UNITED STATES
SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

FORM 10-K

(Mark One)

☑ **ANNUAL REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934**

For the Fiscal Year Ended December 31, 2016

OR

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

For the Transition Period from to

Commission File Number: 001-31918

IDERA PHARMACEUTICALS, INC.

(Exact name of Registrant as specified in its charter)

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

(617) 679-5500

(Registrant's telephone number, including area code)

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

Title of Class:	**Name of Each Exchange on Which Registered**
Common Stock, $.001 par value	**Nasdaq Capital 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 ☐ No ☑

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 ☐ No ☑

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

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

Indicate by check mark if disclosure of delinquent filers pursuant to Item 405 of Regulation S-K (§ 229.405) is not contained herein, and will not be contained, to the best of the registrant's knowledge, in definitive proxy or information statements incorporated by reference in Part III of this Form 10-K or any amendment to this Form 10-K. ☐

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 ☐ Accelerated filer ☑ Non-accelerated filer ☐ Smaller reporting company ☐
(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 ☐ No ☑

The aggregate market value of the voting and non-voting common equity held by non-affiliates of the registrant was $145,406,315 based on the last sale price of the registrant's common stock as reported on the Nasdaq Capital Market on June 30, 2016. As of February 15, 2017, the registrant had 149,093,717 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 7, 2017 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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IMO® and Idera® are our trademarks. All other trademarks and service marks appearing in this Annual Report on Form 10-K are the property of their respective owners.

FORWARD-LOOKING STATEMENTS

This Annual Report on Form 10-K and the documents we incorporate by reference contain 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, the Exchange Act. All statements, other than statements of historical fact, included or incorporated in this report regarding our strategy, future operations, collaborations, intellectual property, cash resources, 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," "would" and similar expressions are intended to identify forward-looking statements, although not all forward-looking statements contain these identifying words. We cannot guarantee that we actually will achieve the plans, intentions or expectations disclosed in our forward-looking statements and you should not place undue reliance on our forward-looking statements. There are a number of important factors that could cause our actual results to differ materially from those indicated or implied by forward-looking statements. These important factors include those set forth below under Part I, Item 1A "Risk Factors." These factors and the other cautionary statements made in this Annual Report on Form 10-K and the documents we incorporate by reference should be read as being applicable to all related forward-looking statements whenever they appear in this Annual Report on Form 10-K and the documents we incorporate by reference. 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 Securities and Exchange Commission 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.

PART I.

Item 1. *Business.*

Overview

We are a clinical-stage biopharmaceutical company focused on the discovery, development and commercialization of novel oligonucleotide therapeutics for oncology and rare diseases. We use two distinct proprietary drug discovery technology platforms to design and develop drug candidates: our Toll-like receptor, or TLR, targeting technology and our third-generation antisense, or 3GA, technology. We developed these platforms based on our scientific expertise and pioneering work with synthetic oligonucleotides as therapeutic agents. Using our TLR targeting technology, we design synthetic oligonucleotide-based drug candidates to modulate the activity of specific TLRs. Using our 3GA technology, we are developing drug candidates to turn off the messenger RNA, or mRNA, associated with disease causing genes. We believe that our 3GA technology may potentially reduce the immunotoxicity and increase the potency of earlier generation antisense and RNA interference, or RNAi, technologies.

Our business strategy is focused on the clinical development of drug candidates for oncology and rare diseases characterized by small, well-defined patient populations with serious unmet medical needs. We believe we can develop and commercialize these targeted therapies on our own. To the extent we seek to develop drug candidates for broader disease indications, we may explore potential collaborative alliances to support development and commercialization.

INTERNAL RESEARCH AND DEVELOPMENT PROGRAMS

Drug Candidate(s)	Indication / Application	Development Status
Programs for the Modulation of Specific Toll-like Receptors		
Immuno-oncology		
IMO-2125	Anti-PD-1 Refractory Metastatic Melanoma	Phase 1/2 clinical trial in combination with ipilimumab and pembrolizumab Anticipated completion of enrollment in ipilimumab combination arm of the Phase 2 portion of the trial in the second half of 2017.
	Refractory Solid Tumors	Phase 1 monotherapy trial in multiple tumor types – Anticipated initiation in 2017. Phase 2 trial in combination with various checkpoint inhibitors in multiple tumor types – Anticipated initiation in the second half of 2017.
Rare Diseases		
IMO-8400	Dermatomyositis	Phase 2 clinical trial – Anticipated completion of trial enrollment in the second half of 2017. Data anticipated to be available in early 2018.
Third-generation Antisense		
IDRA-008	Undisclosed Liver Target for Rare Disorder	Research / IND-enabling activities underway – Anticipated IND submission in the first half 2018.

EXTERNAL RESEARCH AND DEVELOPMENT PROGRAMS

Drug Candidate(s)	Indication / Application	Status
3GA Compound	Renal Target	Collaboration with GSK for undisclosed renal targets entered into in 2015. Candidate selection by GSK anticipated in the first half 2018.
IMO-9200	Non-malignant Gastrointestinal Disorders	Exclusive license and collaboration agreement with Vivelix entered into in 2016.

TLR Modulation Technology Platform

TLRs are key receptors of the immune system and play a role in innate and adaptive immunity. As a result, we believe TLRs are potential therapeutic targets for the treatment of a broad range of diseases. Using our chemistry-based platform, we have designed TLR agonists and antagonists to act by modulating the activity of targeted TLRs. A TLR agonist is a compound that stimulates an immune response through the targeted TLR. A TLR antagonist is a compound that inhibits an immune response by blocking the targeted TLR.

Our TLR agonist lead drug candidate IMO-2125 is an agonist of TLR9. Our TLR antagonist lead drug candidate is IMO-8400, which is an antagonist of TLR7, TLR8 and TLR9.

We are evaluating IMO-2125 for the treatment by intra-tumoral injection of multiple oncology indications both in combination with checkpoint inhibitors and as monotherapy. We are developing IMO-8400 for the treatment of a rare disease called dermatomyositis.

Intra-tumoral IMO-2125 Development Program in Immuno-oncology

Advancements in cancer immunotherapy have included the approval and late-stage development of multiple checkpoint inhibitors, which are therapies that target mechanisms by which tumor cells evade detection by the immune system. Despite these advancements, many patients fail to respond to these therapies. For instance, approximately fifty percent of patients with melanoma fail to respond to therapy with approved checkpoint inhibitors. Current published data suggests that the lack of response to checkpoint inhibition is related to a non-immunogenic tumor micro environment. Because TLR9 agonists stimulate the immune system, we believe that there is a scientific rationale to evaluate the combination of intra-tumoral injection of our TLR9 agonists with checkpoint inhibitors. Specifically, we believe that intra-tumoral injection of our TLR9 agonists activates a local immune response in the injected tumor, which may complement the effect of the systemically administered checkpoint inhibitors. In studies in preclinical cancer models conducted in our laboratories, intra-tumoral injection of TLR9 agonists has potentiated the anti-tumor activity of multiple checkpoint inhibitors in multiple tumor models. These data have been presented at a number of scientific conferences from 2014 through 2016. We believe that these data support evaluation of combination regimens including the combination of a TLR9 agonist and a checkpoint inhibitor for the treatment of cancer.

We are initially developing IMO-2125 for use in combination with checkpoint inhibitors for the treatment of patients with anti-PD1 refractory metastatic melanoma. We believe, based on internally conducted commercial research, that in the United States, by 2025, approximately 20,000 people will have metastatic melanoma and approximately 13,000 of those people will have metastatic melanoma that is anti-PD1 refractory. We also believe that TLR9 agonists may be useful in other tumor types that are unaddressable with current immunotherapy due in part to low mutation load and low dendritic cell infiltration, which include non-small cell lung cancer, head and neck cancer, renal cell cancer and bladder cancer. We believe, based on internal commercial research that we conducted, that in the United States, by 2025, approximately 160,000 people will have tumor types that are addressable with current immunotherapy and approximately 70,000 of those people will have tumor types that are anti-PD1 refractory.

In June 2015, we entered into a strategic research alliance with the University of Texas, MD Anderson Cancer Center, or MD Anderson, to commence clinical development of IMO-2125 in combination with checkpoint inhibitors. In December 2015, we initiated a Phase 1/2 clinical trial to assess the safety and efficacy of IMO-2125, administered intra-tumorally, in combination with ipilimumab, a CTLA4 antibody marketed as Yervoy® by Bristol-Myers Squibb Company, in patients with metastatic melanoma (refractory to treatment with a PD1 inhibitor, also referred to as anti-PD1 refractory).

We subsequently amended the trial protocol to enable an additional arm to study the combination of IMO-2125 with pembrolizumab, an anti-PD1 antibody marketed as Keytruda® by Merck & Co. in the same patient population. In the Phase 1 portion of this clinical trial, escalating doses of IMO-2125 ranging from 4 mg through 32 mg in the ipilimumab arm and ranging from 8 mg through 32 mg in the pembrolizumab arm are being administered intra-tumorally into a selected tumor lesion, together with the standard dosing regimen of ipilimumab or pembrolizumab, administered intravenously. The primary objectives of the Phase 1 portion of the trial include characterizing the safety of the combinations and determining the recommended Phase 2 dose. A secondary objective of the Phase 1 portion of the trial is describing the anti-tumor activity of IMO-2125 when administered intra-tumorally in combination with ipilimumab or pembrolizumab. The primary objectives of the Phase 2 portion of the trial will be to characterize the safety of the combinations and determine the activity of the combinations utilizing immune-related response criteria. Additionally, a secondary objective of the Phase 2 portion of the trial will be to assess treatment response using traditional RECIST criteria. Serial biopsies will be taken of selected injected and non-injected tumor lesions to assess immune changes and response assessments. We anticipate that the entire Phase 1/2 trial may enroll approximately 60 to 80 patients across both ipilimumab and pembrolizumad arms.

In September 2016, we disclosed early clinical results from the 4 mg and 8 mg dosing cohorts of the Phase 1 ipilimumab combination portion of the trial in which three of six evaluable patients demonstrated clinical responses (one complete response and two partial responses). We also disclosed that the drug was well tolerated through the initial dosing of the 16 mg dosing cohort. We have completed enrollment in the dose escalation phase in the ipilimumab arm of the trial as well as the 8 mg dosing cohort in the pembrolizumab arm of the trial. We presented available translational, efficacy and safety data findings from the 4 mg, 8 mg and 16 mg dosing cohorts in the ipilimumab arm during an oral presentation at the Society for Immunotherapy of Cancer (SITC) Annual Meeting in November 2016. In February 2017, we provided a further update in a poster session at the joint meeting of the American Society of Clinical Oncology (ASCO)-SITC Meeting here we disclosed that the drug was well tolerated through the initial dosing of the 32mg mg dosing cohort with ipilimumab as well as through the initial dosing of the first, i.e. 8mg, cohort with pembrolizumab.

We plan to transition to the Phase 2 portion of the clinical trial following determination of the recommended Phase 2 dose. We anticipate that in the Phase 2 portion of the trial for the ipilimumab combination arm, additional patients will receive intra-tumoral IMO-2125 in combination with ipilimumab at the recommended dose determined by the Phase 1 portion of the trial. We anticipate that the Phase 2 portion of the trial will enroll a total of 21 patients at multiple clinical sites.

Additionally, we are planning to initiate a Phase 1 trial with IMO-2125 administered as a single agent intra-tumorally in multiple tumor types. We are also planning to initiate a Phase 2 clinical trial with IMO-2125 administered intra-tumorally together with other checkpoint inhibitors in multiple tumor types.

IMO-8400 in Rare Diseases

We have initiated clinical development of IMO-8400 for the treatment of rare diseases. We have selected dermatomyositis as the first rare disease for which we are developing IMO-8400. We selected this indication for development based on the reported increase in TLR expression in this disease state, expression of cytokines indicative of key TLR-mediated pathways and the presence of auto-antibodies that can induce TLR-mediated immune responses.

We considered that multiple independent research studies across a broad range of autoimmune diseases, including both dermatomyositis and psoriasis, have demonstrated that the over-activation of TLRs plays a critical role in disease maintenance and progression. In autoimmune diseases, endogenous nucleic acids released from damaged or dying cells initiate signaling cascades through TLRs, leading to the induction of multiple pro-inflammatory cytokines. This inflammation causes further damage to the body's own tissues and organs and the release of more self-nucleic acids, creating a self-sustaining autoinflammatory cycle that contributes to chronic inflammation in the affected tissue, promoting disease progression.

We believe that we demonstrated proof of concept for our approach of using TLRs to inhibit the over-activation of specific TLRs for the treatment of psoriasis and potentially other autoimmune diseases in a randomized, double-blind, placebo-controlled Phase 2 clinical trial of IMO-8400 that we conducted in patients with moderate to severe plaque psoriasis, a well-characterized autoimmune disease. In this trial, we evaluated IMO-8400 at four subcutaneous dose levels of 0.075 mg/kg, 0.15 mg/kg, 0.3 mg/kg, and 0.6 mg/kg, versus placebo, administered once weekly for 12 weeks in 46 patients. The trial met its primary objective as IMO-8400 was well tolerated at all dose levels with no treatment-related

discontinuations, treatment-related serious adverse events or dose reductions. The trial also met its secondary objective of demonstrating clinical activity in psoriasis patients, as assessed by the Psoriasis Area Severity Index.

Dermatomyositis is a rare, debilitating, inflammatory muscle and skin disease associated with significant morbidity, decreased quality of life and an increased risk of premature death. While the cause of dermatomyositis is not well understood, the disease process involves immune system attacks against muscle and skin that lead to inflammation and tissue damage. Major symptoms can include progressive muscle weakness, severe skin rash, calcium deposits under the skin (calcinosis), difficulty swallowing (dysphagia) and interstitial lung disease. We believe, based on internally conducted commercial research, that dermatomyositis affects approximately 25,000 people in the United States, and is about twice as common in women as men, with a typical age of onset between 45 and 65 years in adults. Dermatomyositis represents one form of myositis, a spectrum of inflammatory muscle diseases that also includes juvenile dermatomyositis, polymyositis and inclusion body myositis.

In December 2015, we initiated a Phase 2, randomized, double-blind, placebo-controlled clinical trial designed to assess the safety, tolerability and treatment effect of IMO-8400 in adult patients with dermatomyositis. Eligibility criteria include evidence of active skin involvement. Patients in the trial are randomized to one of three groups to receive once weekly subcutaneous injections of: placebo, 0.6 mg/kg of IMO-8400 or 1.8 mg/kg of IMO-8400, in each case, for a period of 24 weeks. The trial is expected to enroll approximately 36 patients and is being conducted at approximately 22 centers in the United States, the United Kingdom, Hungary and Sweden. The primary efficacy endpoint is the change from baseline in the Cutaneous Dermatomyositis Disease Area and Severity Index (CDASI), a validated outcome measure of skin disease. Additional exploratory endpoints include muscle strength and function (which are among the International Myositis Assessment & Clinical Studies Group (IMACS) core set measures), patient-reported quality of life and biochemical markers of disease activity.

Third-generation Antisense (3GA)

Third-generation Antisense (3GA) Technology to Target mRNA

We are developing our 3GA technology to "turn off" the mRNA associated with disease causing genes. We have designed 3GA oligonucleotides to specifically address challenges associated with earlier generation antisense and RNAi technologies.

Our focus is on creating 3GA candidates targeted to specific genes to treat cancer and rare diseases. Our key considerations in identifying disease indications and gene targets in our 3GA program include: strong evidence that the disease is caused by a specific protein; clear criteria to identify a target patient population; biomarkers for early assessment of clinical proof of concept; a targeted therapeutic mechanism of action; unmet medical need to allow for a rapid development path to approval and commercial opportunity. To date we have created 22 novel 3GA compounds for specific gene targets that are potentially applicable across a wide variety of therapeutic areas. These areas include rare diseases, oncology, autoimmune disorders, metabolic conditions, single point mutations and others. Our current activities with respect to these compounds range from cell culture through investigational new drug, or IND, application-enabling toxicology.

In January 2017, we announced that we had selected our first candidate to enter clinical development. We are planning to develop IDRA-008 for a well-established liver target with available pre-clinical animal models and well-known clinical endpoints. IDRA-008 has potential for both broad and rare disease applications.

In November 2015, we entered into a collaboration and license agreement with GlaxoSmithKline Intellectual Property Development Limited, or GSK, to license, research, develop and commercialize pharmaceutical compounds from our 3GA technology for the treatment of selected targets in renal disease, which agreement we refer to as the GSK Agreement. Under this collaboration, we are creating multiple development candidates to address the initial target designated by GSK. From the population of identified development candidates, GSK may designate one development candidate in its sole discretion to move forward into clinical development. Once GSK designates a development candidate, GSK would be solely responsible for the development and commercialization activities for that designated development candidate.

Additional Programs

IMO-9200 for Autoimmune Disease. We have developed a second novel synthetic oligonucleotide antagonist of TLR7, TLR8, and TLR9, IMO-9200, as a drug candidate for potential use in selected autoimmune disease indications. In 2015, we completed a Phase 1 clinical trial of IMO-9200 in healthy subjects as well as additional preclinical studies of IMO-9200 for autoimmune diseases. In 2015, we determined not to proceed with the development of IMO-9200 because the large autoimmune disease indications for which IMO-9200 had been developed did not fit within the strategic focus of our company. In November 2016, we entered into an exclusive license and collaboration agreement with Vivelix Pharmaceuticals, Ltd., or Vivelix, granting Vivelix worldwide rights to develop and market IMO-9200, an antagonist of TLR7, 8, and 9, for non-malignant gastrointestinal disorders, which agreement we refer to as the Vivelix Agreement.

IMO-8400 for B-Cell Lymphomas. In December 2013, we initiated a Phase 1/2 clinical trial of IMO-8400 in patients with Waldenström's macroglobulinemia, and in March 2014, we initiated a Phase 1/2 clinical trial of IMO-8400 in diffuse large B-cell lymphoma, or DLBCL, harboring the MYD88 L265P oncogenic mutation.

In September 2016, we announced that we had suspended internal development of IMO-8400 for B-cell lymphomas, including our ongoing trials in Waldenström's macroglobulinemia and DLBCL. We are exploring strategic alternatives for IMO-8400 in these indications. This decision was based upon our prioritization of the clinical development plans for IMO-2125 and our assessment that the level of clinical activity seen in the Waldenström's macroglobulinemia trial would not support the development of IMO-8400 for these indications as a monotherapy, the very slow enrollment rate in DLBCL and our commercial assessment. The trial of IMO-8400 in DLBCL is now closed. We plan to finish treating patients in the trial of IMO-8400 in Waldenström's macroglobulinemia but enrollment of new patients has been suspended. In these trials under our B-cell lymphoma program, IMO-8400 was generally well tolerated at all dose levels evaluated, with only one treatment-related discontinuation due to adverse events and no dose reductions. The treatment-related discontinuation involved a single patient who experienced a serious adverse event that was possibly related to IMO-8400.

In October 2016, we presented interim clinical data from the Phase 1/2 clinical trial of IMO-8400 in Waldenström's macroglobulinemia, which showed signals of positive clinical activity as well as safety in the first four dosing cohorts of the trial.

Collaborative Alliances

We may explore potential collaborative alliances to support development and commercialization of our TLR agonists and antagonists. We may also seek to enter into additional collaborative alliances with pharmaceutical companies with respect to applications of our 3GA program. We are currently party to collaborations with Vivelix, GSK, Abbott Molecular, and Merck & Co.

Vivelix

In November 2016, we entered into the Vivelix Agreement, granting Vivelix worldwide rights to develop and market IMO-9200, an antagonist of TLR 7, 8 and 9, for non-malignant gastrointestinal disorders (the GI Field or Field as defined in the Vivelix Agreement) and certain back-up compounds to IMO-9200.

In accordance with the Vivelix Agreement, a Joint Research Committee or JRC, was formed with equal representation from us and Vivelix. The responsibilities of the JRC, include, but are not limited to monitoring the progress of the research program, advising on the designation of back-up compounds, sharing information between the parties and dealing with disputes that may arise between the parties. If a dispute cannot be resolved by the JRC, Vivelix has final decision making authority.

In connection with the Vivelix Agreement, we transferred certain drug material to Vivelix for Vivelix’s use in its development activities. Vivelix is solely responsible for the development and commercialization of IMO-9200 and any designated back-up compounds to IMO-9200.

If requested by Vivelix pursuant to the Vivelix Agreement, we will create, characterize and perform research on back-up compounds. Such activity is to be mutually agreed upon and moderated by the JRC. The research period commenced with the execution of the agreement and will last for one year. Vivelix may extend the research period by up

to two one year periods. During the research period, the parties will agree on the number of full time equivalents to work on the program. Vivelix will reimburse us at an annual market rate for the services rendered.

Vivelix has certain rights under the agreement whereby it may (i) exercise the right of first refusal, (ii) the right of first negotiation to obtain an exclusive license for any compound controlled by us that has activity in the field of inflammatory bowel disease and (iii) the right to request an expanded Field beyond the GI Field.

Under the terms of the Vivelix Agreement, we received an upfront, non-refundable fee of $15 million. In addition, we will be eligible for future IMO-9200 related development, regulatory and sales milestone payments totaling up to $140 million, including development and regulatory milestones totaling up to $65 million and sales milestones totaling up to $75 million, and escalating royalties ranging from the mid single-digits to low double-digits of global net sales, which percentages are subject to reduction under agreed upon circumstances. Additionally, under the terms of the agreement and if requested by and at Vivelix's expense, we are responsible for developing potential back-up compounds to IMO-9200. As it relates to back-up compounds, we will be eligible for related designation payments and development, regulatory sales and milestone payments totaling up to $52.5 million, including development and regulatory milestones totaling up to $35 million and sales milestones totaling up to $17.5 million, and escalating royalties ranging from the mid single-digits to low double-digits of global net sales, which percentages are subject to reduction under agreed upon circumstances.

GlaxoSmithKline Intellectual Property Development Limited

In November 2015, we entered into the GSK Agreement to license, research, develop and commercialize pharmaceutical compounds from our 3GA technology for the treatment of selected targets in renal disease. The initial collaboration term is currently anticipated to last between two and four years from signing. In connection with the GSK Agreement, GSK identified an initial target for us to attempt to identify a potential population of development candidates to address such target under a mutually agreed upon research plan, currently estimated to take 27 months to complete. From the population of identified development candidates, GSK may designate one development candidate in its sole discretion to move forward into clinical development. Once GSK designates a development candidate, GSK would be solely responsible for the development and commercialization activities for that designated development candidate.

At any time during the first two years of the GSK Agreement, GSK has the option to select up to two additional targets, for further research under mutually agreed upon research plans. GSK may then designate one development candidate for each additional target, at which time GSK would have sole responsibility to develop and commercialize each such designated development candidate.

In accordance with the GSK Agreement, a Joint Steering Committee, or JSC, was formed with equal representation from us and GSK. The responsibilities of the JSC, include, but are not limited to monitoring the progress of the collaboration, reviewing research plans and dealing with disputes that may arise between the parties. If a dispute cannot be resolved by the JSC, GSK has final decision making authority.

Under the terms of the GSK Agreement, we received a $2.5 million upfront, non-refundable, non-creditable cash payment upon the execution of the GSK Agreement. We are eligible to receive up to approximately $100 million in license, research, clinical development and commercialization milestone payments. Approximately $9 million of these milestone payments are payable by GSK upon the identification of the additional targets, the completion of current and future research plans and the designation of development candidates. Approximately $89 million is payable by GSK upon the achievement of clinical milestones and commercial milestones. In addition, we are eligible to receive royalty payments based on net sales of licensed products following commercialization at varying rates of up to five percent on annual net sales, as defined in the GSK Agreement.

Abbott Molecular

In May 2014, we entered into a development and commercialization agreement with Abbott Molecular for the development of an in vitro companion diagnostic for use in our clinical development programs to treat certain genetically defined forms of B-cell lymphoma with IMO-8400. The agreement provides for the development and subsequent commercialization by Abbott Molecular of a companion diagnostic test utilizing polymerase chain reaction technology to identify with high sensitivity and specificity the presence in tumor biopsy samples of the oncogenic mutation referred to scientifically as MYD88 L265P. Under the agreement, Abbott Molecular is primarily responsible for developing and

obtaining regulatory approvals for the companion diagnostic in accordance with an agreed development plan and regulatory plan and for making the companion diagnostic test commercially available in accordance with an agreed commercialization plan. Abbott Molecular will retain all proceeds from commercialization of the companion diagnostic test. Subject to the terms of the agreement, we are required to pay Abbott Molecular fees and fund Abbott Molecular's development of the companion diagnostic test in an approximate aggregate amount of $6.7 million over an approximately five year development period, which includes clinical trial site costs and Abbott Molecular's costs of preparation and filing fees for regulatory submissions for the companion diagnostic with the U.S. Food and Drug Administration, or FDA. This amount is subject to increase if Abbott Molecular incurs additional expenses in order to meet unexpected material requirements or obligations not included in the agreement or if we are required to conduct additional or different clinical trials which result in Abbott Molecular incurring additional costs.

The parties' activities pursuant to the agreed development, regulatory and commercialization plans are governed by a joint steering committee, with Abbott Molecular retaining final decision making authority, subject to its obligations under the agreement, for development, manufacture and marketing of the companion diagnostic and our retaining final decision making authority, subject to our obligations under the agreement, for the development, manufacture and marketing of IMO-8400.

Under the agreement, each party grants the other party specified intellectual property licenses to enable the other party to perform its obligations and exercise its rights under the agreement, including license grants enabling Abbott Molecular to develop and commercialize the companion diagnostic test for use with IMO-8400 and enabling us to develop and commercialize IMO-8400 with Abbott Molecular's companion diagnostic test. The licenses granted by the parties to one another generally survive termination of the agreement. Abbott Molecular remains free to develop its companion diagnostic test for use with third party therapeutic products, and we remain free to engage third party diagnostics companies to develop other companion diagnostic tests for use with IMO-8400.

We are permitted to terminate the agreement upon 90 days written notice to Abbott Molecular and, under circumstances specified in the agreement, payment of a termination fee and wind-down costs. The parties also may terminate the agreement based on uncured material breaches by or the bankruptcy or insolvency of the other party, and each party has the right to terminate the agreement in the event of specified permanent injunctions based on infringement of third party intellectual property rights.

Merck & Co.

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, TLR8, and TLR9 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, TLR8, and TLR9 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. 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.

In April 2014, we entered into an amendment to the agreement. As a result of this amendment, Merck & Co.'s rights under the agreement were limited to specified TLR7, TLR8, and TLR9 agonists that Merck & Co. selected in January 2012, and we regained the rights to pursue our other independently discovered TLR7, TLR8, and TLR9 agonists for use as vaccine adjuvants in the fields of cancer, infectious diseases and Alzheimer's disease so that we now have the right to pursue our TLR7, TLR8, and TLR9 agonists for use as vaccine adjuvants in all fields. Merck & Co.'s obligations under the agreement to pay us milestone payments and royalties continue in effect with respect to the specified TLR7, TLR8, and TLR9 agonists. However, in connection with this amendment, we agreed that, to the extent that we license to third parties any TLR7, TLR8, and TLR9 agonists for use as vaccine adjuvants in the fields of cancer, infectious diseases and Alzheimer's disease and receive income under such licenses, Merck & Co. may credit against any milestone payments and royalties it owes to us an amount equal to 15% of the license income received by us under the third-party licenses, up to a maximum of $60.0 million in credits.

Licensing Agreements

We have not licensed any rights to our TLR technology to any third party other than under the Vivelix Agreement and our exclusive license and research collaboration agreement with Merck & Co. We have not in-licensed any technology for our TLR program. We have licensed specified rights related to early generation antisense technology to certain parties. We also have in-licensed certain rights related to antisense technology. We have licensed specific rights related to 3GA technology for renal disease to GSK.

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 research collaborations may require us to supply compounds and 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, have an automatic paid-up, royalty-free non-exclusive license 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 terminated with limited notice.

Research and Development Expenses

For the years ended December 31, 2016, 2015 and 2014, we spent approximately $39.8 million, $33.7 million, and $27.5 million, respectively, on research and development activities.

Patents, Proprietary Rights and Trade Secrets

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

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

- Novel chemical entities that function as agonists of TLR3, TLR7, TLR8 or TLR9;
- Novel chemical entities that function as antagonists of TLR7, TLR8 or TLR9;
- Use of our novel chemical entities and chemical modifications to treat and prevent a variety of diseases; and
- Composition and use of our 3GA compounds to treat and prevent a variety of diseases.

As of February 15, 2017, we owned more than 45 U.S. patents and patent applications and more than 80 patents and patent applications throughout the rest of the world for our TLR-targeted immune modulation technologies. These patents and patent applications include claims covering the chemical compositions of matter and methods of use of our IMO compounds, such as IMO-8400, IMO-9200 and IMO-2125, as well as other compounds. These patents expire at various dates ranging from 2023 to 2034. With respect to IMO-8400, we have three issued U.S. patents that cover the chemical composition of matter of IMO-8400 and certain methods of its use that have an earliest statutory expiration date in 2031. With respect to IMO-9200, we have one issued U.S. patent and two U.S. patent applications that cover the chemical composition for IMO-9200 and methods of its use that have an earliest statutory expiration date in 2034. With respect to IMO 2125, we have an issued U.S. patent that covers the chemical composition of matter of IMO-2125 and methods of its use that will expire in 2025.

As of February 15, 2017, we owned two issued U.S. patents, 21 issued foreign patents, seven pending U.S. patent applications and 12 foreign patent applications related to our 3GA compounds and methods of their use. The issued patents covering our 3GA technologies have earliest statutory expiration date in 2030.

In addition to our TLR-targeted and 3GA patent portfolios, we are the owner of or hold licenses to patents and patent applications related to antisense technology. As of February 15, 2017, our antisense patent portfolio includes four U.S. patents. 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 in-licensed patents expire at various dates through 2021.

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.

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 or to determine the appropriate term for an issued patent. In addition, the United States Patent and Trademark Office, or USPTO, 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, even if the eventual outcome is favorable to 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.

The term of individual patents depends upon the legal term for patents in the countries in which they are obtained. In most countries, including the United States, the patent term is 20 years from the earliest filing date of a non-provisional patent application. In the United States, a patent's term may be lengthened by patent term adjustment, which compensates a patentee for administrative delays by the United States Patent and Trademark Office, or USPTO, in examining and granting a patent, or may be shortened if a patent is terminally disclaimed over an earlier filed patent. The term of a patent that covers a drug, biological product or medical device approved pursuant to a pre-market approval may also be eligible for patent term extension when FDA approval is granted, provided statutory and regulatory requirements are met. The length of the patent term extension is related to the length of time the drug is under regulatory review while the patent is in force. The Drug Price Competition and Patent Term Restoration Act of 1984, or the Hatch-Waxman Act, permits a patent term extension of up to five years beyond the expiration date set for the patent. Patent extension cannot extend the remaining term of a patent beyond a total of 14 years from the date of product approval, only one patent applicable to each regulatory review period may be granted an extension and only those claims reading on the approved drug are extended. Similar provisions are available in Europe and other foreign jurisdictions to extend the term of a patent that covers an approved drug.

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.

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 a limited number of contract manufacturers through the issuance of work 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 current Good Manufacturing Practices, or cGMP, regulations for use in clinical trials. We will ultimately depend on contract manufacturers for the manufacture of our products for commercial sale, if and when our drug candidates are approved. Contract manufacturers are subject to extensive governmental regulation.

Under our collaborative agreement with Merck & Co., Merck & Co. is responsible for manufacturing the drug candidates. Under our collaborative agreement with GSK, GSK is responsible for manufacturing clinical drug candidates. Under our collaborative agreement with Vivelix, Vivelix is responsible for manufacturing clinical drug candidates.

Competition

We are developing our TLR-targeted drug candidates for use in our immuno-oncology program and in the treatment of certain rare diseases. Through our clinical alliance partner MD Anderson, we also initiated a Phase 1/2 clinical trial of IMO-2125, administered intra-tumorally, in combination with ipilimumab, a CTLA4 antibody, in patients with metastatic melanoma in the fourth quarter of 2015. We also initiated a Phase 2 clinical trial of IMO-8400 in patients with dermatomyositis in the fourth quarter of 2015. We also entered into a collaborative alliance agreement with GSK and expect to continue to seek to enter into additional collaborative alliances with pharmaceutical companies with respect to applications of our 3GA technology program. For all of these disease areas, there are many other companies, public and private, that are actively engaged in discovery, development, and commercializing products and technologies that may compete with our drug candidates and programs, including TLR-targeted compounds as well as non-TLR-targeted therapeutics.

We are aware of other companies including Dynavax, Mologen AG, BioLineRx Ltd., Innate Immunotherapeutics Ltd., VentiRx Pharmaceuticals Inc., Telormedix S.A., Gilead Sciences Inc., GlaxoSmithKline plc, AstraZeneca plc, Checkmate Pharmaceuticals, Inc. and Hoffmann-La Roche that are developing TLR agonists and antagonists for various indications, including oncology and rare diseases.

Application of TLR Agonists in Immuno-Oncology

Immuno-oncology, which utilizes a patient's own immune system to combat cancer, is currently an active area of research for biotechnology and pharmaceutical companies. Interest in immuno-oncology is driven by efficacy data in cancers with historically bleak outcomes and the potential to achieve a cure or functional cure for some patients. As such, we expect that our efforts in this field will be competitive with a wide variety of different approaches. Any one of these competitive approaches may result in the development of novel technologies that are more effective, safer or less costly than any that we are developing. In addition, Dynavax is conducting a Phase 1/2 clinical trial of an investigational TLR9 agonist in combination with checkpoint inhibitors.

IMO-8400 Development Program for Dermatomyositis

Many of the drug development programs in dermatomyositis are focusing on expanding the use of drugs approved in different indications through investigator sponsored studies such as the ongoing studies of the monoclonal antibodies, belimumab and tocilizumab. In addition, Novartis is developing a competitive anti-inflammatory approach with its new investigational drug, BAF312, a sphingosine-1-phosphate receptor modulator aimed at inhibiting the migration of lymphocytes to the location of inflammation. We are not aware of other new chemical or molecular entities being developed for the treatment of dermatomyositis.

Third-generation Antisense (3GA) Technology to Target RNA

We are developing 3GA drug candidates that we have created using our proprietary technology, to inhibit the production of disease-associated proteins by targeting RNA. We also face competition from other companies working to develop novel drugs using technologies that may compete with our 3GA technology. We are aware of multiple companies that are developing technologies that use oligonucleotide-based compounds to inhibit the production of disease associated proteins. These technologies include, but are not limited to, antisense technology as well as RNAi. In the field of antisense technologies, we compete with multiple companies, including Ionis and its partners, as well as WAVE Life Sciences and its partner. Ionis is currently marketing an antisense drug, Kynamro, and Biogen recently received FDA approval for its antisense drug Spinraza for spinal muscular atrophy. Ionis has over two dozen antisense drug candidates in clinical trials. In the field of RNAi, we compete with Alnylam, Dicerna, Miragen, and their respective partners. For example, Alnylam is developing multiple RNAi-based technologies and has six drug candidates in clinical trials. Any of the competing

companies may develop gene-silencing technologies more rapidly and more effectively than us, and antisense technology and RNAi may become the preferred technology for drugs that target RNA in order to inhibit the production of disease-associated proteins.

Some of these potentially competitive products have been in development or commercialized for years, in some cases by large, well established pharmaceutical companies. Many of the marketed products 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 products 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 is planned for our drug candidates upon commercialization, potentially less attractive, from a cost perspective, to buyers.

We recognize that other companies, including large pharmaceutical companies, may be developing or have plans to develop products and technologies that may compete with ours. 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, and marketing and selling approved products. 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.

We anticipate that the competition with our drug candidates and technologies will be based on a number of factors including product efficacy, safety, availability, and price. The timing of market introduction of our drug candidates 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, protect our intellectual property, and to secure sufficient capital resources for the period between technological conception and commercial sales.

Government Regulation

Government authorities in the United States, at the federal, state and local level, and in other countries and jurisdictions, including the European Union, extensively regulate, among other things, the research, development, testing, manufacture, quality control, approval, packaging, storage, recordkeeping, labeling, advertising, promotion, distribution, marketing, post-approval monitoring and reporting, and import and export of pharmaceutical products. The processes for obtaining regulatory approvals in the United States and in foreign countries and jurisdictions, along with subsequent compliance with applicable statutes and regulations and other regulatory authorities, require the expenditure of substantial time and financial resources.

Review and Approval of Drugs in the United States

In the United States, the FDA regulates drugs under the Federal Food, Drug, and Cosmetic Act, or FDCA, and associated implementing regulations. The failure to comply with the FDCA and other applicable U.S. requirements at any time during the product development process, approval process or after approval may subject an applicant and/or sponsor to a variety of administrative or judicial sanctions, including refusal by the FDA to approve pending applications, withdrawal of an approval, imposition of a clinical hold, issuance of warning letters and other types of letters, product recalls, product seizures, total or partial suspension of production or distribution, injunctions, fines, refusals of government contracts, restitution, disgorgement of profits, or civil or criminal investigations and penalties brought by the FDA and the Department of Justice, or DOJ, or other governmental entities.

An applicant seeking approval to market and distribute a new drug product in the United States must typically undertake the following:

- completion of preclinical laboratory tests, animal studies and formulation studies in compliance with the FDA's good laboratory practice, or GLP, regulations;

- submission to the FDA of an IND, which must take effect before human clinical trials may begin in the United States;

- approval by an independent institutional review board, or IRB, representing each clinical site before each clinical trial may be initiated;

- performance of adequate and well-controlled human clinical trials in accordance with good clinical practices, or GCP, to establish the safety and efficacy of the proposed drug product for each indication;

- preparation and submission to the FDA of a new drug application, or NDA;

- review of the product candidate by an FDA advisory committee, where appropriate or if applicable;

- satisfactory completion of one or more FDA inspections of the manufacturing facility or facilities at which the product, or components thereof, are produced to assess compliance with cGMP requirements and to assure that the facilities, methods and controls are adequate to preserve the product's identity, strength, quality and purity;

- satisfactory completion of FDA audits of clinical trial sites to assure compliance with GCPs and the integrity of the clinical data;

- payment of user fees and securing FDA approval of the NDA; and

- compliance with any post-approval requirements, including Risk Evaluation and Mitigation Strategies, or REMS, where applicable, and post-approval studies required by the FDA.

Preclinical Studies

Preclinical studies include laboratory evaluation of the purity and stability of the manufactured drug substance or active pharmaceutical ingredient and the formulated drug or drug product, as well as *in vitro* and animal studies to assess the safety and activity of the drug for initial testing in humans and to establish a rationale for therapeutic use. The conduct of preclinical studies is subject to federal regulations and requirements, including GLP regulations. The results of the preclinical tests, together with manufacturing information, analytical data, any available clinical data or literature and plans for clinical studies, among other things, are submitted to the FDA as part of an IND. Additional preclinical testing, such as animal tests of reproductive adverse events and carcinogenicity, may continue after the IND is submitted.

Human Clinical Studies in Support of an NDA

Clinical trials involve the administration of the investigational product to human subjects under the supervision of qualified investigators in accordance with GCP requirements, which include, among other things, the requirement that all research subjects provide their informed consent in writing before their participation in any clinical trial. Clinical trials are conducted under written study protocols detailing, among other things, the objectives of the study, inclusion and exclusion criteria, the parameters to be used in monitoring safety and the effectiveness criteria to be evaluated. A protocol for each clinical trial and any subsequent protocol amendments must be submitted to the FDA as part of the IND. An IND automatically becomes effective 30 days after receipt by the FDA, unless before that time the FDA raises concerns or questions related to a proposed clinical trial and places the trial on clinical hold. In such a case, the IND sponsor and the FDA must resolve any outstanding concerns before the clinical trial can begin.

Typically, the FDA will require one IND for early development studies where the sponsor is uncertain of the indication or dosage form of the proposed product, where the drug is being developed for closely related indications within a single review division at FDA, or where there are multiple closely-related routes of administration using the same dosage formulation. On the other hand, multiple INDs may be required where there are two or more unrelated conditions being developed or where multiple dosage forms are being extensively investigated or where multiple routes of administration are being evaluated.

In addition to the foregoing IND requirements, an IRB representing each institution participating in the clinical trial must review and approve the plan for any clinical trial before it commences at that institution, and the IRB must

conduct continuing review and reapprove the study at least annually. The IRB must review and approve, among other things, the study protocol and informed consent information to be provided to study subjects. An IRB must operate in compliance with FDA regulations. Information about certain clinical trials must be submitted within specific timeframes to the National Institutes of Health for public dissemination on their ClinicalTrials.gov website.

Human clinical trials are typically conducted in three sequential phases, which may overlap or be combined:

Phase 1: The drug is initially introduced into healthy human subjects or patients with the target disease (e.g. cancer) or condition and tested for safety, dosage tolerance, absorption, metabolism, distribution, excretion and, if possible, to gain an early indication of its effectiveness and to determine optimal dosage.

Phase 2: The drug is administered to a limited patient population to identify possible adverse effects and safety risks, to preliminarily evaluate the efficacy of the product for specific targeted diseases and to determine dosage tolerance and optimal dosage.

Phase 3: The drug is administered to an expanded patient population, generally at geographically dispersed clinical trial sites, in well-controlled clinical trials to generate enough data to statistically evaluate the efficacy and safety of the product for approval, to establish the overall risk-benefit profile of the product, and to provide adequate information for the labeling of the product.

Progress reports detailing the results of the clinical trials must be submitted at least annually to the FDA and more frequently if serious adverse events occur. In addition, IND safety reports must be submitted to the FDA for any of the following: serious and unexpected suspected adverse reactions; findings from other studies or animal or in vitro testing that suggest a significant risk in humans exposed to the drug; and any clinically important increase in the case of a serious suspected adverse reaction over that listed in the protocol or investigator brochure. Phase 1, Phase 2 and Phase 3 clinical trials may not be completed successfully within any specified period, or at all. Furthermore, the FDA, the sponsor or the data monitoring committee for a clinical trial may suspend or terminate the clinical trial at any time on various grounds, including a finding that the research subjects are being exposed to an unacceptable health risk. Similarly, an IRB can suspend or terminate approval of a clinical trial at its institution, or an institution it represents, if the clinical trial is not being conducted in accordance with the IRB's requirements or if the drug has been associated with unexpected serious harm to patients. The FDA will typically inspect one or more clinical sites to assure compliance with GCP and the integrity of the clinical data submitted.

Section 505(b)(2) NDAs

NDAs for most new drug products are based on two full clinical studies which must contain substantial evidence of the safety and efficacy of the proposed new product. These applications are submitted under Section 505(b)(1) of the FDCA. The FDA is, however, authorized to approve an alternative type of NDA under Section 505(b)(2) of the FDCA. This type of application allows the applicant to rely, in part, on the FDA's previous findings of safety and efficacy for a similar product, or published literature. Specifically, Section 505(b)(2) applies to NDAs for a drug for which the investigations made to show whether or not the drug is safe for use and effective in use and relied upon by the applicant for approval of the application "were not conducted by or for the applicant and for which the applicant has not obtained a right of reference or use from the person by or for whom the investigations were conducted."

Thus, Section 505(b)(2) authorizes the FDA to approve an NDA based on safety and effectiveness data that were not developed by the applicant. NDAs filed under Section 505(b)(2) may provide an alternate and potentially more expeditious pathway to FDA approval for new or improved formulations or new uses of previously approved products. If the Section 505(b)(2) applicant can establish that reliance on the FDA's previous approval is scientifically appropriate, the applicant may eliminate the need to conduct certain preclinical or clinical studies of the new product. The FDA may also require companies to perform additional studies or measurements to support the change from the approved product. The FDA may then approve the new drug candidate for all or some of the label indications for which the referenced product has been approved, as well as for any new indication sought by the Section 505(b)(2) applicant.

Submission of an NDA to the FDA

Assuming successful completion of required clinical testing and other requirements, the results of the preclinical and clinical studies, together with detailed information relating to the product's chemistry, manufacture, controls and

proposed labeling, among other things, are submitted to the FDA as part of an NDA requesting approval to market the drug product for one or more indications. Under federal law, the submission of most NDAs is additionally subject to an application user fee, which for federal fiscal year 2017 is $2,038,100. The sponsor of an approved NDA is also subject to annual product and establishment user fees, which for 2017 are $97,750 per product and $512,200 per establishment.

The FDA conducts a preliminary review of an NDA within 60 calendar days of its receipt and strives to inform the sponsor by the 74th day after the FDA's receipt of the submission to determine whether the application is sufficiently complete to permit substantive review. The FDA may request additional information rather than accept an NDA for filing. In this event, the application must be resubmitted with the additional information. The resubmitted application is also subject to review before the FDA accepts it for filing. Once the submission is accepted for filing, the FDA begins an in-depth substantive review.

The FDA has agreed to specified performance goals in the review process of NDAs. Under the agreement, 90% of applications seeking approval of New Molecular Entities, or NMEs, are meant to be reviewed within ten months from the date on which the FDA accepts the NDA for filing, and 90% of applications for NMEs that have been designated for "priority review" are meant to be reviewed within six months of the filing date. For applications seeking approval of drugs that are not NMEs, the ten-month and six-month review periods run from the date that the FDA receives the application. The review process may be extended by the FDA for three additional months to consider new information or clarification provided by the applicant to address an outstanding deficiency identified by the FDA following the original submission.

Before approving an NDA, the FDA typically will inspect the facility or facilities where the product is or will be manufactured. These pre-approval inspections cover all facilities associated with an NDA submission, including drug component manufacturing (such as active pharmaceutical ingredients), finished drug product manufacturing, and control testing laboratories. The FDA will not approve an application unless it determines that the manufacturing processes and facilities are in compliance with cGMP requirements and adequate to assure consistent production of the product within required specifications. Additionally, before approving an NDA, the FDA will typically inspect one or more clinical sites to assure compliance with GCP.

In addition, as a condition of approval, the FDA may require an applicant to develop a REMS. REMS use risk minimization strategies beyond the professional labeling to ensure that the benefits of the product outweigh the potential risks. To determine whether a REMS is needed, the FDA will consider the size of the population likely to use the product, seriousness of the disease, expected benefit of the product, expected duration of treatment, seriousness of known or potential adverse events, and whether the product is a new molecular entity. REMS can include medication guides, physician communication plans for healthcare professionals, and elements to assure safe use, or ETASU. ETASU may include, but are not limited to, special training or certification for prescribing or dispensing, dispensing only under certain circumstances, special monitoring, and the use of patient registries. The FDA may require a REMS before approval or post-approval if it becomes aware of a serious risk associated with use of the product. The requirement for a REMS can materially affect the potential market and profitability of a product.

The FDA is required to refer an application for a novel drug to an advisory committee or explain why such referral was not made. Typically, an advisory committee is a panel of independent experts, including clinicians and other scientific experts, that reviews, evaluates and provides a recommendation as to whether the application should be approved and under what conditions. The FDA is not bound by the recommendations of an advisory committee, but it considers such recommendations carefully when making decisions.

Fast Track, Breakthrough Therapy and Priority Review Designations

The FDA is authorized to designate certain products for expedited review if they are intended to address an unmet medical need in the treatment of a serious or life-threatening disease or condition. These programs are fast track designation, breakthrough therapy designation and priority review designation.

Specifically, the FDA may designate a product for fast track review if it is intended, whether alone or in combination with one or more other drugs, for the treatment of a serious or life-threatening disease or condition, and it demonstrates the potential to address unmet medical needs for such a disease or condition. For fast track products, sponsors may have greater interactions with the FDA and the FDA may initiate review of sections of a fast track product's NDA before the application is complete. This rolling review may be available if the FDA determines, after preliminary evaluation of clinical data submitted by the sponsor, that a fast track product may be effective. The sponsor must also

provide, and the FDA must approve, a schedule for the submission of the remaining information and the sponsor must pay applicable user fees. However, the FDA's time period goal for reviewing a fast track application does not begin until the last section of the NDA is submitted. In addition, the fast track designation may be withdrawn by the FDA if the FDA believes that the designation is no longer supported by data emerging in the clinical trial process.

Second, in 2012, Congress enacted the Food and Drug Administration Safety and Innovation Act, or FDASIA. This law established a new regulatory scheme allowing for expedited review of products designated as "breakthrough therapies." A product may be designated as a breakthrough therapy if it is intended, either alone or in combination with one or more other drugs, to treat a serious or life-threatening disease or condition and preliminary clinical evidence indicates that the product may demonstrate substantial improvement over existing therapies on one or more clinically significant endpoints, such as substantial treatment effects observed early in clinical development. The FDA may take certain actions with respect to breakthrough therapies, including holding meetings with the sponsor throughout the development process; providing timely advice to the product sponsor regarding development and approval; involving more senior staff in the review process; assigning a cross-disciplinary project lead for the review team; and taking other steps to design the clinical trials in an efficient manner.

Third, the FDA may designate a product for priority review if it is a drug that treats a serious condition and, if approved, would provide a significant improvement in safety or effectiveness. The FDA determines, on a case-by-case basis, whether the proposed drug represents a significant improvement when compared with other available therapies. Significant improvement may be illustrated by evidence of increased effectiveness in the treatment of a condition, elimination or substantial reduction of a treatment-limiting drug reaction, documented enhancement of patient compliance that may lead to improvement in serious outcomes, and evidence of safety and effectiveness in a new subpopulation. A priority designation is intended to direct overall attention and resources to the evaluation of such applications, and to shorten the FDA's goal for taking action on a marketing application from ten months to six months.

Accelerated Approval Pathway

The FDA may grant accelerated approval to a drug for a serious or life-threatening condition that provides meaningful therapeutic advantage to patients over existing treatments based upon a determination that the drug has an effect on a surrogate endpoint that is reasonably likely to predict clinical benefit. The FDA may also grant accelerated approval for such a condition when the product has an effect on an intermediate clinical endpoint that can be measured earlier than an effect on irreversible morbidity or mortality, or IMM, and that is reasonably likely to predict an effect on irreversible morbidity or mortality or other clinical benefit, taking into account the severity, rarity, or prevalence of the condition and the availability or lack of alternative treatments. Drugs granted accelerated approval must meet the same statutory standards for safety and effectiveness as those granted traditional approval.

For the purposes of accelerated approval, a surrogate endpoint is a marker, such as a laboratory measurement, radiographic image, physical sign, or other measure that is thought to predict clinical benefit, but is not itself a measure of clinical benefit. Surrogate endpoints can often be measured more easily or more rapidly than clinical endpoints. An intermediate clinical endpoint is a measurement of a therapeutic effect that is considered reasonably likely to predict the clinical benefit of a drug, such as an effect on IMM. The FDA has limited experience with accelerated approvals based on intermediate clinical endpoints, but has indicated that such endpoints generally may support accelerated approval where the therapeutic effect measured by the endpoint is not itself a clinical benefit and basis for traditional approval, if there is a basis for concluding that the therapeutic effect is reasonably likely to predict the ultimate clinical benefit of a drug.

The accelerated approval pathway is most often used in settings in which the course of a disease is long and an extended period of time is required to measure the intended clinical benefit of a drug, even if the effect on the surrogate or intermediate clinical endpoint occurs rapidly. Thus, accelerated approval has been used extensively in the development and approval of drugs for treatment of a variety of cancers in which the goal of therapy is generally to improve survival or decrease morbidity and the duration of the typical disease course requires lengthy and sometimes large trials to demonstrate a clinical or survival benefit.

The accelerated approval pathway is usually contingent on a sponsor's agreement to conduct, in a diligent manner, additional post-approval confirmatory studies to verify and describe the drug's clinical benefit. As a result, a drug candidate approved on this basis is subject to rigorous post-marketing compliance requirements, including the completion of Phase 4 or post-approval clinical trials to confirm the effect on the clinical endpoint. Failure to conduct required post-approval studies, or confirm a clinical benefit during post-marketing studies, would allow the FDA to withdraw the drug

from the market on an expedited basis. All promotional materials for drug candidates approved under accelerated regulations are subject to prior review by the FDA.

The FDA's Decision on an NDA

On the basis of the FDA's evaluation of the NDA and accompanying information, including the results of the inspection of the manufacturing facilities, the FDA may issue an approval letter or a complete response letter. An approval letter authorizes commercial marketing of the product with specific prescribing information for specific indications. A complete response letter generally outlines the deficiencies in the submission and may require substantial additional testing or information in order for the FDA to reconsider the application. If and when those deficiencies have been addressed to the FDA's satisfaction in a resubmission of the NDA, the FDA will issue an approval letter. The FDA has committed to reviewing such resubmissions in two or six months depending on the type of information included. Even with submission of this additional information, the FDA ultimately may decide that the application does not satisfy the regulatory criteria for approval.

If the FDA approves a product, it may limit the approved indications for use for the product, require that contraindications, warnings or precautions be included in the product labeling, require that post-approval studies, including Phase 4 clinical trials, be conducted to further assess the drug's safety after approval, require testing and surveillance programs to monitor the product after commercialization, or impose other conditions, including distribution restrictions or other risk management mechanisms, including REMS, which can materially affect the potential market and profitability of the product. The FDA may prevent or limit further marketing of a product based on the results of post-market studies or surveillance programs. After approval, many types of changes to the approved product, such as adding new indications, manufacturing changes and additional labeling claims, are subject to further testing requirements and FDA review and approval.

FDA Regulation of Companion Diagnostics.

FDA officials have issued guidance that addresses issues critical to developing *in vitro* companion diagnostics, such as when the FDA will require that the diagnostic and the drug be approved simultaneously. The guidance issued in August 2014 states that if safe and effective use of a therapeutic product depends on an *in vitro* diagnostic, then the FDA generally will require approval or clearance of the diagnostic at the same time that the FDA approves the therapeutic product.

The FDA previously has required *in vitro* companion diagnostics intended to select the patients who will respond to the drug candidate to obtain pre-market approval, or PMA, simultaneously with approval of the drug.

The PMA process, including the gathering of clinical and preclinical data and the submission to and review by the FDA, can take several years or longer. It involves a rigorous premarket review during which the applicant must prepare and provide the FDA with reasonable assurance of the device's safety and effectiveness and information about the device and its components regarding, among other things, device design, manufacturing and labeling. PMA applications are subject to an application fee, which exceeds $250,000 for most PMAs.

Post-Approval Requirements

Drugs manufactured or distributed pursuant to FDA approvals are subject to pervasive and continuing regulation by the FDA, including, among other things, requirements relating to recordkeeping, periodic reporting, product sampling and distribution, advertising and promotion and reporting of adverse experiences with the product. After approval, most changes to the approved product, such as adding new indications or other labeling claims, are subject to prior FDA review and approval. There also are continuing, annual user fee requirements for any marketed products and the establishments at which such products are manufactured, as well as new application fees for supplemental applications with clinical data.

In addition, drug manufacturers and other entities involved in the manufacture and distribution of approved drugs are required to register their establishments with the FDA and state agencies, and are subject to periodic unannounced inspections by the FDA and these state agencies for compliance with cGMP requirements. Changes to the manufacturing process are strictly regulated and often require prior FDA approval before being implemented. FDA regulations also require investigation and correction of any deviations from cGMP and impose reporting and documentation requirements

upon the sponsor and any third-party manufacturers that the sponsor may decide to use. Accordingly, manufacturers must continue to expend time, money, and effort in the area of production and quality control to maintain cGMP compliance.

Once an approval is granted, the FDA may withdraw the approval if compliance with regulatory requirements and standards is not maintained or if problems occur after the product reaches the market. Later discovery of previously unknown problems with a product, including adverse events of unanticipated severity or frequency, or with manufacturing processes, or failure to comply with regulatory requirements, may result in revisions to the approved labeling to add new safety information; imposition of post-market studies or clinical trials to assess new safety risks; or imposition of distribution or other restrictions under a REMS program. Other potential consequences include, among other things:

- restrictions on the marketing or manufacturing of the product, suspension of the approval, complete withdrawal of the product from the market or product recalls;
- fines, warning letters or holds on post-approval clinical trials;
- refusal of the FDA to approve pending NDAs or supplements to approved NDAs, or suspension or revocation of product license approvals;
- product seizure or detention, or refusal to permit the import or export of products; or
- injunctions or the imposition of civil or criminal penalties.

The FDA strictly regulates marketing, labeling, advertising and promotion of products that are placed on the market. Drugs may be promoted only for the approved indications and in accordance with the provisions of the approved label. The FDA and other agencies actively enforce the laws and regulations prohibiting the promotion of off-label uses, and a company that is found to have improperly promoted off-label uses may be subject to significant liability.

In addition, the distribution of prescription pharmaceutical products is subject to the Prescription Drug Marketing Act, or PDMA, as well as the Drug Supply Chain Security Act, or DSCA, which regulate the distribution and tracing of prescription drugs and prescription drug samples at the federal level, and set minimum standards for the registration and regulation of drug distributors by the states. Both the PDMA and state laws limit the distribution of prescription pharmaceutical product samples and impose requirements to ensure accountability in distribution. The DSCA imposes requires to ensure accountability in distribution and to identify and remove counterfeit and other illegitimate products from the market.

Hatch-Waxman Patent Certification and the 30-Month Stay

Upon approval of an NDA or a supplement thereto, NDA sponsors are required to list with the FDA each patent with claims that cover the applicant's product or an approved method of using the product. Each of the patents listed by the NDA sponsor is published in the Orange Book. When an Abbreviated New Drug Application, or ANDA, or 505(b)(2) applicant files its application with the FDA, the applicant is required to certify to the FDA concerning any patents listed for the reference product in the Orange Book, except for patents covering methods of use for which the ANDA applicant is not seeking approval.

Specifically, the applicant must certify with respect to each patent that:

- the required patent information has not been filed;
- the listed patent has expired;
- the listed patent has not expired, but will expire on a particular date and approval is sought after patent expiration; or
- the listed patent is invalid, unenforceable or will not be infringed by the new product.

A certification that the new product will not infringe the already approved product's listed patents or that such patents are invalid or unenforceable is called a Paragraph IV certification. If the applicant does not challenge the listed patents or indicates that it is not seeking approval of a patented method of use, the application will not be approved until all the listed patents claiming the referenced product have expired (other than method of use patents involving indications for which the ANDA applicant is not seeking approval).

If the ANDA or 505(b)(2) applicant has provided a Paragraph IV certification to the FDA, the applicant must also send notice of the Paragraph IV certification to the NDA and patent holders once the ANDA or 505(b)(2) application has been accepted for filing by the FDA. The NDA and patent holders may then initiate a patent infringement lawsuit in response to the notice of the Paragraph IV certification. The filing of a patent infringement lawsuit within 45 days after the receipt of a Paragraph IV certification automatically prevents the FDA from approving the ANDA or 505(b)(2) application until the earlier of 30 months after the receipt of the Paragraph IV notice, expiration of the patent, or a decision in the infringement case that is favorable to the ANDA applicant.

Pediatric Studies and Exclusivity

Under the Pediatric Research Equity Act of 2003, an NDA or supplement thereto must contain data that are adequate to assess the safety and effectiveness of the drug product for the claimed indications in all relevant pediatric subpopulations, and to support dosing and administration for each pediatric subpopulation for which the product is safe and effective. With enactment of the FDASIA in 2012, sponsors must also submit pediatric study plans prior to the assessment data. Those plans must contain an outline of the proposed pediatric study or studies the applicant plans to conduct, including study objectives and design, any deferral or waiver requests, and other information required by regulation. The applicant, the FDA, and the FDA's internal review committee must then review the information submitted, consult with each other, and agree upon a final plan. The FDA or the applicant may request an amendment to the plan at any time.

The FDA may, on its own initiative or at the request of the applicant, grant deferrals for submission of some or all pediatric data until after approval of the product for use in adults, or full or partial waivers from the pediatric data requirements. Additional requirements and procedures relating to deferral requests and requests for extension of deferrals are contained in the FDASIA. Unless otherwise required by regulation, the pediatric data requirements do not apply to products with orphan designation.

Pediatric exclusivity is another type of non-patent marketing exclusivity in the United States and, if granted, provides for the attachment of an additional six months of marketing protection to the term of any existing regulatory exclusivity, including the non-patent and orphan exclusivity. This six-month exclusivity may be granted if an NDA sponsor submits pediatric data that fairly respond to a written request from the FDA for such data. The data do not need to show the product to be effective in the pediatric population studied; rather, if the clinical trial is deemed to fairly respond to the FDA's request, the additional protection is granted. If reports of requested pediatric studies are submitted to and accepted by the FDA within the statutory time limits, whatever statutory or regulatory periods of exclusivity or patent protection cover the product are extended by six months. This is not a patent term extension, but it effectively extends the regulatory period during which the FDA cannot approve another application.

Orphan Drug Designation and Exclusivity

Under the Orphan Drug Act, the FDA may designate a drug product as an "orphan drug" if it is intended to treat a rare disease or condition (generally meaning that it affects fewer than 200,000 individuals in the United States, or more in cases in which there is no reasonable expectation that the cost of developing and making a drug product available in the United States for treatment of the disease or condition will be recovered from sales of the product). A company must request orphan product designation before submitting an NDA. If the request is granted, the FDA will disclose the identity of the therapeutic agent and its potential use. Orphan product designation does not convey any advantage in or shorten the duration of the regulatory review and approval process.

If a product with orphan status receives the first FDA approval for the disease or condition for which it has such designation or for a select indication or use within the rare disease or condition for which it was designated, the product generally will receive orphan product exclusivity. Orphan product exclusivity means that the FDA may not approve any other applications for the same product for the same indication for seven years, except in certain limited circumstances. Competitors may receive approval of different products for the indication for which the orphan product has exclusivity

and may obtain approval for the same product but for a different indication. If a drug or drug product designated as an orphan product ultimately receives marketing approval for an indication broader than what was designated in its orphan product application, it may not be entitled to exclusivity.

Patent Term Restoration and Extension

A patent claiming a new drug product may be eligible for a limited patent term extension under the Drug Price Competition and Patent Term Restoration Act of 1984, which permits a patent restoration of up to five years for patent term lost during product development and the FDA regulatory review. The restoration period granted is typically one-half the time between the effective date of an IND and the submission date of an NDA, plus the time between the submission date of an NDA and the ultimate approval date. Patent term restoration cannot be used to extend the remaining term of a patent past a total of 14 years from the product's approval date. Only one patent applicable to an approved drug product is eligible for the extension, and the application for the extension must be submitted prior to the expiration of the patent in question. A patent that covers multiple drugs for which approval is sought can only be extended in connection with one of the approvals. The USPTO reviews and approves the application for any patent term extension or restoration in consultation with the FDA.

The 21st Century Cures Act

On December 13, 2016, President Obama signed the 21st Century Cures Act, or the Cures Act, into law. The Cures Act is designed to modernize and personalize healthcare, spur innovation and research, and streamline the discovery and development of new therapies through increased federal funding of particular programs. It authorizes increasing funding for FDA to spend on innovation projects. The new law also amends the Public Health Service Act to reauthorize and expand funding for the National Institutes of Health. The Act establishes the NIH Innovation Fund to pay for the cost of development and implementation of a strategic plan, early stage investigators and research. It also charges NIH with leading and coordinating expanded pediatric research. Further, the Cures Act directs the Centers for Disease Control and Prevention to expand surveillance of neurological diseases.

With amendments to the FDCA and the Public Health Service Act, Title III of the Cures Act seeks to accelerate the discovery, development, and delivery of new medicines and medical technologies. To that end, and among other provisions, the Cures Act reauthorizes the priority review voucher program for certain drugs intended to treat rare pediatric diseases; creates a new priority review voucher program for drug applications determined to be material threat medical countermeasure applications; revises the FDCA to streamline review of combination product applications; requires FDA to evaluate the potential use of "real world evidence" to help support approval of new indications for approved drugs; provides a new "limited population" approval pathway for antibiotic and antifungal drugs intended to treat serious or life-threatening infections; and authorizes FDA to designate a drug as a "regenerative advanced therapy," thereby making it eligible for certain expedited review and approval designations.

Review and Approval of Drug Products in the European Union

In order to market any product outside of the United States, a company must also comply with numerous and varying regulatory requirements of other countries and jurisdictions regarding quality, safety and efficacy and governing, among other things, clinical trials, marketing authorization, commercial sales and distribution of drug products. Whether or not it obtains FDA approval for a product, the company would need to obtain the necessary approvals by the comparable foreign regulatory authorities before it can commence clinical trials or marketing of the product in those countries or jurisdictions. The approval process ultimately varies between countries and jurisdictions and can involve additional product testing and additional administrative review periods. The time required to obtain approval in other countries and jurisdictions might differ from and be longer than that required to obtain FDA approval. Regulatory approval in one country or jurisdiction does not ensure regulatory approval in another, but a failure or delay in obtaining regulatory approval in one country or jurisdiction may negatively impact the regulatory process in others.

Clinical Trial Approval in the EU

Pursuant to the European Clinical Trials Directive, a system for the approval of clinical trials in the European Union has been implemented through national legislation of the member states. Under this system, an applicant must obtain approval from the competent national authority of a European Union member state in which the clinical trial is to be conducted. Furthermore, the applicant may only start a clinical trial after a competent ethics committee has issued a

favorable opinion. Clinical trial application must be accompanied by an investigational medicinal product dossier with supporting information prescribed by the European Clinical Trials Directive and corresponding national laws of the member states and further detailed in applicable guidance documents. In April 2014, the EU adopted a new Clinical Trials Regulation, which will be directly applicable to and binding without the need for any national implementing legislation. Under the new coordinated procedure for the approval of clinical trials, the sponsor of a clinical trial will be required to submit a single application for approval of a clinical trial to a reporting EU Member State (RMS) through an EU Portal. The submission procedure will be the same irrespective of whether the clinical trial is to be conducted in a single EU Member State or in more than one EU Member State. The Clinical Trials Regulation also aims to streamline and simplify the rules on safety reporting for clinical trials.

Orphan Drug Designation and Exclusivity

Regulation 141/2000 provides that a drug shall be designated as an orphan drug if its sponsor can establish: that the product is intended for the diagnosis, prevention or treatment of a life-threatening or chronically debilitating condition affecting not more than five in ten thousand persons in the European Community when the application is made, or that the product is intended for the diagnosis, prevention or treatment of a life-threatening, seriously debilitating or serious and chronic condition in the European Community and that without incentives it is unlikely that the marketing of the drug in the European Community would generate sufficient return to justify the necessary investment. For either of these conditions, the applicant must demonstrate that there exists no satisfactory method of diagnosis, prevention or treatment of the condition in question that has been authorized in the European Community or, if such method exists, the drug will be of significant benefit to those affected by that condition.

Regulation 847/2000 sets out criteria and procedures governing designation of orphan drugs in the EU. Specifically, an application for designation as an orphan product can be made any time prior to the filing of an application for approval to market the product. Marketing authorization for an orphan drug leads to a ten-year period of market exclusivity. This period may, however, be reduced to six years if, at the end of the fifth year, it is established that the product no longer meets the criteria for orphan drug designation, for example because the product is sufficiently profitable not to justify market exclusivity. Market exclusivity can be revoked only in very selected cases, such as consent from the marketing authorization holder, inability to supply sufficient quantities of the product, demonstration of "clinically relevant superiority" by a similar medicinal product, or, after a review by the Committee for Orphan Medicinal Products, requested by a member state in the fifth year of the marketing exclusivity period (if the designation criteria are believed to no longer apply). Medicinal products designated as orphan drugs pursuant to Regulation 141/2000 shall be eligible for incentives made available by the European Community and by the member states to support research into, and the development and availability of, orphan drugs.

Pharmaceutical Coverage, Pricing and Reimbursement

Significant uncertainty exists as to the coverage and reimbursement status of products approved by the FDA and other government authorities. Sales of products will depend, in part, on the extent to which the costs of the products will be covered by third-party payors, including government health programs in the United States such as Medicare and Medicaid, commercial health insurers and managed care organizations. The process for determining whether a payor will provide coverage for a product may be separate from the process for setting the price or reimbursement rate that the payor will pay for the product once coverage is approved. Third-party payors are increasingly challenging the prices charged, examining the medical necessity, and reviewing the cost-effectiveness of medical products and services and imposing controls to manage costs. Third-party payors may also limit coverage to specific products on an approved list, or formulary, which might not include all of the approved products for a particular indication.

In order to secure coverage and reimbursement for any product that might be approved for sale, a company may need to conduct expensive pharmacoeconomic studies in order to demonstrate the medical necessity and cost-effectiveness of the product, in addition to the costs required to obtain FDA or other comparable regulatory approvals. A payor's decision to provide coverage for a drug product does not imply that an adequate reimbursement rate will be approved. Third-party reimbursement may not be sufficient to maintain price levels high enough to realize an appropriate return on investment in product development.

The containment of healthcare costs also has become a priority of federal, state and foreign governments and the prices of drugs have been a focus in this effort. Governments have shown significant interest in implementing cost-containment programs, including price controls, restrictions on reimbursement and requirements for substitution of generic

products. Adoption of price controls and cost-containment measures, and adoption of more restrictive policies in jurisdictions with existing controls and measures, could further limit a company's revenue generated from the sale of any approved products. Coverage policies and third-party reimbursement rates may change at any time. Even if favorable coverage and reimbursement status is attained for one or more products for which a company or its collaborators receive marketing approval, less favorable coverage policies and reimbursement rates may be implemented in the future. In the European Union, pricing and reimbursement schemes vary widely from country to country. Some countries provide that drug products may be marketed only after a reimbursement price has been agreed. Some countries may require the completion of additional studies that compare the cost-effectiveness of a particular drug candidate to currently available therapies, or so called health technology assessments, in order to obtain reimbursement or pricing approval. For example, the European Union provides options for its member states to restrict the range of drug products for which their national health insurance systems provide reimbursement and to control the prices of medicinal products for human use. European Union member states may approve a specific price for a drug product or may instead adopt a system of direct or indirect controls on the profitability of the company placing the drug product on the market. Other member states allow companies to fix their own prices for drug products, but monitor and control company profits. The downward pressure on health care costs in general, particularly prescription drugs, has become intense. As a result, increasingly high barriers are being erected to the entry of new products. In addition, in some countries, cross-border imports from low-priced markets exert competitive pressure that may reduce pricing within a country. Any country that has price controls or reimbursement limitations for drug products may not allow favorable reimbursement and pricing arrangements.

Healthcare Law and Regulation

Healthcare providers, physicians and third-party payors play a primary role in the recommendation and prescription of drug products that are granted marketing approval. Arrangements with providers, consultants, third-party payors and customers are subject to broadly applicable fraud and abuse and other healthcare laws and regulations. Such restrictions under applicable federal and state healthcare laws and regulations, include the following:

- the federal Anti-Kickback Statute prohibits, among other things, persons from knowingly and willfully soliciting, offering, receiving or providing remuneration, directly or indirectly, in cash or in kind, to induce or reward either the referral of an individual for, or the purchase, order or recommendation of, any good or service, for which payment may be made, in whole or in part, under a federal healthcare program such as Medicare and Medicaid;

- the federal False Claims Act imposes civil penalties, and provides for civil whistleblower or qui tam actions, against individuals or entities for knowingly presenting, or causing to be presented, to the federal government, claims for payment that are false or fraudulent or making a false statement to avoid, decrease or conceal an obligation to pay money to the federal government, with potential liability including mandatory treble damages and significant per-claim penalties, currently set at $5,500 to $11,000 per false claim;

- the federal Health Insurance Portability and Accountability Act of 1996, or HIPAA, imposes criminal and civil liability for executing a scheme to defraud any healthcare benefit program or making false statements relating to healthcare matters;

- HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act and their respective implementing regulations, including the Final Omnibus Rule published in January 2013, also imposes obligations, including mandatory contractual terms, with respect to safeguarding the privacy, security and transmission of individually identifiable health information;

- the federal false statements statute prohibits knowingly and willfully falsifying, concealing or covering up a material fact or making any materially false statement in connection with the delivery of or payment for healthcare benefits, items or services;

- the federal transparency requirements under the Health Care Reform Law, known as the federal Physician Payments Sunshine Act, require manufacturers of drugs, devices, biologics and medical supplies to report to the Centers for Medicare & Medicaid Services, or CMS, within the Department of Health and Human Services information related to payments and other transfers of value to physicians and teaching hospitals and physician ownership and investment interests held by physicians and their immediate family members; and

- analogous state and foreign laws and regulations, such as state anti-kickback and false claims laws, may apply to sales or marketing arrangements and claims involving healthcare items or services reimbursed by non-governmental third-party payors, including private insurers.

Some state laws require pharmaceutical companies to comply with the pharmaceutical industry's voluntary compliance guidelines and the relevant compliance guidance promulgated by the federal government in addition to requiring drug manufacturers to report information related to payments to physicians and other health care providers or marketing expenditures. State and foreign laws also govern the privacy and security of health information in some circumstances, many of which differ from each other in significant ways and often are not preempted by HIPAA, thus complicating compliance efforts.

Healthcare Reform in the United States

A primary trend in the United States healthcare industry and elsewhere is cost containment. There have been a number of federal and state proposals during the last several years regarding the pricing of pharmaceutical and biopharmaceutical products, limiting coverage and reimbursement for drugs and other medical products, government control and other changes to the healthcare system in the United States.

By way of example, the United States and state governments continue to propose and pass legislation designed to reduce the cost of healthcare. In March 2010, the United States Congress enacted the Patient Protection and Affordable Care Act, or the PPACA, which, among other things, includes changes to the coverage and payment for products under government health care programs. Among the provisions of the PPACA of importance to potential drug candidates are:

- an annual, nondeductible fee on any entity that manufactures or imports specified branded prescription drugs and biologic agents, apportioned among these entities according to their market share in certain government healthcare programs, although this fee would not apply to sales of certain products approved exclusively for orphan indications;

- expansion of eligibility criteria for Medicaid programs by, among other things, allowing states to offer Medicaid coverage to certain individuals with income at or below 133% of the federal poverty level, thereby potentially increasing a manufacturer's Medicaid rebate liability;

- expanded manufacturers' rebate liability under the Medicaid Drug Rebate Program by increasing the minimum rebate for both branded and generic drugs and revising the definition of "average manufacturer price," or AMP, for calculating and reporting Medicaid drug rebates on outpatient prescription drug prices and extending rebate liability to prescriptions for individuals enrolled in Medicare Advantage plans;

- addressed a new methodology by which rebates owed by manufacturers under the Medicaid Drug Rebate Program are calculated for drugs that are inhaled, infused, instilled, implanted or injected;

- expanded the types of entities eligible for the 340B drug discount program;

- established the Medicare Part D coverage gap discount program by requiring manufacturers to provide a 50% point-of-sale-discount off the negotiated price of applicable brand drugs to eligible beneficiaries during their coverage gap period as a condition for the manufacturers' outpatient drugs to be covered under Medicare Part D;

- established a new Patient-Centered Outcomes Research Institute to oversee, identify priorities in, and conduct comparative clinical effectiveness research, along with funding for such research;

- established the Independent Payment Advisory Board, or IPAB, which has authority to recommend certain changes to the Medicare program to reduce expenditures by the program that could result in reduced payments for prescription drugs. However, the IPAB implementation has been not been clearly defined. The PPACA provided that under certain circumstances, IPAB recommendations will become law unless Congress enacts legislation that will achieve the same or greater Medicare cost savings; and

- established the Center for Medicare and Medicaid Innovation within CMS to test innovative payment and service delivery models to lower Medicare and Medicaid spending, potentially including prescription drug spending. Funding has been allocated to support the mission of the Center for Medicare and Medicaid Innovation from 2011 to 2019.

Other legislative changes have been proposed and adopted in the United States since the PPACA was enacted. For example, in August 2011, the Budget Control Act of 2011, among other things, created measures for spending reductions by Congress. A Joint Select Committee on Deficit Reduction, tasked with recommending a targeted deficit reduction of at least $1.2 trillion for the years 2012 through 2021, was unable to reach required goals, thereby triggering the legislation's automatic reduction to several government programs. This includes aggregate reductions of Medicare payments to providers of up to 2% per fiscal year, which went into effect in April 2013 and will remain in effect through 2024 unless additional Congressional action is taken. In January 2013, President Obama signed into law the American Taxpayer Relief Act of 2012, which, among other things, further reduced Medicare payments to several providers, including hospitals, imaging centers and cancer treatment centers, and increased the statute of limitations period for the government to recover overpayments to providers from three to five years.

With the new Presidential administration and Congress, there will likely be additional legislative changes, including repeal and replacement of certain provisions of the PPACA. To that end, on January 20, 2017, the President issued an Executive Order Minimizing the Economic Burden of the Patient Protection and Affordable Care Act Pending Repeal. The Executive Order declares that, pending repeal of the PPACA, it is imperative for the executive branch to ensure that the law is being efficiently implemented, take all actions consistent with law to minimize the unwarranted economic and regulatory burdens of the Act, and prepare to afford the States more flexibility and control to create a more free and open healthcare market. The Order directs the Secretary of Health and Human Services and the heads of all other executive departments and agencies with authorities and responsibilities under the PPACA to exercise their authority and discretion to waive, defer, grant exemptions from, or delay the implementation of any provision or requirement of the PPACA that would impose a fiscal burden on any State or a cost, fee, tax, penalty, or regulatory burden on individuals, families, healthcare providers, health insurers, patients, recipients of healthcare services, purchasers of health insurance, or makers of medical devices, products, or medications.

With respect to repeal of the PPACA and its replacement with new legislation, it is unclear when such legislation will be enacted, what it will provide and what impact it will have on the availability of healthcare and containing or lowering the costs of healthcare.

Segment and Geographical Information

We operate in a single operating segment. For segment and geographical financial information, see Note 2(i) to the financial statements appearing elsewhere in this Annual Report on Form 10-K, which are incorporated herein by reference.

Employees

As of February 15, 2017, we employed 62 individuals, 38 of whom are engaged in research and development and 19 of whom 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.

Corporate Information

We were incorporated in Delaware in 1989 and our offices are located at 167 Sidney Street, Cambridge, Massachusetts 02139 and 505 Eagleview Boulevard, Suite 212, Exton, Pennsylvania 19341.

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 13(a) or 15(d) of the Securities Exchange

Act of 1934, as amended, or the Exchange Act, as soon as reasonably practicable after we electronically file or furnish such materials to the Securities and Exchange Commission, or the SEC.

Item 1A. RISK FACTORS.

RISK FACTORS

Investing in our securities 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. Our business, financial condition and results of operations could be materially and adversely affected by any of these and currently unknown risks or uncertainties. In that case, the market price of our common stock could decline, and you may lose all or part of your investment in our securities.

Risks Relating to Our Financial Results and Need for Financing

We will need additional financing, which may be difficult to obtain. Our failure to obtain necessary financing or doing so on unattractive terms could result in the termination of our operations and the sale and license of our assets or otherwise adversely affect our research and development programs and other operations.

We had cash, cash equivalents and investments of approximately $109.0 million at December 31, 2016. We believe that, based on our current operating plan, our existing cash, cash equivalents and investments, will enable us to fund our operations into the second quarter of 2018. Specifically, we believe that our available funds will be sufficient to enable us to:

- participate in an FDA End-of-Phase 1 meeting to obtain FDA feedback on the regulatory pathway for IMO-2125;
- complete our ongoing Phase 1/2 clinical trial of IMO-2125 in combination with ipilimumab or pembrolizumab in anti-PD1 refractory metastatic melanoma and complete the enrollment in the Phase 2 portion of this trial;
- prepare for the initiation of a pivotal Phase 3 clinical trial of IMO-2125 in combination with a checkpoint inhibitor for the treatment of anti-PD1 refractory metastatic melanoma;
- initiate a Phase 1 intra-tumoral monotherapy clinical trial of IMO-2125 in multiple refractory tumor types;
- initiate a Phase 2 multi-arm clinical trial of IMO-2125 in combination with a checkpoint inhibitor in multiple refractory tumor types;
- complete our ongoing Phase 2 clinical trial of IMO-8400 in patients with dermatomyositis; and
- submit an IND and initiate a Phase 1 human clinical proof-of-concept trial of IDRA-008.

We expect that we will need to raise additional funds in order to conduct any other clinical development of our TLR drug candidates or to conduct any other development of our 3GA technology, and to fund our operations. We are seeking and expect to continue to seek additional funding through collaborations, the sale or license of assets or financings of equity or debt securities. We believe the key factors that will affect our ability to obtain funding are:

- the results of our clinical and preclinical development activities in our rare disease program, our immuno-oncology program and our 3GA program, and our ability to advance our drug candidates and 3GA technology on the timelines anticipated;
- the cost, timing, and outcome of regulatory reviews;
- competitive and potentially competitive products and technologies and investors' receptivity to our drug candidates and the technology underlying them in light of competitive products and technologies;
- the receptivity of the capital markets to financings by biotechnology companies generally and companies with drug candidates and technologies such as ours specifically; and
- our ability to enter into additional collaborations with biotechnology and pharmaceutical companies and the success of such collaborations.

In addition, increases in expenses or delays in clinical development may adversely impact our cash position and require additional funds or cost reductions.

Financing may not be available to us when we need it or may not be available to us on favorable or acceptable terms or at all. 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. An equity financing that involves existing stockholders may cause a concentration of ownership. 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 or equity financing may contain terms which are not favorable to us or to our stockholders, such as liquidation and other preferences, or liens or other restrictions on our assets. As discussed in Note 10 to the financial statements appearing elsewhere in this Annual Report on Form 10-K, additional equity financings may also result in cumulative changes in ownership over a three-year period in excess of 50% which would limit the amount of net operating loss and tax credit carryforwards that we may utilize in any one year.

If we are unable to obtain adequate funding on a timely basis or at all, we will be required to terminate, modify or delay preclinical or clinical trials of one or more of our drug candidates, significantly curtail or terminate discovery or development programs for new drug candidates or relinquish rights to portions of our technology, drug candidates and/or products.

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, 2008, and 2009 when our recognition of revenues under license and collaboration agreements resulted in our reporting net income for those years. As of December 31, 2016, we had an accumulated deficit of $538.5 million. Since January 1, 2001, we have primarily been involved in the development of our TLR pipeline. From January 1, 2001 to December 31, 2016, we incurred losses of $278.3 million. We incurred losses of $260.2 million prior to December 31, 2000, during which time we were primarily involved in the development of earlier generation 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. As of December 31, 2016, substantially 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 have not completed development of any drug candidates. 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 drug candidates will become commercially available, or when we will become profitable, if at all. We expect to incur substantial operating losses in future periods.

Risks Relating to Our Business, Strategy and Industry

We are depending heavily on the development of TLR-targeted drug candidates for the treatment of certain rare diseases and in our immuno-oncology program and on the development of our 3GA technology. If we terminate the development of any of our programs or any of our drug candidates in such programs, are unable to successfully develop and commercialize any of our drug candidates, or experience significant delays in doing so, our business may be materially harmed.

We have invested a significant portion of our time and financial resources in the development of TLR-targeted clinical-stage drug candidates as part of our rare disease program. In the future, we intend to invest a significant portion of our time and financial resources in the development of our TLR-targeted candidates for the treatment of certain rare diseases and in our immuno-oncology program. We also plan to invest substantial time and resources to further advance the development of drug candidates under our 3GA program. For instance:

- we are conducting a Phase 1/2 clinical trial of IMO-2125, administered intra-tumorally, in combination with ipilimumab or pembrolizumab in patients with anti-PD1 refractory metastatic melanoma;
- we plan to conduct additional clinical trials of IMO-2125 in our immuno-oncology program both as a monotherapy and in combination with checkpoint inhibitors for the treatment of multiple tumor types;
- we are conducting a Phase 2 clinical trial of IMO-8400 in patients with dermatomyositis; and
- we are developing compounds in our 3GA program and plan to initiate a Phase 1 clinical trial of IDRA-008.

We anticipate that our ability to generate product revenues will depend heavily on the successful development and commercialization of our TLR drug candidates in our rare disease and immuno-oncology programs, and the successful identification, development and commercialization of drug candidates in our 3GA program.

Our ability to generate milestone and royalty revenues under our collaborations with Vivelix, GSK and Merck & Co., and under any other collaboration that we enter into with respect to our other programs, will depend on the development and commercialization of the drug candidates being developed under the collaborations.

Our efforts, and the efforts of Vivelix, GSK and Merck & Co., to develop and commercialize compounds are at an early stage and are subject to many challenges. For instance, we previously experienced a setback with respect to our program for IMO-2125 for hepatitis C. In April 2011, we chose to delay initiation of our planned 12-week Phase 2 randomized clinical trial of IMO-2125 plus ribavirin in treatment-naïve, genotype 1 hepatitis C virus, or HCV, patients based on observations of lymphoproliferative malignancies in an ongoing 26-week chronic nonclinical toxicology study of IMO-2125 in rodents. We subsequently completed a 39-week chronic nonclinical toxicology study of IMO-2125 in non-human primates in which there were no similar observations. Additionally, in September 2016, we discontinued our development program of IMO-8400 for the treatment of B-cell lymphomas and suspended our ongoing Phase 1/2 clinical trials of IMO-8400 in patients with Waldenström's macroglobulinemia and in patients with DLBCL harboring the MYD88 L265P oncogenic mutation due to several factors, including the lack of a strong clinical signal for Waldenström's macroglobulinemia patients and the inability to adequately enroll patients with DLBCL.

We have entered into and expect to continue to seek to enter into collaborative alliances with pharmaceutical companies to advance our TLR agonists and antagonist candidates and with respect to additional applications of our 3GA technology program. Our previous setbacks with respect to our program for IMO-2125 in patients with chronic hepatitis C virus and our program for IMO-8400 in patients with B-cell lymphomas could negatively impact our ability to license any of such compounds, or any of our other compounds, particularly related compounds, to a third party.

Our ability to successfully develop and commercialize these drug candidates, or other potential drug candidates, will depend on our ability to overcome these recent challenges and on several factors, including the following:

- the drug candidates demonstrating activity in clinical trials;
- the drug candidates demonstrating an acceptable safety profile in nonclinical toxicology studies and during clinical trials;
- timely enrollment in clinical trials of IMO-8400, IMO-2125 and other drug candidates, which may be slower than anticipated, potentially resulting in significant delays;
- satisfying conditions imposed on us and/or our collaborators by the FDA or equivalent foreign regulatory authorities regarding the scope or design of clinical trials;
- the ability to demonstrate to the satisfaction of the FDA, or equivalent foreign regulatory authorities, the safety and efficacy of the drug candidates through current and future clinical trials;
- timely receipt of necessary marketing approvals from the FDA and equivalent foreign regulatory authorities;
- the ability to combine our drug candidates and the drug candidates being developed by our collaborators and any other collaborators safely and successfully with other therapeutic agents;
- achieving and maintaining compliance with all regulatory requirements applicable to the products;
- establishment of commercial manufacturing arrangements with third-party manufacturers;

- the ability to secure orphan drug exclusivity for our drug candidates either alone or in combination with other products;
- the successful commercial launch of the drug candidates, assuming FDA approval is obtained, whether alone or in combination with other products;
- acceptance of the products as safe and effective by patients, the medical community, and third-party payors;
- competition from other companies and their therapies;
- changes in treatment regimens;
- favorable market conditions in which to raise additional capital;
- the strength of our intellectual property portfolio in the United States and abroad; and
- a continued acceptable safety and efficacy profile of the drug candidates following marketing approval.

We are in the early stages of developing our TLR9 agonists in combination with checkpoint inhibitors, which is a novel technology, and our efforts may not be successful or result in any approved and marketable products.

In June 2015, we entered into a strategic clinical research alliance with MD Anderson to advance clinical development of TLR9 agonists in combination with checkpoint inhibitors. We initiated the first trial from the research alliance, a Phase 1/2 clinical trial to assess the safety and efficacy of IMO-2125, administered intra-tumorally in combination with ipilimumab, a CTLA4 antibody, in patients with metastatic melanoma (anti-PD1 refractory) in the fourth quarter of 2015. While we have evaluated the safety profile of IMO-2125 in previous trials, in those trials we evaluated the safety profile of IMO-2125 by subcutaneous injection and not by intra-tumoral injection. In addition, while, as a marketed product, the safety profile of ipilimumab is known, the safety profile of the combination of IMO-2125 and ipilimumab has not been evaluated in previous trials. These factors may result in participating subjects experiencing serious adverse events or undesirable side effects or exposure to unacceptable health risks requiring us to suspend or terminate any clinical trials that we may conduct of IMO-2125 in combination with ipilimumab, or any other checkpoint inhibitor. Furthermore, we have expanded the Phase 1/2 clinical trial to include the assessment of safety and efficacy of IMO-2125, administered intra-tumorally in combination with pembrolizumab, an anti-PD1 antibody in patients with metastatic melanoma (anti-PD1 refractory). While, as a marketed product, the safety profile of pembrolizumab is known, the safety profile of the combination of IMO-2125 and pembrolizumab has not been evaluated in previous trials and may result in participating subjects experiencing serious adverse events or undesirable side effects or exposure to unacceptable health risks requiring us to suspend or terminate any clinical trials that we may conduct of IMO-2125 in combination with pembrolizumab, or any other checkpoint inhibitor.

In September 2016, we disclosed early clinical results from the Phase 1 portion of our ongoing Phase 1/2 clinical trial of IMO-2125. It is important to note that the clinical responses reported from the first two dosing cohorts of the Phase 1 portion of the trial were observed in only three of the patients enrolled through the second cohort, were achieved in an open-label setting, are not statistically significant, and might not be achieved by any other patient treated with IMO-2125. In February 2017, we provided a further update in a poster session at the joint meeting of the American Society of Clinical Oncology (ASCO)-SITC Meeting where we disclosed that the drug was well tolerated through the initial dosing of the 32mg mg dosing cohort with ipilimumab as well as through the initial dosing of the first, i.e. 8mg, cohort with pembrolizumab. These additional interim results as well as final results from this trial and results of future trials may not be positive or consistent with the results of this trial we have observed to date.

We are in the early stages of developing our 3GA program, which is a novel technology, and our efforts may not be successful or result in any approved and marketable products.

We are in the early stages of developing our 3GA technology program, and the scientific evidence to support the feasibility of developing drugs based on this technology is preliminary. Further, neither we nor any other company has received regulatory approval to market therapeutics utilizing 3GA drug candidates.

The future success of our 3GA technology program depends on our success in identifying and developing marketable products based on such technology. Although the results of our preclinical studies to date have been supportive of the viability of this technology, it is unknown whether these results are indicative of results that may be obtained in any

future clinical trials that we may conduct. We are currently undertaking an analysis of priority oncology and rare disease indications for development of drug candidates generated from our 3GA technology. We are also conducting preliminary analysis of 3GA compounds for undisclosed potential gene targets.

However, many steps must be successfully achieved prior to the declaration of a 3GA drug candidate and the initiation of clinical development. Given the level of uncertainty of our ability to successfully achieve these many steps and the uncertainty of the drug discovery and clinical development processes in general, there can be no assurance that we will succeed in developing any marketable products as a result of our efforts with respect to our 3GA technology program.

If we experience delays or difficulties in the enrollment of patients in clinical trials, our receipt of necessary regulatory approvals could be delayed or prevented.

We may not be able to initiate or continue clinical trials for our drug candidates if we are unable to locate and enroll a sufficient number of eligible patients to participate in these trials as required by the FDA or similar regulatory authorities outside the United States. For example, we recently suspended our clinical trial of IMO-8400 in patients with DLBCL harboring the MYD88 L265P oncogenic mutation due to difficulty in enrolling patients. Additionally, because there are a limited number of patients with dermatomyositis, or other rare diseases having indications for which we may determine to develop our TLR antagonists, our ability to enroll eligible patients in any clinical trials for these indications may be limited or may result in slower enrollment than we anticipated. In addition, some of our competitors have ongoing clinical trials for drug candidates that treat the same indications as our drug candidates, and patients who would otherwise be eligible for our clinical trials may instead enroll in clinical trials of our competitors' drug candidates.

Patient enrollment is affected by other factors including the:

- severity of the disease under investigation;
- eligibility criteria for the trial in question;
- perceived risks and benefits of the TLR-targeted drug candidates under study;
- efforts to facilitate timely enrollment in clinical trials;
- availability of competing clinical trials or other therapies;
- patient referral practices of physicians;
- ability to monitor patients adequately during and after treatment; and
- proximity and availability of clinical trial sites for prospective patients.

Our inability to enroll a sufficient number of patients for our clinical trials would result in significant delays and could require us to abandon one or more clinical trials altogether. Enrollment delays in our clinical trials may result in increased development costs for our drug candidates, which would cause the value of our company to decline and limit our ability to obtain additional financing.

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

In order to obtain regulatory approvals for the commercial sale of our drug candidates, 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 or other equivalent foreign regulatory agencies may not allow us 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. For example, in September 2016, we disclosed positive early data from the first two dosing cohorts of the Phase 1 portion of our ongoing Phase 1/2 clinical trial of IMO-2125. In February 2017, we provided a further update in a poster session at the joint meeting of the American Society of Clinical Oncology (ASCO)-SITC Meeting where we disclosed that the drug was well tolerated through the initial dosing of the 32mg mg dosing cohort with ipilimumab as well as through the initial dosing of the first, i.e. 8mg, cohort with pembrolizumab. There is no assurance that any interim results or the final results of our ongoing Phase 1/2 clinical trial or any future trial of IMO-2125 will be positive or consistent with results previously reported. 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, effects seen in nonclinical studies, even if not observed in clinical trials, may result in limitations or restrictions on clinical trials. Numerous unforeseen events may occur during, or as a result of, preclinical testing, nonclinical testing or the clinical trial process that could delay or inhibit the ability to receive regulatory approval or to commercialize drug products.

Other companies developing drugs targeted to TLRs have experienced setbacks in clinical trials. These setbacks may result in enhanced scrutiny by regulators or institutional review boards, or IRBs, of clinical trials of our drug candidates, including our TLR-targeted drug candidates, which could result in regulators or IRBs prohibiting the commencement of clinical trials, requiring additional nonclinical studies as a precondition to commencing clinical trials or imposing restrictions on the design or scope of clinical trials that could slow enrollment of trials, increase the costs of trials or limit the significance of the results of trials. Such setbacks could also adversely impact the desire of investigators to enroll patients in, and the desire of patients to enroll in, clinical trials of our drug candidates.

Other events that could delay or inhibit conduct of our clinical trials include:

- regulators or IRBs 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 subjects experience serious adverse events or undesirable side effects or are exposed to unacceptable health risks;
- regulators or IRBs may hold, suspend or terminate clinical research for various reasons, including noncompliance with regulatory requirements, issues identified through inspections of manufacturing or clinical trial operations or clinical trial sites, or if, in their opinion, the participating subjects are being exposed to unacceptable health risks;
- 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, or similar policy under foreign regulatory authorities. Employment of such debarred persons, even if inadvertent, may result in delays in the FDA's or foreign equivalent's review or approval of our drug candidates, or the rejection of data developed with the involvement of such person(s);
- we or our contract manufacturers may be unable to manufacture sufficient quantities of our drug candidates for use in clinical trials;
- the cost of our clinical trials may be greater than we currently anticipate making continuation and/or completion improbable; and
- our drug candidates may not cause the desired effects or may cause undesirable side effects or our drug candidates may have other unexpected characteristics.

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 drug candidates.

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 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 drug candidate development costs, delay any potential revenues, reduce the potential length of patent exclusivity 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;
- 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 or proposed clinical trial design;
- obtaining additional financing;
- obtaining IRB 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, or oligonucleotides, targeted to TLRs and on 3GA drug candidates. Neither we nor any other company have obtained regulatory approval to market such TLR-targeted drug candidates or 3GA oligonucleotides as therapeutic drugs, and no such products currently are being marketed. The results of preclinical studies with TLR-targeted compounds may not be indicative of results that may be obtained in clinical trials, and results we have obtained in the 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 or of 3GA drug candidates 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.

Moreover, only one oligonucleotide antisense drug, Kynamro®, has been approved by the FDA for marketing in the United States since 1998 and is currently being marketed.

As such, oligonucleotides as a chemical class of drug candidates have limited precedence for successful late-stage development and regulatory approval. As we progress our oligonucleotide drug candidates into Phase 2 clinical trials involving patients with severe disease and as we conduct long-term nonclinical toxicology studies, we expect to encounter an increased risk of generating clinical adverse events and nonclinical toxicology study results that will require careful interpretation. In animal toxicology studies, we have observed adverse treatment-related effects on serum complement as well as evidence of adverse kidney, vascular, and heart pathology in longer term dosing of animals with our oligonucleotide compounds, which we believe are consistent with data previously generated with other third party oligonucleotides. Given

the limited experience in assessing the relevance of oligonucleotide-related adverse animal toxicology findings to humans, the clinical and regulatory context for interpreting the significance of such events and results is not well established.

As a result of these factors, we may never succeed in obtaining regulatory approval to market any product. Furthermore, the commercial success of any of our drug candidates for which we may obtain marketing approval from the FDA or other regulatory authorities will depend upon their acceptance by patients, the medical community, and third-party payors as clinically useful, safe, and cost-effective. In addition, if products being developed by our competitors have negative clinical trial results or otherwise are viewed negatively, the perception of our technologies and market acceptance of our drug candidates could be impacted negatively.

Our setbacks with respect to our TLR-targeted compounds, together with the setbacks experienced by other companies developing oligonucleotides-based compounds and TLR-targeted compounds, may result in a negative perception of our technology and our TLR-targeted compounds, impact our ability to obtain marketing approval of these drug candidates and adversely affect acceptance of our technology and our TLR-targeted compounds by patients, the medical community and third-party payors.

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 drug candidates 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.

We are developing our TLR-targeted drug candidates for use in the treatment of certain rare diseases and in our immuno-oncology program. We are conducting a Phase 2 clinical trial of IMO-8400 in patients with dermatomyositis. In addition, through our clinical alliance partner MD Anderson, we are conducting a Phase 1/2 clinical trial of IMO-2125, administered intra-tumorally, in combination with ipilimumab, a CTLA4 antibody, or pembrolizumab in patients with metastatic melanoma and plan to initiate additional clinical trials of IMO-2125 in our immuno-oncology program both as a monotherapy and in combination with checkpoint inhibitors for the treatment of multiple tumor types. We also entered into a collaborative alliance agreement with GSK, and expect to seek to enter into additional collaborative alliances with pharmaceutical companies with respect to applications of our 3GA technology program. For all of these disease areas, there are many other companies, public and private, that are actively engaged in discovery, development, and commercializing products and technologies that may compete with our drug candidates and programs, including TLR-targeted compounds as well as non-TLR-targeted therapeutics.

Many of the drug development programs in dermatomyositis are focusing on expanding the use of drugs approved in different indications through investigator sponsored studies such as the ongoing studies of the monoclonal antibodies, belimumab and tocilizumab. We are not aware of other new chemical or molecular entities being developed for the treatment of dermatomyositis.

We are aware of other companies including Dynavax, Mologen AG, BioLineRx Ltd., Innate Immunotherapeutics Ltd., VentiRx Pharmaceuticals Inc., Telormedix S.A., Gilead Sciences Inc., GlaxoSmithKline plc, AstraZeneca plc, Checkmate Pharmaceuticals, Inc. and Hoffmann-La Roche that are developing TLR agonists and antagonists for various indications, including oncology and rare diseases.

Immuno-oncology, which utilizes a patient's own immune system to combat cancer, is currently an active area of research for biotechnology and pharmaceutical companies. Interest in immuno-oncology is driven by recent efficacy data in cancers with historically bleak outcomes and the potential to achieve a cure or functional cure for some patients. As such, our efforts in this field will be competitive with a wide variety of different approaches. Any one of these competitive approaches may result in the development of novel technologies that are more effective, safer or less costly than any that we are developing. In addition, Dynavax is conducting a Phase 1/2 clinical trial of an investigational TLR9 agonist in combination with checkpoint inhibitors and Checkmate is conducting a Phase 1b clinical trial of an investigational TLR9 agonist in combination with a checkpoint inhibitor.

We are also developing 3GA drug candidates that we have created using our proprietary technology to inhibit the production of disease-associated proteins by targeting RNA. We also face competition from other companies working to develop novel drugs using technologies that may compete with our 3GA technology. We are aware of multiple companies that are developing technologies that use oligonucleotide-based compounds to inhibit the production of disease associated proteins. These technologies include, but are not limited to, antisense technology as well as RNAi. In the field of antisense technologies, we compete with multiple companies, including Ionis and its partners, as well as WAVE Life Sciences and its partner. Ionis is currently marketing an antisense drug, Kynamro, and Biogen recently received FDA approval for its antisense drug Spinraza for spinal muscular atrophy. Ionis has over two dozen antisense drug candidates in clinical trials. In the field of RNAi, our primary competition is with Alnylam, Dicerna, Miragen, and their respective partners. For example, Alnylam is developing multiple RNAi-based technologies and has six drug candidates in clinical trials. Any of the competing companies may develop gene-silencing technologies more rapidly and more effectively than us, and antisense technology and RNAi may become the preferred technology for drugs that target RNA in order to inhibit the production of disease-associated proteins.

Some of these potentially competitive products have been in development or commercialized for years, in some cases by large, well established pharmaceutical companies. Many of the marketed products 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 products 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 is planned for our drug candidates upon commercialization, potentially less attractive, from a cost perspective, to buyers.

We recognize that other companies, including large pharmaceutical companies, may be developing or have plans to develop products and technologies that may compete with ours. 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, and marketing and selling approved products. 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.

We anticipate that the competition with our drug candidates and technologies will be based on a number of factors including product efficacy, safety, availability, and price. The timing of market introduction of our drug candidates 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, 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 Mr. Vincent Milano and Dr. Sudhir Agrawal. Mr. Milano serves as our President and Chief Executive Officer, and Dr. Agrawal serves as our President of Research.

We are a party to employment agreements with Mr. Milano and Dr. Agrawal. Mr. Milano's employment agreement is terminable upon 15 days prior written notice at the election of either party and immediately in the event of a termination for cause (as defined therein). Dr. Agrawal's employment agreement expires on October 19, 2019, but automatically extends annually for additional one-year periods. 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 Mr. Milano or 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.

Risks Related to Regulatory Approval and Marketing of Our Drug Candidates and Other Legal Compliance Matters

Even if we complete the necessary preclinical studies and clinical trials, the marketing approval process is expensive, time-consuming and uncertain and may prevent us from obtaining approvals for the commercialization of some or all of our drug candidates. As a result, we cannot predict when or if we, or any future collaborators, will obtain marketing approval to commercialize a drug candidate.

Our drug candidates and the activities associated with their development and commercialization, including their design, testing, manufacture, safety, efficacy, recordkeeping, labeling, storage, approval, marketing, promotion, sale and distribution, export and import are subject to extensive regulation by the FDA and comparable foreign regulatory authorities, whose laws and regulations may differ from country to country. We are not permitted to market our drug candidates in the United States or in other countries until we, or any future collaborators, receive approval of an NDA from the FDA or marketing approval from applicable regulatory authorities outside of the United States.

All of the drug candidates that we are developing, or may develop in the future, will require additional research and development, extensive preclinical studies, nonclinical testing, 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. Securing marketing approval requires the submission of extensive preclinical and clinical data and supporting information to regulatory authorities for each therapeutic indication to establish the drug candidate's safety and purity. Securing marketing approval also requires the submission of information about the product manufacturing process to, and inspection of manufacturing facilities by, the regulatory authorities.

Since our inception, we have conducted clinical trials of a number of compounds and are planning to initiate clinical trials for a number of additional disease indications. Specifically:

- we are conducting a Phase 1/2 clinical trial of IMO-2125, administered intra-tumorally, in combination with ipilimumab or pembrolizumab in patients with anti-PD1 refractory metastatic melanoma;
- we plan to conduct additional clinical trials of IMO-2125 in our immuno-oncology program both as a monotherapy and in combination with checkpoint inhibitors for the treatment of multiple tumor types;
- we are conducting a Phase 2 clinical trial of IMO-8400 in patients with dermatomyositis; and
- we are developing compounds in our 3GA program and plan to initiate a Phase 1 clinical trial of IDRA-008.

The FDA and other regulatory authorities may not approve any of our potential products for any indication.

We may need to address a number of technological challenges in order to complete development of our drug candidates. 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. In addition, changes in marketing approval policies during the development period, changes in or the enactment of additional statutes or regulations, or changes in regulatory review for each submitted product application, may cause delays in the approval or rejection of an application. The FDA and comparable authorities in other countries have substantial discretion in the approval process and may refuse to accept any application or may decide that our data is insufficient for approval and require additional preclinical, clinical or other studies. In addition, varying interpretations of the data obtained from preclinical and clinical testing could delay, limit or prevent marketing approval of a drug candidate.

Any delay in obtaining or failure to obtain required approvals could materially adversely affect our ability or that of any collaborators we may have to generate revenue from the particular drug candidate, which likely would result in significant harm to our financial position and adversely impact our stock price.

Our failure to obtain marketing approval in foreign jurisdictions would prevent our drug candidates from being marketed abroad, and any approval we are granted for our drug candidates in the United States would not assure approval of drug candidates in foreign jurisdictions.

In order to market and sell our drugs in the European Union and many other jurisdictions, we, and any future collaborators, must obtain separate marketing approvals and comply with numerous and varying regulatory requirements. The approval procedure varies among countries and can involve additional testing. The time required to obtain approval may differ substantially from that required to obtain FDA approval. The marketing approval process outside of the United States generally includes all of the risks associated with obtaining FDA approval. In addition, in many countries outside of the United States, it is required that the drug be approved for reimbursement before the drug can be approved for sale in that country. We, and any future collaborators, may not obtain approvals from regulatory authorities outside of the United States on a timely basis, if at all. Approval by the FDA does not ensure approval by regulatory authorities in other countries or jurisdictions, and approval by one regulatory authority outside of the United States does not ensure approval by regulatory authorities in other countries or jurisdictions or by the FDA.

Even if we, or any future collaborators, obtain marketing approvals for our drug candidates, the terms of approvals and ongoing regulation of our drugs may limit how we, or they, manufacture and market our drugs, which could materially impair our ability to generate revenue.

Once marketing approval has been granted, an approved drug and its manufacturer and marketer are subject to ongoing review and extensive regulation. We, and any future collaborators, must therefore comply with requirements concerning advertising and promotion for any of our drug candidates for which we or they obtain marketing approval. Promotional communications with respect to prescription drugs are subject to a variety of legal and regulatory restrictions and must be consistent with the information in the drug's approved labeling. Thus, we, and any future collaborators, may not be able to promote any drugs we develop for indications or uses for which they are not approved.

In addition, manufacturers of approved drugs and those manufacturers' facilities are required to comply with extensive FDA requirements, including ensuring that quality control and manufacturing procedures conform to cGMPs, which include requirements relating to quality control and quality assurance as well as the corresponding maintenance of records and documentation and reporting requirements. We, our contract manufacturers, our future collaborators and their contract manufacturers could be subject to periodic unannounced inspections by the FDA to monitor and ensure compliance with cGMPs.

Accordingly, assuming we, or our future collaborators, receive marketing approval for one or more of our drug candidates, we, and our future collaborators, and our and their contract manufacturers will continue to expend time, money and effort in all areas of regulatory compliance, including manufacturing, production, product surveillance and quality control.

If we, and our future collaborators, are not able to comply with post-approval regulatory requirements, we, and our future collaborators, could have the marketing approvals for our drugs withdrawn by regulatory authorities and our, or our future collaborators', ability to market any future drugs could be limited, which could adversely affect our ability to achieve or sustain profitability. Further, the cost of compliance with post-approval regulations may have a negative effect on our operating results and financial condition.

Moreover, legislative and regulatory proposals have been made to expand post-approval requirements and restrict sales and promotional activities for pharmaceutical products. We cannot be sure whether additional legislative changes will be enacted, or whether the FDA regulations, guidance or interpretations will be changed, or what the impact of such changes on the marketing approvals of our drug candidates, if any, may be. In addition, increased scrutiny by the United States Congress of the FDA's approval process may significantly delay or prevent marketing approval, as well as subject us and any collaborators to more stringent product labeling and post-marketing testing and other requirements.

Any of our drug candidates for which we, or our future collaborators, obtain marketing approval in the future could be subject to post-marketing restrictions or withdrawal from the market and we, and our future collaborators, may be subject to substantial penalties if we, or they, fail to comply with regulatory requirements or if we, or they, experience unanticipated problems with our drugs following approval.

Any of our drug candidates for which we, or our future collaborators, obtain marketing approval in the future, as well as the manufacturing processes, post-approval studies and measures, labeling, advertising and promotional activities for such drug, among other things, will be subject to continual requirements of and review by the FDA and other regulatory authorities. These requirements include submissions of safety and other post-marketing information and reports, registration and listing requirements, requirements relating to manufacturing, quality control, quality assurance and corresponding maintenance of records and documents, requirements regarding the distribution of samples to physicians and recordkeeping. Even if marketing approval of a drug candidate is granted, the approval may be subject to limitations on the indicated uses for which the drug may be marketed or to the conditions of approval, including the requirement to implement a Risk Evaluation and Mitigation Strategy, which could include requirements for a restricted distribution system.

The FDA may also impose requirements for costly post-marketing studies or clinical trials and surveillance to monitor the safety or efficacy of a drug. The FDA and other agencies, including the Department of Justice, or the DOJ, closely regulate and monitor the post-approval marketing and promotion of drugs to ensure that they are manufactured, marketed and distributed only for the approved indications and in accordance with the provisions of the approved labeling. The FDA imposes stringent restrictions on manufacturers' communications regarding off-label use and if we, or our future collaborators, do not market any of our drug candidates for which we, or they, receive marketing approval for only their approved indications, we, or they, may be subject to warnings or enforcement action for off-label marketing. Violation of the FDCA and other statutes, including the False Claims Act, relating to the promotion and advertising of prescription drugs may lead to investigations or allegations of violations of federal and state health care fraud and abuse laws and state consumer protection laws.

In addition, later discovery of previously unknown adverse events or other problems with our drugs or their manufacturers or manufacturing processes, or failure to comply with regulatory requirements, may yield various results, including:

- litigation involving patients taking our drug;
- restrictions on such drugs, manufacturers or manufacturing processes;
- restrictions on the labeling or marketing of a drug;
- restrictions on drug distribution or use;
- requirements to conduct post-marketing studies or clinical trials;
- warning letters or untitled letters;
- withdrawal of the drugs from the market;
- refusal to approve pending applications or supplements to approved applications that we submit;
- recall of drugs;
- fines, restitution or disgorgement of profits or revenues;
- suspension or withdrawal of marketing approvals;
- damage to relationships with any potential collaborators;
- unfavorable press coverage and damage to our reputation;
- refusal to permit the import or export of drugs;
- drug seizure; or

- injunctions or the imposition of civil or criminal penalties.

We may not be able to obtain orphan drug exclusivity for applications of our TLR drug candidates.

Regulatory authorities in some jurisdictions, including the United States and Europe, may designate drugs for relatively small patient populations as orphan drugs. Under the Orphan Drug Act, the FDA may designate a product as an orphan drug if it is a drug intended to treat a rare disease or condition, which is generally defined as a patient population of fewer than 200,000 individuals in the United States.

Generally, if a product with an orphan drug designation subsequently receives the first marketing approval for the indication for which it has such designation, the product is entitled to a period of marketing exclusivity, which precludes the European Medicines Agency, or EMA, or the FDA from approving another marketing application for the same drug for the same indication for that exclusivity period. The applicable period is seven years in the United States and ten years in Europe. The European exclusivity period can be reduced to six years if a drug no longer meets the criteria for orphan drug designation or if the drug is sufficiently profitable such that market exclusivity is no longer justified. Orphan drug exclusivity may be lost if the FDA or EMA determines that the request for designation was materially defective or if the manufacturer is unable to assure sufficient quantity of the drug to meet the needs of patients with the rare disease or condition.

The FDA had granted us orphan drug designation for IMO-8400 for the treatment of Waldenström's macroglobulinemia and the treatment of DLBCL. However, there can be no assurance that we will obtain orphan drug designation or exclusivity for any other disease indications for which we develop IMO-8400, for IMO-2125, or for our other drug candidates. Even if we obtain orphan drug exclusivity for a product, that exclusivity may not effectively protect the product from competition because different drugs can be approved for the same condition. Even after an orphan drug is approved, the FDA can subsequently approve the same drug for the same condition if the FDA concludes that the later drug is clinically superior in that it is shown to be safer, more effective or makes a major contribution to patient care.

A fast track designation by the FDA may not actually lead to a faster development or regulatory review or approval process, and does not increase the likelihood that drug candidates will receive marketing approval.

We intend to seek fast track designation for some applications of our drug candidates. If a drug is intended for the treatment of a serious or life-threatening condition and the drug demonstrates the potential to address unmet medical needs for this condition, the drug sponsor may apply for FDA fast track designation. The FDA has broad discretion whether or not to grant this designation, so even if we believe a particular drug candidate is eligible for this designation, we cannot assure you that the FDA would decide to grant it. Even if we do receive fast track designation, we may not experience a faster development process, review or approval compared to conventional FDA procedures. The FDA may withdraw fast track designation if it believes that the designation is no longer supported by data from our clinical development program.

A breakthrough therapy designation by the FDA for any application of our drug candidates may not lead to a faster development or regulatory review or approval process, and it does not increase the likelihood that those drug candidates will receive marketing approval.

We may seek a breakthrough therapy designation for some applications of our drug candidates. A breakthrough therapy is defined as a drug that is intended, alone or in combination with one or more other drugs, to treat a serious or life-threatening disease or condition, and preliminary clinical evidence indicates that the drug may demonstrate substantial improvement over existing therapies on one or more clinically significant endpoints, such as substantial treatment effects observed early in clinical development. For drugs and biologics that have been designated as breakthrough therapies, interaction and communication between the FDA and the sponsor of the trial can help to identify the most efficient path for clinical development while minimizing the number of patients placed in ineffective control regimens. Drugs designated as breakthrough therapies by the FDA are also eligible for accelerated approval.

Designation as a breakthrough therapy is within the discretion of the FDA. Accordingly, even if we believe an application of one of our drug candidates meets the criteria for designation as a breakthrough therapy, the FDA may disagree and instead determine not to make such designation. In any event, the receipt of a breakthrough therapy designation for a drug candidate may not result in a faster development process, review or approval compared to drugs

considered for approval under conventional FDA procedures and does not assure ultimate approval by the FDA. In addition, even if one or more of our drug candidates qualify as breakthrough therapies, the FDA may later decide that the products no longer meet the conditions for qualification or decide that the time period for FDA review or approval will not be shortened.

If we are required by the FDA to obtain approval of a companion diagnostic in connection with and as a condition to approval of a drug candidate, and we do not obtain or we experience delays in obtaining FDA approval of a diagnostic device, we will not be able to commercialize the drug candidate and our ability to generate revenue will be materially impaired.

According to FDA guidance, if the FDA determines that a companion diagnostic device is essential to the safe and effective use of a novel therapeutic product or indication, the FDA generally will not approve the therapeutic product or new therapeutic product indication if the companion diagnostic is not also approved or cleared for that indication. Under the Federal Food, Drug, and Cosmetic Act, companion diagnostics are regulated as medical devices and the FDA has generally required companion diagnostics intended to select the patients who will respond to cancer treatment to obtain Premarket Approval, or a PMA. The PMA process, including the gathering of clinical and preclinical data and the submission to and review by the FDA, involves a rigorous premarket review during which the applicant must prepare and provide the FDA with reasonable assurance of the device's safety and effectiveness and information about the device and its components regarding, among other things, device design, manufacturing and labeling. PMA approval is not guaranteed and may take considerable time, and the FDA may ultimately respond to a PMA submission with a not approvable determination based on deficiencies in the application and require additional clinical trial or other data that may be expensive and time-consuming to generate and that can substantially delay approval.

We do not have experience or capabilities in developing or commercializing diagnostics and plan to rely on third parties or collaborators to perform these functions. Companion diagnostics are subject to regulation by the FDA and similar regulatory authorities outside the United States as medical devices and require separate regulatory approval prior to commercialization.

If we, any third parties that we engage to assist us or any of our collaborators are unable to successfully develop companion diagnostics for our TLR antagonist drug candidates, or experience delays in doing so:

- the development of our TLR antagonist drug candidates may be adversely affected if we are unable to appropriately select patients for enrollment in our clinical trials;
- our TLR antagonist drug candidates may not receive marketing approval if their safe and effective use depends on a companion diagnostic; and
- we may not realize the full commercial potential of any TLR antagonist drug candidates that receive marketing approval if, among other reasons, we are unable to appropriately identify patients with the specific oncogenic mutation targeted by our TLR antagonist drug candidates.

If any of these events were to occur, our business would be harmed, possibly materially.

We have only limited experience in regulatory affairs and our drug candidates 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 obtain 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.

Our relationships with healthcare providers and physicians and third-party payors will be subject to applicable anti-kickback, fraud and abuse and other healthcare laws and regulations, which could expose us to criminal sanctions, civil penalties, contractual damages, reputational harm and diminished profits and future earnings.

Healthcare providers, physicians and third party payors will play a primary role in the recommendation and prescription of any drugs for which we obtain marketing approval. Our future arrangements with third party payors, healthcare providers and physicians may expose us to broadly applicable fraud and abuse and other healthcare laws and regulations that may constrain the business or financial arrangements and relationships through which we market, sell and distribute any drugs for which we obtain marketing approval. These include the following:

- Anti-Kickback Statute—the federal healthcare anti-kickback statute prohibits, among other things, persons from knowingly and willfully soliciting, offering, receiving or providing remuneration, directly or indirectly, in cash or in kind, to induce or reward, or in return for, either the referral of an individual for, or the purchase, order or recommendation or arranging of, any good or service, for which payment may be made under a federal healthcare program such as Medicare and Medicaid;
- False Claims Act—the federal False Claims Act imposes criminal and civil penalties, including through civil whistleblower or qui tam actions, against individuals or entities for, among other things, knowingly presenting, or causing to be presented false or fraudulent claims for payment by a federal healthcare program or making a false statement or record material to payment of a false claim or avoiding, decreasing or concealing an obligation to pay money to the federal government, with potential liability including mandatory treble damages and significant per-claim penalties, currently set at $5,500 to $11,000 per false claim;
- HIPAA—the federal Health Insurance Portability and Accountability Act of 1996, or HIPAA, imposes criminal and civil liability for executing a scheme to defraud any healthcare benefit program or making false statements relating to healthcare matters, and, as amended by the Health Information Technology for Economic and Clinical Health Act and its implementing regulations, also imposes obligations, including mandatory contractual terms and technical safeguards, with respect to maintaining the privacy, security and transmission of individually identifiable health information;
- Transparency Requirements—federal laws require applicable manufacturers of covered drugs to report payments and other transfers of value to physicians and teaching hospitals; and
- Analogous State and Foreign Laws—analogous state and foreign fraud and abuse laws and regulations, such as state anti-kickback and false claims laws, can apply to sales or marketing arrangements and claims involving healthcare items or services and are generally broad and are enforced by many different federal and state agencies as well as through private actions.

Some state laws require pharmaceutical companies to comply with the pharmaceutical industry's voluntary compliance guidelines and the relevant compliance guidance promulgated by the federal government and require drug manufacturers to report information related to payments and other transfers of value to physicians and other healthcare providers or marketing expenditures. State and foreign laws also govern the privacy and security of health information in some circumstances, many of which differ from each other in significant ways and often are not pre-empted by HIPAA, thus complicating compliance efforts.

Efforts to ensure that our business arrangements with third parties will comply with applicable healthcare laws and regulations will involve substantial costs. It is possible that governmental authorities will conclude that our business practices may not comply with current or future statutes, regulations or case law involving applicable fraud and abuse or other healthcare laws and regulations. If our operations are found to be in violation of any of these laws or any other governmental regulations that may apply to us, we may be subject to significant civil, criminal and administrative penalties, damages, fines, imprisonment, exclusion of products from government funded healthcare programs, such as Medicare and Medicaid, and the curtailment or restructuring of our operations. If any of the physicians or other healthcare providers or entities with whom we expect to do business is found to be not in compliance with applicable laws, they may be subject to criminal, civil or administrative sanctions, including exclusions from government funded healthcare programs.

Current and future legislation may increase the difficulty and cost for us and any collaborators to obtain marketing approval of our drug candidates and affect the prices we, or they, may obtain.

In the United States and some foreign jurisdictions, there have been a number of legislative and regulatory changes and proposed changes regarding the healthcare system that could, among other things, prevent or delay marketing approval of our drug candidates, restrict or regulate post-approval activities and affect our ability, or the ability of any collaborators, to profitably sell any products for which we, or they, obtain marketing approval. We expect that current laws, as well as other healthcare reform measures that may be adopted in the future, may result in more rigorous coverage criteria and in additional downward pressure on the price that we, or any collaborators, may receive for any approved products.

For example, in March 2010, President Obama signed into law the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Affordability Reconciliation Act, or collectively the PPACA. Among the provisions of the PPACA of potential importance to our business and our drug candidates are the following:

- an annual, non-deductible fee on any entity that manufactures or imports specified branded prescription products and biologic agents;
- an increase in the statutory minimum rebates a manufacturer must pay under the Medicaid Drug Rebate Program;
- a new methodology by which rebates owed by manufacturers under the Medicaid Drug Rebate Program are calculated for products that are inhaled, infused, instilled, implanted or injected;
- expansion of healthcare fraud and abuse laws, including the civil False Claims Act and the federal Anti-Kickback Statute, new government investigative powers and enhanced penalties for noncompliance;
- a new Medicare Part D coverage gap discount program, in which manufacturers must agree to offer 50% point-of-sale discounts off negotiated prices of applicable brand products to eligible beneficiaries during their coverage gap period, as a condition for the manufacturer's outpatient products to be covered under Medicare Part D;
- extension of manufacturers' Medicaid rebate liability to individuals enrolled in Medicaid managed care organizations;
- expansion of eligibility criteria for Medicaid programs;
- expansion of the entities eligible for discounts under the Public Health Service pharmaceutical pricing program;
- new requirements to report certain financial arrangements with physicians and teaching hospitals;
- a new requirement to annually report product samples that manufacturers and distributors provide to physicians;
- a new Patient-Centered Outcomes Research Institute to oversee, identify priorities in, and conduct comparative clinical effectiveness research, along with funding for such research;
- a new Independent Payment Advisory Board, which has authority to recommend certain changes to the Medicare program to reduce expenditures by the program that could result in reduced payments for prescription products; and
- established the Center for Medicare and Medicaid Innovation within the Centers for Medicare & Medicaid Services to test innovative payment and service delivery models.

With the new Administration and Congress, there will likely be additional legislative changes, including repeal and replacement of certain provisions of the Affordable Care Act. To that end, on January 20, 2017, the President issued an Executive Order Minimizing the Economic Burden of the Patient Protection and Affordable Care Act Pending Repeal. The Executive Order declares that, pending repeal of the Affordable Care Act, it is imperative for the executive branch to ensure that the law is being efficiently implemented, take all actions consistent with law to minimize the unwarranted economic and regulatory burdens of the Act, and prepare to afford the States more flexibility and control to create a more free and open healthcare market. The Order directs the Secretary of Health and Human Services and the heads of all other

executive departments and agencies with authorities and responsibilities under the Affordable Care Act to exercise their authority and discretion to waive, defer, grant exemptions from, or delay the implementation of any provision or requirement of the Affordable Care Act that would impose a fiscal burden on any State or a cost, fee, tax, penalty, or regulatory burden on individuals, families, healthcare providers, health insurers, patients, recipients of healthcare services, purchasers of health insurance, or makers of medical devices, products, or medications.

With respect to repeal of the Affordable Care Act and its replacement with new legislation, it is unclear when such legislation will be enacted, what it will provide and what impact it will have on the availability of healthcare and containing or lowering the costs of healthcare. At this point, it remains unclear how a repeal or replacements of these programs might affect the prices we, or our collaborators, may obtain for any of our drug candidates for which marketing approval is obtained.

Laws and regulations governing any international operations we may have in the future may preclude us from developing, manufacturing and selling certain drug candidates outside of the United States and require us to develop and implement costly compliance programs.

We are subject to numerous laws and regulations in each jurisdiction outside the United States in which we operate. The creation, implementation and maintenance of international business practices compliance programs is costly and such programs are difficult to enforce, particularly where reliance on third parties is required.

The FCPA prohibits any U.S. individual or business from paying, offering, authorizing payment or offering of anything of value, directly or indirectly, to any foreign official, political party or candidate for the purpose of influencing any act or decision of the foreign entity in order to assist the individual or business in obtaining or retaining business. The FCPA also obligates companies whose securities are listed in the United States to comply with certain accounting provisions requiring the company to maintain books and records that accurately and fairly reflect all transactions of the corporation, including international subsidiaries, and to devise and maintain an adequate system of internal accounting controls for international operations. The anti-bribery provisions of the FCPA are enforced primarily by the DOJ. The Securities and Exchange Commission, or SEC, is involved with enforcement of the books and records provisions of the FCPA.

Compliance with the FCPA is expensive and difficult, particularly in countries in which corruption is a recognized problem. In addition, the FCPA presents particular challenges in the pharmaceutical industry, because, in many countries, hospitals are operated by the government, and doctors and other hospital employees are considered foreign officials. Certain payments to hospitals in connection with clinical trials and other work have been deemed to be improper payments to government officials and have led to FCPA enforcement actions.

Various laws, regulations and executive orders also restrict the use and dissemination outside of the United States, or the sharing with certain non-U.S. nationals, of information classified for national security purposes, as well as certain products and technical data relating to those products. Our expansion outside of the United States, has required, and will continue to require, us to dedicate additional resources to comply with these laws, and these laws may preclude us from developing, manufacturing, or selling certain drugs and drug candidates outside of the United States, which could limit our growth potential and increase our development costs. The failure to comply with laws governing international business practices may result in substantial penalties, including suspension or debarment from government contracting. Violation of the FCPA can result in significant civil and criminal penalties. Indictment alone under the FCPA can lead to suspension of the right to do business with the U.S. government until the pending claims are resolved. Conviction of a violation of the FCPA can result in long-term disqualification as a government contractor. The termination of a government contract or relationship as a result of our failure to satisfy any of our obligations under laws governing international business practices would have a negative impact on our operations and harm our reputation and ability to procure government contracts. The SEC also may suspend or bar issuers from trading securities on U.S. exchanges for violations of the FCPA's accounting provisions.

Governments outside of the United States tend to impose strict price controls, which may adversely affect our revenues from the sales of drugs, if any.

In some 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 considerable time after the receipt of marketing approval for a drug. To obtain reimbursement or pricing approval in some

countries, we, or our future collaborators, may be required to conduct a clinical trial that compares the cost-effectiveness of our drug to other available therapies. If reimbursement of our drugs is unavailable or limited in scope or amount, or if pricing is set at unsatisfactory levels, our business could be materially harmed.

If we fail to comply with environmental, health and safety laws and regulations, we could become subject to fines or penalties or incur costs that could have a material adverse effect on our business.

We are subject to numerous environmental, health and safety laws and regulations, including those governing laboratory procedures and the handling, use, storage, treatment and disposal of hazardous materials and wastes. Our operations involve the use of hazardous and flammable materials, including chemicals and biological and radioactive materials. Our operations also produce hazardous waste products. We generally contract with third parties for the disposal of these materials and wastes. We cannot eliminate the risk of contamination or injury from these materials. In the event of contamination or injury resulting from our use of hazardous materials, we could be held liable for any resulting damages, and any liability could exceed our resources. We also could incur significant costs associated with civil or criminal fines and penalties.

Although we maintain workers' compensation insurance to cover us for costs and expenses we may incur due to injuries to our employees resulting from the use of hazardous materials, this insurance may not provide adequate coverage against potential liabilities. We do not maintain insurance for environmental liability or toxic tort claims that may be asserted against us in connection with our storage or disposal of biological, hazardous or radioactive materials.

In addition, we may incur substantial costs in order to comply with current or future environmental, health and safety laws and regulations. These current or future laws and regulations may impair our research, development or commercialization efforts. Failure to comply with these laws and regulations also may result in substantial fines, penalties or other sanctions.

Our employees may engage in misconduct or other improper activities, including non-compliance with regulatory standards and requirements, which could cause significant liability for us and harm our reputation.

We are exposed to the risk of employee fraud or other misconduct, including intentional failures to comply with FDA regulations or similar regulations of comparable foreign regulatory authorities, provide accurate information to the FDA or comparable foreign regulatory authorities, comply with manufacturing standards we have established, comply with federal and state healthcare fraud and abuse laws and regulations and similar laws and regulations established and enforced by comparable foreign regulatory authorities, report financial information or data accurately or disclose unauthorized activities to us. Employee misconduct could also involve the improper use of information obtained in the course of clinical trials, which could result in regulatory sanctions and serious harm to our reputation. It is not always possible to identify and deter employee misconduct, and the precautions we take to detect and prevent this activity may not be effective in controlling unknown or unmanaged risks or losses or in protecting us from governmental investigations or other actions or lawsuits stemming from a failure to be in compliance with such laws, standards or regulations. If any such actions are instituted against us, and we are not successful in defending ourselves or asserting our rights, those actions could have a significant impact on our business and results of operations, including the imposition of significant fines or other sanctions.

Risks Relating to Collaborators

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

Historically, an important element of our business strategy has included 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 2006, we entered into an exclusive license and research collaboration with Merck & Co. to research, develop, and commercialize vaccine products containing our TLR7, TLR8 and TLR9 agonists in the fields of cancer, infectious diseases, and Alzheimer's disease. In November 2015, we entered into a collaboration and license agreement with GSK for the development of our 3GA technology for certain renal indications and in November 2016, we entered into a license agreement with Vivelix granting them exclusive rights for the development of IMO-9200 for non-malignant indication of the GI tract.

Any collaboration 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. Our existing collaborations and any potential future collaborations have risks, including the following:

- our collaborators may control the development of the drug candidates being developed with our technologies and compounds including the timing of development;
- our collaborators may control the development of the companion diagnostic to be developed for use in conjunction with our drug candidates 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 or right to use technology and intellectual property 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 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;
- our collaborators may not comply with all applicable regulatory requirements, or may fail to report safety data in accordance with all applicable regulatory requirements;
- 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. For example, we have a strategic collaboration with Merck & Co., which merged with Schering-Plough Corporation, which has been involved with certain TLR-targeted research and development programs. Although the merger has not affected our collaboration with Merck & Co. to date, management of the combined company could determine to reduce the efforts and resources that the combined company will apply to its strategic collaboration with us or terminate the strategic collaboration. The ability of our drug candidates to reach their potential could be limited if our collaborators decrease or fail to increase spending relating to such drug candidates;
- our collaborators may under fund or not commit sufficient resources to the testing, marketing, distribution or development of our drug candidates; 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.

Given these risks, it is possible that any collaborative alliance into which we enter may not be successful. Collaborations with pharmaceutical companies and other third parties often are terminated or allowed to expire by the other party. The termination or expiration of our agreement with Vivelix, GSK, or Merck & Co. or any other collaboration agreement that we enter into in the future may adversely affect us financially and could harm our business reputation.

If we are unable to establish additional collaborative alliances, our business may be materially harmed.

Collaborators provide the necessary resources and drug development experience to advance our compounds in their programs. We have entered into and expect to continue to seek to enter into collaborative alliances with pharmaceutical companies to advance our TLR agonist and antagonist candidates and with respect to additional applications of our 3GA technology program. 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 certain rare diseases and in our immuno-oncology program and on 3GA drug candidates. We believe that additional resources will be required to advance compounds in all of these areas. If we do not reach agreements with additional collaborators in the future, we may not be able to obtain the expertise and resources necessary to achieve our business objectives, our ability to advance our compounds will be jeopardized and we may fail to meet our business objectives.

We may have difficulty establishing additional collaborative alliances, particularly with respect to our TLR-targeted drug candidates and technology and our 3GA technology. For example, potential collaborators may note that our prior TLR collaborations with Novartis and with Merck KGaA have been terminated. Potential collaborators may also be reluctant to establish collaborations with respect to IMO-2125 or IMO-8400, given our setbacks with respect to these drug candidates. We also face, and expect to continue to face, significant competition in seeking appropriate collaborators.

Even if a potential partner were willing to enter into a collaborative alliance with respect to our TLR-targeted compounds or technology or our 3GA technology, the terms of such a collaborative alliance may not be on terms that are favorable to us. 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 on a timely basis.

Risks Relating to Intellectual Property

If we are unable to obtain and maintain 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 and maintain valid and enforceable 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 our trade secrets.

We do not know whether any of our currently pending 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, held unenforceable, narrowed in the course of a post-issuance proceeding or circumvented, and the rights granted thereunder may not provide us proprietary protection or competitive advantages against competitors with similar technology. Moreover, intellectual property laws may change and negatively impact our ability to obtain issued patents covering our technologies or to enforce any patents that issue. 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.

As of February 15, 2017, we owned more than 45 U.S. patents and patent applications and more than 80 patents and patent applications throughout the rest of the world for our TLR-targeted immune modulation technologies. These patents and patent applications include claims covering the chemical compositions of matter and methods of use of our IMO compounds, such as IMO-8400, IMO-9200 and IMO-2125, as well as other compounds. These patents expire at various dates ranging from 2023 to 2034. With respect to IMO-8400, we have three issued U.S. patents that cover the chemical composition of matter of IMO-8400 and certain methods of its use that have an earliest statutory expiration date in 2031. With respect to IMO-9200, we have one issued U.S. patent and two U.S. patent applications that cover the chemical composition for IMO-9200 and methods of its use that will expire in 2034. With respect to IMO-2125, we have an issued U.S. patent that covers the chemical composition of matter of IMO-2125 and methods of its use that will expire in 2025.

As of February 15, 2017, we owned two issued U.S. patents, 21 issued foreign patents, seven pending U.S. patent applications and 12 foreign patent applications related to our 3GA technology and methods of its use. The issued patents covering our 3GA technologies have earliest statutory expiration dates in 2030.

In addition to our TLR-targeted and 3GA patent portfolios, we are the owner of or hold licenses to patents and patent applications related to antisense technology. As of February 15, 2017, our antisense patent portfolio includes four U.S. patents. 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 in-licensed patents expire at various dates through 2021.

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.

Although we have many issued patents and pending patent applications in the United States and other countries, we may not have rights under certain third-party patents or patent applications related to our compounds under development. Third parties may own or control these patents and patent applications in the United States and abroad. In particular, we are aware of certain third-party U.S. patents that contain claims related to immunostimulatory polynucleotides and their use to stimulate an immune response, as well as to antisense technology. Although we do not believe any of our TLR or antisense compounds under development infringe any valid claim of these patents, we cannot be assured that the holder of such patents would not seek to assert such patents against us or, if the holder did, that the courts would not interpret the claims of such patents more broadly than we believe appropriate and determine that we are in infringement of such patents. In addition, there may be other patents and patent applications related to our current or future drug candidates of which we are not aware. Therefore, in some cases, in order to develop, manufacture, sell or import some of our drug candidates, 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 third-party patents that might issue from U.S. 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, or may be delayed in doing so. Either of these results could have a material adverse effect on our business.

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, require us to stop our development and commercialization efforts or result in our patents being invalidated, interpreted narrowly or limited.

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.

In addition to litigation, we may become involved in patent office proceedings, including oppositions, reexaminations, supplemental examinations and inter partes reviews involving our patents or the patents of third parties.

We may initiate such proceedings or have such proceedings brought against us. An adverse determination in any such proceeding, or in litigation, could reduce the scope of, or invalidate, our patent rights, allow third parties to commercialize our technology or products and compete directly with us, without payment to us, or result in our inability to manufacture or commercialize products without infringing third-party patent rights. In addition, if the breadth or strength of protection provided by our patents and patent applications is threatened, it could dissuade companies from collaborating with us to license, develop or commercialize current or future drug candidates. An adverse determination in a proceeding involving a patent in our portfolio could result in the loss of protection or a narrowing in the scope of protection provided by that patent.

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. In a patent office proceeding, such as an opposition, reexamination or inter partes review, our patents may be narrowed or invalidated.

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, and no manufacturing facilities or infrastructure, we are dependent on third-party manufacturers to manufacture drug candidates 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 drug candidates, 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 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 drug candidates, if approved. 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.

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

Reliance on third-party manufacturers entails risks to which we would not be subject if we manufactured drug candidates 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 or otherwise, 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 drug candidates that becomes necessary for the manufacture of our drug candidates; and
- reliance upon third-party manufacturers to assist us in preventing inadvertent disclosure or theft of our proprietary knowledge.

Any contract manufacturers with which we enter into manufacturing arrangements will be subject to ongoing periodic, unannounced inspections by the FDA, or foreign equivalent, and corresponding state and foreign agencies or their designees to ensure compliance with cGMP requirements and other governmental regulations and corresponding foreign standards. Any failure by our third-party manufacturers to comply with such requirements, regulations or standards could lead to a delay in the conduct of our clinical trials, or a delay in, or failure to obtain, regulatory approval of any of our drug candidates. Such failure could also result in sanctions being imposed, including fines, injunctions, civil penalties, delays, suspension or withdrawal of approvals, product seizures or recalls, imposition of operating restrictions, total or partial suspension of production or distribution, or criminal prosecution.

Additionally, contract manufacturers may not be able to manufacture our drug candidates at a cost or in quantities necessary to make them commercially viable. As of February 15, 2017, 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 substance or drug product is manufactured or a change of a third-party manufacturer, may require prior FDA review and approval in accordance with the FDA's cGMP and New Drug Application/biologics license application regulations. Contract manufacturers may also be subject to comparable foreign requirements. This review may be costly and time-consuming and could delay or prevent the launch of a drug candidate. 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 drug candidates, 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 drug candidates 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 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 drug candidates and our business may suffer.

We do not have the ability to independently conduct the clinical trials required to obtain regulatory approval for our drug candidates. We depend on independent clinical investigators, contract research organizations, and other third-party service providers in the conduct of the clinical trials of our drug candidates and expect to continue to do so. We have contracted with contract research organizations to manage our ongoing Phase 2 clinical trial of IMO-8400 in patients with dermatomyositis, and our Phase 1/2 clinical trial of IMO-2125, administered intra-tumorally, in combination with ipilimumab or pembrolizumab, in patients with metastatic melanoma and expect to contract with such organizations for future clinical trials. 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 and foreign regulatory agencies require us to comply with certain standards, commonly referred to as good clinical practices, and applicable regulatory requirements, for conducting, recording, and reporting the results of 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 at all, or may not conduct our clinical trials in accordance with regulatory requirements

or our stated protocols. If these third parties fail to carry out their obligations, we may need to enter into new arrangements with alternative third parties. This could be difficult, costly or impossible, and our preclinical studies or clinical trials may need to be extended, delayed, terminated or repeated, and we may not be able to obtain regulatory approval in a timely fashion, or at all, for the applicable drug candidate, or to commercialize such drug candidate being tested in such studies or trials. 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 research, clinical, quality and corporate 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 or others in the medical community. For example, current cancer treatments like chemotherapy and radiation therapy are well established in the medical community, and doctors may continue to rely on these treatments. If our products do not achieve an adequate level of acceptance, we may not generate product revenue and we may not become profitable. The degree of market acceptance of our products, 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 patients, 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, Improvement, and Modernization Act of 2003. While the program established by this statute may increase demand for our products if we were to 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 or may otherwise negotiate the price they are willing to pay.

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 drug candidates. 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.

In March 2010, the Patient Protection and Affordable Care Act and the Health Care and Education Reconciliation Act became law. These health care reform laws are intended to broaden access to health insurance; reduce or constrain the growth of health care spending, especially Medicare spending; enhance remedies against fraud and abuse; add new transparency requirements for health care and health insurance industries; impose new taxes and fees on certain sectors of the health industry; and impose additional health policy reforms. Among the new fees is an annual assessment on makers of branded pharmaceuticals and biologics, under which a company's assessment is based primarily on its share of branded drug sales to federal health care programs. Such fees could affect our future prospects for profitability. Although it is too early to determine the effect of the health care legislation on our future prospects for profitability and financial condition, the law appears likely to continue the pressure on pharmaceutical pricing, especially under the Medicare program, and may also increase our regulatory burdens and operating costs.

Third-party payors are challenging the prices charged for medical products and services, and many third-party payors limit reimbursement for newly-approved health care products. These third-party payors may base their coverage and reimbursement on the coverage and reimbursement rate paid by carriers for Medicare beneficiaries. Furthermore, many such payors are investigating or implementing methods for reducing health care costs, such as the establishment of capitated or prospective payment systems. Cost containment pressures have led to an increased emphasis on the use of cost-effective products by health care providers. 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 limit the price we might establish for products that we or our current or future collaborators may develop or sell, which would result in lower product revenues or royalties payable 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 Ownership of Our Common Stock

Our corporate governance structure, including provisions in our certificate of incorporation and by-laws 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 and by-laws 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.

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.

We have two significant securityholders. If these securityholders choose to act together, they could exert substantial influence over our business. In addition, in connection with any merger, consolidation or sale of all or substantially all of our assets, they would be entitled to receive consideration in excess of their reported beneficial ownership of our common stock.

As of February 15, 2017, Baker Bros. Advisors LP, and certain of its affiliated funds, which we refer to collectively as Baker Brothers, held 10,286,483 shares of our common stock, warrants to purchase up to 20,316,327 shares of our common stock at an exercise price of $0.47 per share and pre-funded warrants to purchase up to 22,151,052 shares of our common stock at an exercise price of $0.01 per share. In addition, two members of our board of directors are affiliates of Baker Brothers. Under the terms of the warrants and pre-funded warrants issued to Baker Brothers, Baker Brothers is not permitted to exercise such warrants to the extent that such exercise would result in Baker Brothers (and its affiliates) beneficially owning more than 4.999% of the number of shares of our common stock outstanding immediately after giving effect to the issuance of shares of common stock issuable upon exercise of such warrants. Baker Brothers has the right to increase this beneficial ownership limitation in its discretion on 61 days' prior written notice to us, provided that in no event is Baker Brothers permitted to exercise such warrants to the extent that such exercise would result in Baker Brothers (and its affiliates) beneficially owning more than 19.99% of the number of shares of our common stock outstanding or the combined voting power of our securities outstanding immediately after giving effect to the issuance of shares of common stock issuable upon exercise of such warrants. After giving effect to the 4.999% beneficial ownership limitation currently in effect with respect to the warrants and pre-funded warrants held by Baker Brothers, as of February 15, 2017, Baker Brothers beneficially owned 7.1% of our outstanding common stock. If the warrants and pre-funded warrants held by Baker Brothers could be exercised without this limitation, then as of February 15, 2017, Baker Brothers would have beneficially owned 27.6% of our common stock. The information in this paragraph is based on a Schedule 13G filed with the SEC on February 16, 2016 and a Schedule 13D filed with the SEC on October 11, 2016, on Form 4s filed with the SEC on April 5, 2016, July 6, 2016, October 11, 2016 and January 5, 2017 and on information provided to us by Baker Brothers. On February 9, 2015, we entered into a registration rights agreement with Baker Brothers, pursuant to which we agreed to file registration statements to register for resale the shares of our common stock, including shares issuable upon the exercise of warrants, held by Baker Brothers. We filed a registration statement under this agreement in the first quarter of 2016.

As of February 15, 2017, entities affiliated with Pillar Invest Corporation, which we refer to collectively as the Pillar Investment Entities, held 21,724,158 shares of our common stock and warrants to purchase up to 9,152,081 shares of our common stock at exercise prices ranging from $0.47 per share to $0.70 per share. In addition, one member of our board of directors is an affiliate of the Pillar Investment Entities. As of February 15, 2017, the Pillar Investment Entities beneficially owned 19.6% of our outstanding common stock. The Pillar Investment Entities are subject to contractual limitations that limit their ability to exercise any securities held by them that are exercisable into shares of our common stock to the extent that such exercise would result in the Pillar Investment Entities and their affiliates beneficially owning more than 19.99% of the number of shares of our common stock outstanding or the combined voting power of our securities outstanding immediately after giving effect to the issuance of shares of common stock issuable upon exercise of such securities. The information in this paragraph is based on information provided to us by the Pillar Investment Entities and on Form 4s filed with the SEC on November 7, 2016 and January 5, 2017, a Form 3 filed with the SEC on October 12, 2016 and a Schedule 13D/A filed with the SEC on October 17, 2016.

Although there are contractual limitations on the beneficial ownership of Baker Brothers and the Pillar Investment Entities, which we refer to collectively as our significant securityholders, if our significant securityholders were to exercise their warrants for common stock and were to choose to act together, they could be able to exert substantial influence over our business. This concentration of voting power could delay, defer or prevent a change of control, entrench our management and the board of directors or delay or prevent a merger, consolidation, takeover or other business combination involving us on terms that other stockholders may desire. In addition, conflicts of interest could arise in the future between us, on the one hand, and either or both of our significant securityholders on the other hand, concerning potential competitive business activities, business opportunities, the issuance of additional securities and other matters. Furthermore in the event of a sale of our company, whether by merger, sale of all or substantially all of our assets or otherwise, our significant securityholders would be entitled to receive, with respect to each share of common stock issuable upon exercise of the warrants then held by them and without regard to the beneficial ownership limitations imposed on the conversion or exercise of such securities, the same amount and kind of securities, cash or property as they would have been entitled to receive if such securities had been converted into or exercised for shares of our common stock immediately prior to such sale of our company. Because the significant securityholders would receive this sale consideration with respect to warrants not included in their reported beneficial ownership of our common stock, in the event of a sale of our company, they would be entitled to receive a significantly larger portion of the total proceeds distributable to the holders of our securities than is represented by their reported beneficial ownership of our common stock.

Our stock price has been and may in the future be extremely volatile. In addition, because our common stock has historically been traded at low volume levels, 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 and may in the future be volatile. During the period from January 1, 2016 to February 15, 2017, the closing sales price of our common stock ranged from a high of $3.00 per share to a low of $1.32 per share. The stock market has also experienced periods of significant price and volume fluctuations 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:

- our cash resources;
- timing and results of nonclinical studies and 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;

- our ability to maintain the listing of our common stock on The Nasdaq Capital Market or an alternative national securities exchange;
- variations in our financial results or those of companies that are perceived to be similar to us;
- the terms of any financing consummated 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.

Because we do not intend to pay dividends on our common stock, investor returns will be limited to any increase in the value of our stock.

We have never declared or paid any cash dividends on our common stock. In addition, under the terms of our loan and security agreement with Oxford Finance LLC, we are required to obtain the prior written consent of Oxford Finance LLC in order to declare or pay a cash dividend on our common stock in an amount in excess of $500,000 in any fiscal year. We currently intend to retain all available funds and any future earnings to support our operations and finance the growth and development of our business and do not anticipate declaring or paying any cash dividends on our common stock for the foreseeable future. Any return to stockholders will therefore be limited to the appreciation of their stock, if any.

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

None.

Item 2. ***Properties.***

We lease approximately 27,000 square feet of laboratory and office space located in Cambridge, Massachusetts. The lease expires on August 31, 2022 subject to a five-year renewal option exercisable by us. We also lease approximately 11,000 square feet of office space located in Exton, Pennsylvania. The lease expires on May 31, 2020 subject to a three-year renewal option exercisable by us. We have specified rights to sublease these facilities.

Item 3. ***Legal Proceedings.***

None.

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

Not applicable.

PART II.

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

Market Information

Our common stock is listed under the symbol "IDRA" on the Nasdaq Capital Market.

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 Capital Market.

	High	Low
2015		
First Quarter	$ 5.48	$ 3.25
Second Quarter	3.92	2.65
Third Quarter	4.16	2.27
Fourth Quarter	4.42	2.65
2016		
First Quarter	$ 3.10	$ 1.50
Second Quarter	2.14	1.19
Third Quarter	3.33	1.52
Fourth Quarter	2.66	1.43

Holders

As of February 15, 2017, we had approximately 98 common stockholders of record registered on our books, excluding shares held through banks and brokers.

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. Under the terms of our loan and security agreement with Oxford Finance LLC, we are required to obtain the prior written consent of Oxford Finance LLC in order to declare or pay a cash dividend on our common stock in an amount in excess of $500,000 in any fiscal year.

Recent Sales of Unregistered Securities

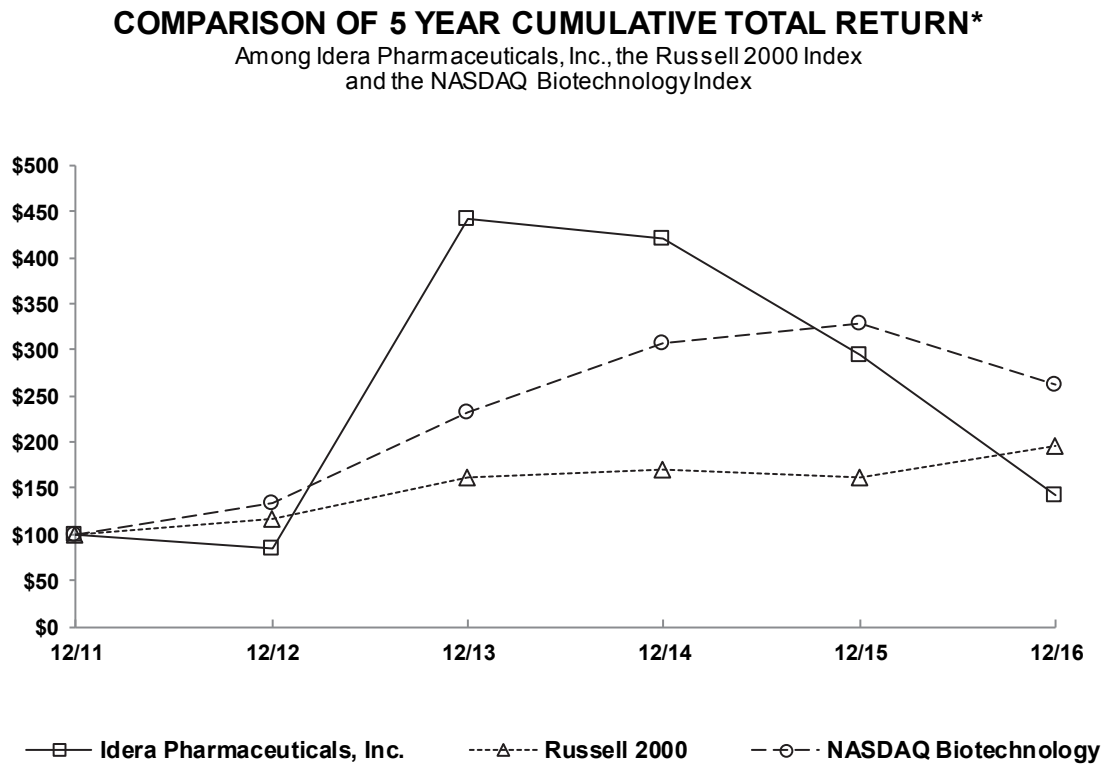
In November 2016, we issued 1,370,000 shares of our common stock in unregistered sales to holders of warrants upon the exercise of such warrants. We issued the 1,370,000 shares upon the payment of a warrant exercise price of $1.46 per share. We received approximately $2.0 million of cash proceeds in the aggregate upon the exercise of the foregoing warrants.

The issuance of shares of our common stock upon exercise of outstanding warrants described above were exempt from registration under the Securities Act of 1933, as amended, and Rule 506 of Regulation D promulgated thereunder as not involving a public offering. The shares of common stock issued by us upon these warrant exercises have been registered for resale by the holders under our Registration Statement on Form S-3, File No. 333-178405.

Comparative Stock Performance

The information included under the heading "Comparative Stock Performance" in Item 5 of this Annual Report on Form 10-K is "furnished" and not "filed" and shall not be deemed to be "soliciting material" or subject to Regulation 14A, shall not be deemed "filed" for purposes of Section 18 of the Exchange Act or otherwise subject to the liabilities of that section, nor shall it be deemed incorporated by reference in any filing under the Securities Act of 1933, as amended, or the Securities Act, or the Exchange Act.

The comparative stock performance graph shown below compares cumulative stockholder return on our common stock from December 31, 2011 through December 31, 2016, with the cumulative total return of the Russell 2000 Index and the Nasdaq Biotechnology Index. This graph assumes an investment of $100 on December 31, 2011 in our common stock and in each of the indices and assumes that dividends are reinvested.



	12/31/11	12/31/12	12/31/13	12/31/14	12/31/15	12/31/16
IDERA PHARMACEUTICALS, INC.	$ 100.00	$ 84.76	$ 440.95	$ 420.00	$ 294.29	$ 142.86
RUSSELL 2000 INDEX	$ 100.00	$ 116.35	$ 161.52	$ 169.43	$ 161.95	$ 196.45
NASDAQ BIOTECHNOLOGY INDEX	$ 100.00	$ 134.68	$ 232.37	$ 307.67	$ 328.76	$ 262.08

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 elsewhere in this Annual Report on Form 10-K.

	Year Ended December 31,				
	2016	2015	2014	2013	2012
	(In thousands, except per share data)				
Statement of Operations and Comprehensive Loss Data:					
Alliance revenue	$ 16,199	$ 249	$ 73	$ 47	$ 51
Operating expenses:					
Research and development	39,824	33,699	27,493	10,475	13,673
General and administrative	15,132	15,396	11,332	7,741	6,279
Total operating expenses	54,956	49,095	38,825	18,216	19,952
Loss from operations	(38,757)	(48,846)	(38,752)	(18,169)	(19,901)
Other income (expense):					
Decrease in fair value of warrant liability	—	—	—	—	675
Interest income	415	357	66	11	9
Interest expense	(80)	(105)	(27)	—	—
Foreign currency exchange gain (loss)	33	39	71	(68)	(23)
Net loss before extinguishment of convertible preferred stock, and preferred stock accretion and dividends	$ (38,389)	$ (48,555)	$ (38,642)	$ (18,226)	$ (19,240)
Loss on extinguishment of convertible preferred stock, and preferred stock accretion and dividends	—	—	519	2,866	3,210
Net loss applicable to common stockholders	$ (38,389)	$ (48,555)	$ (39,161)	$ (21,092)	$ (22,450)
Basic and diluted net loss per share applicable to common stockholders[(1)]	$ (0.30)	$ (0.42)	$ (0.47)	$ (0.48)	$ (0.81)
Shares used in computing basic and diluted net loss per common share applicable to common stockholders[(1)]	127,597	115,092	82,827	43,906	27,639
Net loss	(38,389)	(48,555)	(38,642)	(18,226)	(19,240)
Other comprehensive gain (loss):					
Unrealized gain (loss) on available-for-sale securities	117	(117)	(10)	(7)	—
Other comprehensive gain (loss):	117	(117)	(10)	(7)	—
Comprehensive loss	$ (38,272)	$ (48,672)	$ (38,652)	$ (18,233)	$ (19,240)
Balance Sheet Data:					
Cash, cash equivalents and investments	$ 109,014	$ 87,157	$ 48,571	$ 35,592	$ 10,096
Working capital	101,691	56,427	35,384	25,867	6,163
Total assets	113,231	92,276	51,426	36,867	10,823
Capital lease obligations	15	22	21	9	12
Note payable	501	762	870	—	—
Redeemable preferred stock	—	—	—	—	5,921
Accumulated deficit	(538,470)	(500,081)	(451,526)	(412,884)	(394,658)
Total stockholders' equity	103,349	83,582	43,402	32,452	706

(1) Computed on the basis described in Note 12 to the 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 a clinical-stage biopharmaceutical company focused on the discovery, development and commercialization of novel oligonucleotide therapeutics for oncology and rare diseases. We use two distinct proprietary drug discovery technology platforms to design and develop drug candidates: our Toll-like receptor, or TLR, targeting technology and our third-generation antisense, or 3GA, technology. We developed these platforms based on our scientific expertise and pioneering work with synthetic oligonucleotides as therapeutic agents. Using our TLR targeting technology, we design synthetic oligonucleotide-based drug candidates to modulate the activity of specific TLRs. Using our 3GA technology, we are developing drug candidates to turn off the messenger RNA, or mRNA, associated with disease causing genes. We believe that our 3GA technology may potentially reduce the immunotoxicity and increase the potency of earlier generation antisense and RNA interference, or RNAi, technologies.

Our business strategy is focused on the clinical development of drug candidates for oncology and rare diseases characterized by small, well-defined patient populations with serious unmet medical needs. We believe we can develop and commercialize these targeted therapies on our own. To the extent we seek to develop drug candidates for broader disease indications, we may explore potential collaborative alliances to support development and commercialization.

Our TLR-targeted clinical-stage drug candidates are IMO-2125 and IMO-8400. IMO-2125 is an agonist of TLR9 and IMO-8400 is an antagonist of TLR7, TLR8 and TLR9.

At December 31, 2016, we had an accumulated deficit of $538.5 million. We expect to incur substantial operating losses in future periods. We do not expect to generate product revenue, sales-based milestones or royalties from our development programs until we successfully complete development and obtain marketing approval for drug candidates, either alone or in collaborations with third parties, which we expect will take a number of years. In order to commercialize our drug candidates, we need to complete clinical development and comply with comprehensive regulatory requirements.

Critical Accounting Policies and Estimates

This management's discussion and analysis of financial condition and results of operations is based on our financial statements, which have been prepared in accordance with accounting principles generally accepted in the United States. The preparation of these financial statements requires management to make estimates and assumptions that affect the reported amounts of assets and liabilities and the disclosure of contingent assets and liabilities at the date of the financial statements and the reported amounts of revenues and expenses during the reporting period. On an ongoing basis, management evaluates its estimates and judgments, including those related to stock-based compensation. Management bases its estimates and judgments on historical experience and on various other factors that are believed to be reasonable under the circumstances, the results of which form the basis for making judgments about the carrying values of assets and liabilities that are not readily apparent from other sources. Actual results may differ from these estimates under different assumptions or conditions.

We regard an accounting estimate or assumption underlying our financial statements as a "critical accounting estimate" where:

- the nature of the estimate or assumption is material due to the level of subjectivity and judgment necessary to account for highly uncertain matters or the susceptibility of such matters to change; and

- the impact of the estimates and assumptions on financial condition or operating performance is material.

Our significant accounting policies are described in Note 2 to our financial statements appearing elsewhere in this Annual Report on Form 10-K. Not all of these significant policies, however, fit the definition of critical accounting policies and estimates. We believe that our accounting policies relating to revenue recognition, stock-based compensation and research and development prepayments, accruals and related expenses fit the description of critical accounting estimates and judgments.

Revenue Recognition

We recognize revenue in accordance with the Financial Accounting Standards Board's, or FASB, Accounting Standards Codification, or ASC, Topic 605, *Revenue Recognition*. Accordingly, revenue is recognized for each unit of accounting when all of the following criteria are met:

- persuasive evidence of an arrangement exists;
- delivery has occurred or services have been rendered;
- the seller's price to the buyer is fixed or determinable; and
- collectability is reasonably assured.

Amounts received prior to satisfying the revenue recognition criteria are recognized as deferred revenue in our balance sheet. Amounts expected to be recognized as revenue within the 12 months following the balance sheet date are classified as deferred revenue, current. Amounts not expected to be recognized as revenue within the 12 months following the balance sheet date are classified as deferred revenue, net of current portion.

Our revenues have primarily been generated through collaborative research, development and/or commercialization agreements. The terms of these agreements typically may include payment to us of one or more of the following: nonrefundable, up-front license fees, research, development and commercial milestone payments, other contingent payments due based on the activities of the counterparty or the reimbursement by licensees of costs associated with patent maintenance. Each of these types of revenue are recorded as Alliance revenues in our statement of operations.

For each collaborative research, development and/or commercialization agreement, which results in revenues, we determine (i) whether multiple deliverables exist, (ii) whether the delivered elements have value to the customer on a stand-alone basis, (iii) how the deliverables should be separated or combined and (iv) how the consideration should be allocated to the deliverables.

Arrangement consideration that is fixed or determinable is allocated among the separate units of accounting using the relative selling price method. Then, the applicable revenue recognition criteria in ASC 605 are applied to each of the separate units of accounting in determining the appropriate period and pattern of recognition. We determine the selling price of a unit of accounting following the hierarchy of evidence prescribed by ASC 605-25. Accordingly, we determine the estimated selling price for units of accounting within each arrangement using vendor-specific objective evidence, or VSOE, of selling price, if available, third-party evidence, or TPE, of selling price if VSOE is not available, or best estimate of selling price, or BESP, if neither VSOE nor TPE is available. We typically use BESP to estimate the selling price, since we generally do not have VSOE or TPE of selling price for our units of accounting. Determining the BESP for a unit of accounting requires significant judgment. In developing the BESP for a unit of accounting, we consider applicable market conditions and relevant entity-specific factors, including factors that were contemplated in negotiating the agreement with the customer and estimated costs. We validate the BESP for units of accounting by evaluating whether changes in the key assumptions used to determine the BESP will have a significant effect on the allocation of arrangement consideration between multiple units of accounting.

Options are considered substantive if, at the inception of the arrangement, we are at risk as to whether the collaborator will choose to exercise the option. Factors that we consider in evaluating whether an option is substantive include the overall objective of the arrangement, the benefit the collaborator might obtain from the arrangement without exercising the option, the cost to exercise the option and the likelihood that the option will be exercised. For arrangements under which an option is considered substantive, we do not consider the item underlying the option to be a deliverable at the inception of the arrangement and the associated option fees are not included in allocable arrangement consideration, assuming the option is not priced at a significant and incremental discount. Conversely, for arrangements under which an option is not considered substantive or if an option is priced at a significant and incremental discount, we would consider the item underlying the option to be a deliverable at the inception of the arrangement and a corresponding amount would be included in allocable arrangement consideration. The license to the first product candidate is considered a deliverable at the inception of the arrangement but options to license any additional product candidates are substantive options and therefore are not considered deliverables at inception.

We recognize arrangement consideration allocated to each unit of accounting when all of the revenue recognition criteria in ASC 605 are satisfied for that particular unit of accounting. We will recognize as revenue arrangement consideration attributed to licenses that have standalone value from the other deliverables to be provided in an arrangement upon delivery. We will recognize as revenue arrangement consideration attributed to licenses that do not have standalone value from the other deliverables to be provided in an arrangement over our estimated performance period as the arrangement would be accounted for as a single unit of accounting.

Our multiple element revenue arrangements may include the following:

Up-front License Fees: If a license does not have stand-alone value, we recognize revenues from nonrefundable, up-front license fees on a straight-line basis over the contracted or estimated period of performance of the services under the related agreement, unless evidence suggests that revenue is earned or obligations are fulfilled in a different pattern. We evaluate the period of performance each reporting period and adjust the period of performance on a prospective basis if there are changes to be made. If a license were to have stand-alone value and the other criteria of revenue recognition were satisfied, then revenue would be recognized in the period earned.

Milestone Payments: At the inception of an agreement that includes research and development milestone payments, we evaluate whether each milestone is substantive or represents a deliverable of the counterparty to the agreement. We recognize revenues related to substantive milestones in full in the period in which the substantive milestone is achieved if payment is reasonably assured. If a milestone is a deliverable of the counterparty to the agreement, it is considered contingent revenue and is recognized when we are informed by the counterparty that they have achieved it and such amount is reasonably assured of payment.

Research and Development Activities: If we are entitled to reimbursement from our collaborators for specified research and development activities or the reimbursement of costs associated with patent maintenance, we determine whether such funding would result in alliance revenues or an offset to research and development expenses. Reimbursement of patent maintenance costs are recognized during the period in which the related expenses are incurred as alliance revenues in our statement of operations.

Royalties: If we are entitled to receive royalties from our collaborator for product sales, we will recognize royalty revenue in the period of sale of the related product(s), based on the underlying contract terms, provided that the reported sales are reliably measurable and we have no remaining performance obligations, assuming all other revenue recognition criteria are met.

Under the terms of the Vivelix Agreement, we are eligible for future IMO-9200 related development, regulatory and sales milestone payments totaling up to $140 million, including development and regulatory milestones totaling up to $65 million and sales milestones totaling up to $75 million, and escalating royalties ranging from the mid single-digits to low double-digits of global net sales, which percentages are subject to reduction under agreed upon circumstances. As it relates to back-up compounds we are eligible for related designation payments and development, regulatory sales and milestone payments totaling up to $52.5 million, including development and regulatory milestones totaling up to $35 million and sales milestones totaling up to $17.5 million and escalating royalties ranging from the mid single-digits to low double-digits of global net sales, which percentages are subject to reduction under agreed upon circumstances.

Under the terms of the GSK Agreement, we are eligible to receive up to approximately $100 million in license, research, clinical development and commercialization milestone payments, including a $2.5 million upfront, non-refundable, non-creditable cash payment. Approximately $9.0 million of the milestone payments are payable by GSK upon the identification of additional targets, the completion of current and future research plans and the designation of development candidates. Approximately $89.0 million is payable by GSK upon the achievement of clinical milestones and commercial milestones. In addition, we are eligible to receive royalty payments based on net sales of licensed products following commercialization at varying rates of up to five percent on annual net sales, as defined in the GSK Agreement.

Stock-Based Compensation

We recognize all share-based payments to employees and directors as expense in our statements of operations and comprehensive loss based on their fair values. We record compensation expense over an award's requisite service period, or vesting period, based on the award's fair value at the date of grant. Our policy is to charge the fair value of stock

options as an expense, adjusted for forfeitures, on a straight-line basis over the vesting period, which is generally four years for employees and three years for directors.

We use the Black-Scholes option pricing model to estimate the fair value of stock option grants. The Black-Scholes option pricing model relies on a number of key assumptions to calculate estimated fair values, including assumptions as to average risk-free interest rate, expected dividend yield, expected life and expected volatility. For the assumed risk-free interest rate, we use the U.S. Treasury security rate with a term equal to the expected life of the option. Our assumed dividend yield of zero is based on the fact that we have never paid cash dividends to common stockholders and have no present intention to pay cash dividends. We use an expected option life based on actual experience. Our assumption for expected volatility is based on the actual stock-price volatility over a period equal to the expected life of the option.

If factors change and we employ different assumptions for estimating stock-based compensation expense in future periods, or if we decide to use a different valuation model, the stock-based compensation expense we recognize in future periods may differ significantly from what we have recorded in the current period and could materially affect our operating income (loss), net income (loss) and earnings (loss) per share. It may also result in a lack of comparability with other companies that use different models, methods and assumptions. The Black-Scholes option pricing model was developed for use in estimating the fair value of traded options that have no vesting restrictions and are fully transferable. These characteristics are not present in our option grants. Although the Black-Scholes option pricing model is widely used, existing valuation models, including the Black-Scholes option pricing model, may not provide reliable measures of the fair values of our stock-based compensation.

We recorded charges of $6.8 million, $5.4 million, and $4.3 million in our statements of operations and comprehensive loss for the years ended December 31, 2016, 2015 and 2014, respectively, for stock compensation expense attributable to share-based payments made to employees and directors.

Research and Development Prepayments, Accruals and Related Expenses

As part of the process of preparing our financial statements, we are required to estimate our accrued and prepaid expenses for research and development activities performed by third parties, including Clinical Research Organizations, or CROs, and clinical investigators. These estimates are made as of the reporting date of the work completed over the life of the individual study in accordance with agreements established with CROs and clinical trial sites. Some CROs invoice us on a monthly basis, while others invoice upon achievement of milestones and the expense is recorded as services are rendered. We determine the estimates of research and development activities incurred at the end of each reporting period through discussion with internal personnel and outside service providers as to the progress or stage of completion of trials or services, as of the end of each reporting period, pursuant to contracts with clinical trial centers and CROs and the agreed upon fee to be paid for such services. We periodically confirm the accuracy of our estimates with the service providers and make adjustments if necessary. Clinical trial site costs related to patient enrollments are recorded as patients are entered into the trial.

Results of Operations

Years ended December 31, 2016, 2015 and 2014

Alliance Revenue

Alliance revenue increased by approximately $16.0 million from $0.2 million in 2015 to $16.2 million in 2016 and increased approximately $0.1 million from $0.1 million in 2014 to $0.2 million in 2015.

In November 2016, we entered into the Vivelix Agreement, granting Vivelix a worldwide license to develop and market IMO-9200, an antagonist of TLR 7, 8 and 9, for non-malignant gastrointestinal disorders and a license to IMO-9200 and certain back-up compounds to IMO-9200 and transferred to Vivelix certain IMO-9200 drug material. Under the terms of the Vivelix Agreement, we received an upfront, non-refundable fee of $15 million, which was recorded to Alliance revenue in our Statement of Operations.

In November 2015, we entered into an exclusive worldwide collaboration and license agreement with GSK to research, develop and commercialize selected molecules from our 3GA technology for the treatment of selected targets in

renal disease. During 2015, we received a $2.5 million upfront payment in connection with this agreement which is being deferred and recognized as revenue in our Statement of Operations on a straight line basis over a 27-month performance period. Accordingly, we recognized approximately $1.1 million and $0.1 million of Alliance revenue during 2016 and 2015, respectively, and expect to recognize the balance into 2018.

We also recognized revenue from the reimbursement by licensees of costs associated with patent maintenance as alliance revenue in the years ended December 31, 2016, 2015 and 2014.

Research and Development Expenses

Research and development expenses increased by approximately $6.1 million, or 18%, from $33.7 million in 2015 to $39.8 million in 2016 and approximately $6.2 million, or 23%, from $27.5 million in 2014 to $33.7 million in 2015. In the following table, research and development expenses are set forth in five categories which are discussed beneath the table:

(in thousands)	Year Ended December 31,			Annual Percentage Change	
	2016	2015	2014	2016/2015	2015/2014
IMO-8400 external development expense	$ 11,150	$ 9,561	$ 9,602	17%	—
IMO-2125 external development expense	4,187	1,183	—	254%	—
IMO-9200 external development expense	392	2,498	1,663	(84%)	50%
Other drug development expense	14,221	11,847	9,125	20%	30%
Basic discovery expense	9,874	8,610	7,103	15%	21%
	$ 39,824	$ 33,699	$ 27,493	18%	23%

IMO-8400 External Development Expenses. These expenses include external expenses that we have incurred in connection with IMO-8400 since October 2012, when we commenced clinical development of IMO-8400. These external expenses include payments to independent contractors and vendors for drug development activities conducted after the initiation of IMO-8400 clinical development but exclude internal costs such as payroll and overhead expenses. Since October 2012, we have incurred approximately $34.3 million in IMO-8400 external development expenses through December 31, 2016, including costs associated with our Phase 1 clinical trial in healthy subjects; our Phase 2 clinical trial in patients with psoriasis; preparation for and conduct of our Phase 1/2 clinical trial in patients with Waldenström's macroglobulinemia and our Phase 1/2 clinical trial in patients with DLBCL harboring the MYD88 L265P oncogenic mutation, which we discontinued in September 2016; the preparation for and conduct of our ongoing Phase 2 clinical trial in patients with dermatomyositis; the manufacture of additional drug substance for use in our clinical trials; and expenses associated with our collaboration with Abbott Molecular for the development of a companion diagnostic for identification of patients with B-cell lymphoma harboring the MYD88 L265P oncogenic mutation.

The increase in our IMO-8400 external development expenses in 2016, as compared to 2015, was primarily due to increases in costs associated with our ongoing Phase 2 clinical trial in patients with dermatomyositis and costs incurred in connection with the manufacture of additional drug substance for use in our clinical trials in 2016. An increase in the cost of conducting our Phase 1/2 clinical trial in patients with DLBCL harboring the MYD88 L265P oncogenic mutation also contributed to the increase in IMO-8400 external development expenses in 2016. These increases were partially offset by a decrease related to lower enrollment in our Phase 1/2 clinical trial in patients with Waldenström's macroglobulinemia and a decrease in the cost of developing a companion diagnostic for identification of patients with B-cell lymphoma harboring the MYD88 L265P oncogenic mutation as compared to 2015.

The change in our IMO-8400 external development expenses in 2015, as compared to 2014, was due to lower consulting fees in 2015 and lower costs associated with long-term nonclinical safety studies conducted during 2014, partially offset by higher costs incurred in 2015 in connection with our Phase 1/2 clinical trial in patients with Waldenström's macroglobulinemia, our Phase 1/2 clinical trial in patients with DLBCL harboring the MYD88 L265P oncogenic mutation, and our nonclinical studies and Phase 2 clinical trial in patients with dermatomyositis.

We expect our IMO-8400 external development expenses during 2017 to be similar to 2016. In September 2016, we announced that we had suspended the internal clinical development of IMO-8400 for B-cell lymphomas, including our trials in Waldenström's macroglobulinemia and DLBCL. We are exploring strategic alternatives for IMO-8400 in these indications. We expect to continue to incur costs associated with IMO-8400 as we continue our ongoing Phase 2 clinical

trial of IMO-8400 in patients with dermatomyositis, finish treating enrolled patients in our clinical trial of IMO-8400 in Waldenström's macroglobulinemia and wind down our clinical development of IMO-8400 in Waldenström's macroglobulinemia and DLBCL.

IMO-2125 External Development Expenses. These expenses include external expenses that we have incurred in connection with the development of IMO-2125 as part of our immuno-oncology program. These external expenses include payments to independent contractors and vendors for drug development activities conducted after the initiation of IMO-2125 clinical development in immuno-oncology, but exclude internal costs such as payroll and overhead expenses. We commenced clinical development of IMO-2125 as part of our immuno-oncology program in July 2015 and from July 2015 through December 31, 2016 we incurred approximately $5.4 million in IMO-2125 external development expenses as part of our immuno-oncology program, including costs associated with the preparation for and conduct of the ongoing Phase 1/2 clinical trial being conducted under our research alliance with MD Anderson to assess the safety and efficacy of IMO-2125 in combination with ipilimumab and with pembrolizumab in patients with metastatic melanoma, the manufacture of additional drug substance for use in our clinical trials and additional nonclinical studies. The $5.4 million in IMO-2125 external development expenses excludes costs incurred prior to July 2015 with respect to IMO-2125, including costs incurred for the development of IMO-2125 for the treatment of patients with chronic hepatitis C virus which we discontinued in the third quarter of 2011.

We expect our IMO-2125 external development expenses to increase during 2017, as compared to 2016, as we plan to continue our Phase 1/2 clinical trial being conducted under our research alliance with MD Anderson to assess the safety and efficacy of IMO-2125 in combination with ipilimumab and with pembrolizumab in patients with metastatic melanoma, conduct clinical trials of IMO-2125, work on the design and planning for additional clinical trials of IMO-2125 and develop our strategy to optimize IMO-2125, and continue manufacturing activities and nonclinical studies.

IMO-9200 External Development Expenses. These expenses include external expenses that we have incurred in connection with IMO-9200 since October 2014, when we commenced clinical development of IMO-9200. These external expenses include payments to independent contractors and vendors for drug development activities conducted after the initiation of IMO-9200 clinical development but exclude internal costs such as payroll and overhead expenses. We have incurred approximately $4.6 million in IMO-9200 external development expenses from October 2014 through December 31, 2016 including costs associated with our Phase 1 clinical trial in healthy subjects, the manufacture of additional drug substance for use in our clinical and nonclinical trials and additional nonclinical studies. We classified the IMO-9200 external development expenses incurred prior to October 2014 in other drug development expenses.

The decrease in IMO-9200 external development expenses in 2016, as compared to 2015, reflects fewer manufacturing and nonclinical toxicology studies during 2016. We expect our IMO-9200 external development expenses to decrease during 2017, as compared to 2016, as in September 2016, we determined not to proceed with the development of IMO-9200 and, in November 2016, entered into the Vivelix Agreement, granting Vivelix worldwide rights to develop and market IMO-9200 for non-malignant gastrointestinal disorders.

Other Drug Development Expenses. These expenses include external expenses associated with preclinical development of identified compounds in anticipation of advancing these compounds into clinical development. In addition, these expenses include internal costs, such as payroll and overhead expenses, associated with preclinical development and products in clinical development. The external expenses associated with preclinical compounds include payments to contract vendors for manufacturing and the related stability studies, preclinical studies, including animal toxicology and pharmacology studies, and professional fees. Other drug development expenses also include costs associated with compounds that were previously being developed but are not currently being developed.

The increase in other drug development expenses in 2016, as compared to 2015, was primarily due the costs of additional headcount associated with our expanded drug development programs and costs associated with the manufacture of 3GA drug supplies, partially offset by lower consulting costs during 2016. In addition, other drug development expenses in 2015 included costs associated with the manufacture of IMO-2055 drug supply and other drug development expenses of IMO-2125 incurred prior to the commencement of its clinical development in our immuno-oncology program in July 2015. Costs associated with the clinical development of IMO-2125 since July 2015 are included in IMO-2125 external development expenses.

The increase in other drug development expenses in 2015, as compared to 2014, was primarily due to higher consulting costs and additional headcount associated with our expanded drug development programs, and the manufacture

of IMO-2055 drug supply, which we may use in our immuno-oncology program. The increase in other drug development expenses during 2015 was partially offset by higher costs for preclinical studies and manufacturing activities that were incurred during 2014 to support the IND submission for IMO-9200.

Basic Discovery Expenses. These expenses include our internal and external expenses relating to our discovery efforts with respect to our TLR-targeted programs, including agonists and antagonists of TLR3, TLR7, TLR8 and TLR9, and our 3GA program. These expenses reflect payments for laboratory supplies, external research, and professional fees, as well as payroll and overhead expenses. The increase in basic discovery expenses in 2016, as compared to 2015, was primarily due to increases in payroll and stock-based compensation associated with additional research and development headcount, the costs of laboratory supplies and facilities expenses during 2016. The increase in basic discovery expenses in 2016 was partially offset by decreases in external research and recruiting expenses in 2016. The increase in basic discovery expenses in 2015, as compared to 2014, was primarily due to increases in recruiting, external research, stock-based compensation and the accrual of incentive compensation. The increase in basic discovery expenses during 2015 was partially offset by a decrease in the cost of laboratory supplies.

We do not know if we will be successful in developing any drug candidate from our research and development programs. At this time, and without knowing the results from our ongoing clinical trial of IMO-8400, our ongoing clinical trial of IMO-2125, and our ongoing development of compounds in our 3GA program, we cannot reasonably estimate or know the nature, timing, and costs of the efforts that will be necessary to complete the remainder of the development of, or the period, if any, in which material net cash inflows may commence from, any drug candidate from our research and development programs. Moreover, the clinical development of any drug candidate from our research and development programs is subject to numerous risks and uncertainties associated with the duration and cost of clinical trials, which vary significantly over the life of a project as a result of unanticipated events arising during clinical development.

General and Administrative Expenses

General and administrative expenses consist primarily of payroll, stock-based compensation expense, consulting fees and professional legal fees associated with our patent applications and maintenance, our corporate regulatory filing requirements, our corporate legal matters, and our business development initiatives.

General and administrative expenses decreased by approximately $0.3 million, or 2%, from $15.4 million in 2015 to $15.1 million in 2016. The decrease in general and administrative expenses during 2016, as compared to 2015, was primarily due to decreases in corporate legal fees and investor relations expenses, partially offset by increases in payroll, stock compensation, legal fees associated with our patent filing and maintenance, and accounting and auditing fees, including the cost of Sarbanes-Oxley compliance and the related internal control audit.

General and administrative expenses increased by $4.1 million, or 36%, from $11.3 million in 2014, to $15.4 million in 2015. The increase in general and administrative expenses during 2015, as compared to 2014, was primarily due to higher stock-based compensation costs primarily attributable to options granted in the latter part of 2014, higher cash compensation expenses, including additional headcount to support our drug development programs, the hiring of a new Chief Executive Officer in December 2014, the accrual of incentive compensation, and higher patent expenses. The increase in general and administrative expenses during 2015 was partially offset by decreases in consulting and recruiting expenses.

We expect general and administrative expenses to increase during 2017, as compared to 2016, due to additional headcount to support our drug development programs.

Interest Income

Interest income increased by $58,000 from $357,000 in 2015 to $415,000 in 2016 primarily due to fluctuations of investment balances, which were impacted by the investment of funds obtained from our follow-on underwritten public offerings in October 2016 and February 2015 and from warrant and option exercises since June 2015, offset by general spending.

Interest income increased by $291,000, from $66,000 in 2014 to $357,000 in 2015 primarily due to an increase in investment balances, including corporate debt securities, in 2015 resulting from our follow-on underwritten public offering in February 2015 and warrant and option exercises since September 30, 2014.

Interest Expense

Interest expense decreased during 2016, as compared to 2015, primarily due to a decrease in the outstanding principal amount of our note under our loan and security agreement with Oxford Finance LLC.

Interest expense increased during 2015, as compared to 2014 due to interest on our note payable which we incurred pursuant to our loan and security agreement with Oxford Finance LLC executed on September 30, 2014.

Loss on Extinguishment of Convertible Preferred Stock and Preferred Stock Accretion and Dividends

The $519,000 in preferred stock dividends in 2014 reflects $66,000 in dividends accrued on shares of our Series D redeemable convertible preferred stock, or Series D preferred stock, and $453,000 in dividends accrued on shares of our Series E convertible preferred stock, or Series E preferred stock. There were no dividends accrued on our Series D preferred stock or Series E preferred stock during 2016 and 2015 because the Series D preferred stock and Series E preferred stock were converted to common stock during February 2014 and December 2014, respectively.

Net Loss Applicable to Common Stockholders

As a result of the factors discussed above, our net loss applicable to common stockholders was $38.4 million, $48.6 million and $39.2 million for the years ended December 31, 2016, 2015 and 2014, respectively. Since January 1, 2001, we have primarily been involved in the development of our TLR pipeline. From January 1, 2001 through December 31, 2016, we incurred losses of $278.3 million. We also incurred net losses of $260.2 million prior to December 31, 2000 during which time we were primarily involved in the development of earlier generation antisense technology. Since our inception, we had an accumulated deficit of $538.5 million through December 31, 2016. We expect to continue to incur substantial operating losses in the future.

Net Operating Loss Carryforwards

The Tax Reform Act of 1986 contains provisions that limit the amount of net operating loss carryforwards, or NOLs, and tax credit carryforwards that companies may utilize in any one year in the event of cumulative changes in ownership over a three-year period in excess of 50%. We have completed several financings since the effective date of the Tax Reform Act of 1986, which as of December 31, 2016, have resulted in ownership changes in excess of 50% that will significantly limit our ability to utilize our NOL and tax credit carryforwards. In December 2014, we completed a study which determined that a cumulative three-year ownership change in excess of 50% had occurred in November 2012. Our 2016 and 2015 federal and state NOLs and tax credit carryforwards shown below have been adjusted to reflect the ownership change limitations that resulted from this study. We have entered into additional equity transactions since November 2012 that could result in ownership changes that further limit our ability to utilize our NOL and tax credit carryforwards. We have not determined whether any additional ownership change limitations have resulted from equity transactions that have occurred after November 2012.

After adjusting our federal and state NOLs to reflect the ownership change limitations that resulted from this study, as of December 31, 2016, we had cumulative federal and state NOLs of approximately $149.3 million and $138.2 million available to reduce federal and state taxable income, respectively. These NOLs expire through 2036. In addition, after adjusting our federal and state tax credit carryforwards to reflect the ownership change limitations that were identified during this study, as of December 31, 2016, we had cumulative federal and state tax credit carryforwards of $8.4 million and $1.6 million, respectively, available to reduce federal and state income taxes which expire through 2036 and 2031, respectively. Additional ownership change limitations may result from ownership changes that occur after November 2012.

Liquidity and Capital Resources

Sources of Liquidity

We require cash to fund our operating expenses and to make capital expenditures. Historically, we have funded our cash requirements primarily through the following:

- sale of common stock, preferred stock and warrants and warrant exercises;

- debt financing, including capital leases;
- license fees, research funding and milestone payments under collaborative and license agreements; and
- interest income.

Collaborative Alliances. We are currently party to collaborations with Vivelix, GSK, Abbott Molecular and Merck & Co. Under the terms of the Vivelix Agreement, we received an upfront fee of $15 million in November 2016. Under the terms of the GSK Agreement, we received an upfront fee of $2.5 million in November 2015. Under both agreements, we are eligible to receive additional fees based on future activities. The details of these agreements are discussed in Note 6 to the financial statements appearing elsewhere in this Annual Report on Form 10-K.

October 13, 2016 Follow-on Underwritten Public Offering. On October 13, 2016, we closed a follow-on underwritten public offering, in which we sold 25,000,000 shares of common stock at a price to the public of $2.00 per share for aggregate gross proceeds of $50.0 million. On October 28, 2016, we sold an additional 1,225,243 shares of common stock pursuant to the underwriters' 30-day option to purchase additional shares at the public offering price less the underwriting discount. The net proceeds from the offering, including the exercise by the underwriters of their option to purchase additional shares and after deducting underwriters' discounts and commissions and other offering costs and expenses, were approximately $48.8 million.

Warrant Exercises. Warrants to purchase 1,370,000 shares of our common stock were exercised at a per share price of $1.46 during 2016. We received proceeds of $2.0 million from the exercise of these warrants.

Cash Flows

As of December 31, 2016, we had approximately $109.0 million in cash, cash equivalents and investments, a net increase of approximately $21.8 million from December 31, 2015. Net cash used in operating activities totaled $28.2 million during 2016, reflecting our $38.4 million net loss, as adjusted for non-cash income and expenses, including stock-based compensation, depreciation and amortization. Net cash used in operating activities also reflects changes in our prepaid expenses, accounts payable, accrued expenses and other liabilities.

The net cash used in investing activities during 2016 reflects the purchase of $32.7 million of available-for-sale securities, which are investments that we do not have the positive intent to hold to maturity at the time of purchase, the maturity of $2.9 million of available-for-sale securities, the sale of $2.0 million of available-for-sale securities, and payments for the purchase of $0.4 million in property and equipment.

The $50.9 million net cash provided by financing activities during 2016 primarily reflects $49.0 million of the net proceeds from our follow-on underwritten public offering of our securities in October 2016, excluding the $0.2 million of costs that were unpaid at December 31, 2016. Financing activities also includes $2.2 million in net proceeds from the exercise of warrants and employee stock purchases under our 1995 Employee Stock Purchase Plan, or ESPP.

As of December 31, 2015, we had approximately $87.2 million in cash, cash equivalents and investments, a net increase of approximately $38.6 million from December 31, 2014. Net cash used in operating activities totaled $43.0 million during 2015, reflecting our $48.6 million net loss, as adjusted for non-cash income and expenses, including stock-based compensation, depreciation and amortization. Net cash used in operating activities also reflects changes in our prepaid expenses, accounts payable, accrued expenses and other liabilities.

The net cash used in investing activities during 2015 reflects the purchase of $63.1 million of available-for-sale securities, which are investments that we do not have the positive intent to hold to maturity at the time of purchase, the maturity of $29.4 million of available-for-sale securities, the sale of $1.0 million of available-for-sale securities, and payments for the purchase of $0.7 million in property and equipment.

The $83.0 million net cash provided by financing activities during 2015 primarily reflects $80.6 million in net proceeds from our follow-on underwritten public offering of our securities in February 2015 and $2.5 million in net proceeds from employee stock purchases under our ESPP and the exercise of common stock options and warrants.

As of December 31, 2014, we had approximately $48.6 million in cash, cash equivalents and investments, a net increase of approximately $13.0 million from December 31, 2013. Net cash used in operating activities totaled $31.3 million during 2014, reflecting our $38.6 million net loss, as adjusted for non-cash income and expenses, including stock-based compensation, depreciation and amortization. Net cash used in operating activities also reflects changes in our prepaid expenses, accounts payable, accrued expenses and other liabilities.

The net cash used in investing activities during 2014 reflects the purchase of $23.6 million of available-for-sale securities, the maturity of $4.1 million of available-for-sale securities, and payments for the purchase of $1.1 million in property and equipment.

The $45.6 million net cash provided by financing activities during 2014 primarily reflects $37.2 million in net proceeds from our follow-on underwritten public offering of our securities in February 2014, which were partially offset by $0.1 million in costs related to our 2013 financings, $8.5 million in net proceeds from employee stock purchases under our ESPP, and the exercise of common stock options and warrants and $0.8 million in net proceeds from the issuance of the promissory note under the loan and security agreement with Oxford Financial LLC which were partially offset by dividends paid on our Series D preferred stock and our Series E preferred stock.

Funding Requirements

We have incurred operating losses in all fiscal years since our inception except 2002, 2008 and 2009, and we had an accumulated deficit of $538.5 million at December 31, 2016. We expect to incur substantial operating losses in future periods. 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 received no revenues from the sale of drugs. As of February 15, 2017, substantially all of our revenues have been from collaboration 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 do not expect to generate significant additional funds internally until we successfully complete development and obtain marketing approval for products, either alone or in collaboration with third parties, which we expect will take a number of years. In addition, we have no committed external sources of funds.

We had cash, cash equivalents and investments of approximately $109.0 million at December 31, 2016. We believe that, based on our current operating plan, our existing cash, cash equivalents and investments will enable us to fund our operations into the second quarter of 2018. Specifically, we believe that our available funds will be sufficient to enable us to:

- participate in an FDA End-of-Phase 1 meeting to obtain FDA feedback on the regulatory pathway for IMO-2125;
- complete our ongoing Phase 1/2 clinical trial of IMO-2125 in combination with ipilimumab or pembrolizumab in anti-PD1 refractory metastatic melanoma and complete enrollment in the Phase 2 portion of this trial;
- prepare for the initiation of a pivotal Phase 3 clinical trial of IMO-2125 in combination with a checkpoint inhibitor for the treatment of anti-PD1 refractory metastatic melanoma;
- initiate a Phase 1 intra-tumoral monotherapy clinical trial of IMO-2125 in multiple refractory tumor types;
- initiate a Phase 2 multi-arm clinical trial of IMO-2125 in combination with a checkpoint inhibitor in multiple refractory tumor types;
- complete our ongoing Phase 2 clinical trial of IMO-8400 in patients with dermatomyositis; and
- submit an IND and initiate a Phase 1 human clinical proof-of-concept trial of IDRA-008.

We expect that we will need to raise additional funds in order to conduct any other clinical development of our TLR drug candidates or to conduct any other development of our 3GA technology, and to fund our operations. We are seeking and expect to continue to seek additional funding through collaborations, the sale or license of assets or financings of equity or debt securities. We believe that the key factors that will affect our ability to obtain funding are:

- the results of our clinical and preclinical development activities in our rare disease program, our immuno-oncology program and our 3GA program, and our ability to advance our drug candidates and 3GA technology on the timelines anticipated;
- the cost, timing, and outcome of regulatory reviews;
- competitive and potentially competitive products and technologies and investors' receptivity to our drug candidates and the technology underlying them in light of competitive products and technologies;
- the receptivity of the capital markets to financings by biotechnology companies generally and companies with drug candidates and technologies such as ours specifically; and
- our ability to enter into additional collaborations with biotechnology and pharmaceutical companies and the success of such collaborations.

In addition, increases in expenses or delays in clinical development may adversely impact our cash position and require additional funds or cost reductions.

Financing may not be available to us when we need it or may not be available to us on favorable or acceptable terms or at all. 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. An equity financing that involves existing stockholders may cause a concentration of ownership. 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 or equity financing may contain terms which are not favorable to us or to our stockholders, such as liquidation and other preferences, or liens or other restrictions on our assets. As discussed in Note 10 to the financial statements appearing elsewhere in this Annual Report on Form 10-K, additional equity financings may also result in cumulative changes in ownership over a three-year period in excess of 50% which would limit the amount of net operating loss and tax credit carryforwards that we may utilize in any one year.

If we are unable to obtain adequate funding on a timely basis or at all, we will be required to terminate, modify or delay preclinical or clinical trials of one or more of our drug candidates, significantly curtail or terminate discovery or development programs for new drug candidates or relinquish rights to portions of our technology, drug candidates and/or products.

Contractual Obligations

As of December 31, 2016, our contractual commitments were as follows:

	Payments Due by Period				
Contractual Commitment	**Total**	**Less than 1 year**	**1-3 years**	**3-5 years**	**More than 5 years**
			(In thousands)		
Operating lease	$ 11,300	$ 1,842	$ 4,108	$ 4,002	$ 1,348
Loan and security agreement	552	333	219	—	—
Total	$ 11,852	$ 2,175	$ 4,327	$ 4,002	$ 1,348

Our only material lease commitments relate to our facilities in Cambridge, Massachusetts, which expires on August 31, 2022 subject to a five-year renewal option exercisable by us, and Exton, Pennsylvania, which expires on May 31, 2020 subject to a three-year renewal option exercisable by us.

In the normal course of business, we enter into contracts with clinical research organizations, drug manufacturers and other vendors for preclinical and clinical research studies, research and development supplies and other services and products for operating purposes. These contracts generally provide for termination on notice, and therefore are cancellable contracts and not included in the table of contractual obligations and commitments.

Off-Balance Sheet Arrangements

As of December 31, 2016, we had no off-balance sheet arrangements.

New Accounting Pronouncements

New accounting pronouncements are discussed in Note 2(n) in the Notes to the Financial Statements in this Annual Report on Form10-K.

Item 7A. ***Quantitative and Qualitative Disclosures about Market Risk.***

As of December 31, 2016, all material assets and liabilities are in U.S. dollars, which is our functional currency.

We maintain investments in accordance with our investment policy. The primary objectives of our investment activities are to preserve principal, maintain proper liquidity to meet operating needs and maximize yields. Although our investments are subject to credit risk, our investment policy specifies credit quality standards for our investments and limits the amount of credit exposure from any single issue, issuer or type of investment. We regularly review our investment holdings in light of the then current economic environment. At December 31, 2016, all of our invested funds were invested in two money market funds, classified in cash and cash equivalents on the accompanying balance sheet, corporate bonds, municipal bonds and commercial paper classified in short-term investments, and corporate bonds and municipal bonds classified in long-term investments.

Based on a hypothetical ten percent adverse movement in interest rates, the potential losses in future earnings, fair value of risk sensitive financial instruments, and cash flows are immaterial, although the actual effects may differ materially from the hypothetical analysis.

Item 8. ***Financial Statements and Supplementary Data.***

All financial statements required to be filed hereunder are filed as listed under Item 15(a) of this Annual Report on Form 10-K and are incorporated herein by this reference.

Quarterly Operating Results (Unaudited)

The following table presents the unaudited statement of operations and comprehensive loss data for each of the eight quarters in the period ended December 31, 2016. The information for each of these quarters is unaudited, but has been prepared on the same basis as the audited financial statements appearing elsewhere in this Annual Report on Form 10-K. In our opinion, all necessary adjustments, consisting only of normal recurring adjustments, have been made to present fairly the unaudited quarterly results when read in conjunction with the audited financial statements and the notes thereto appearing elsewhere in this document. These operating results are not necessarily indicative of the results of operations that may be expected for any future period.

	Three months ended							
	Dec. 31, 2016	Sep. 30, 2016	Jun. 30, 2016	Mar. 31, 2016	Dec. 31, 2015	Sep. 30, 2015	Jun. 30, 2015	Mar. 31, 2015
	(In thousands, except per share data)							
Statement of Operations and Comprehensive Income (Loss) Data:								
Alliance revenue	$ 15,281	$ 323	$ 301	$ 294	$ 190	$ 20	$ 5	$ 34
Operating expenses:								
Research and development	11,007	9,393	10,128	9,296	8,565	7,454	8,960	8,720
General and administrative	3,531	3,907	3,778	3,916	3,708	4,030	3,821	3,837
Total operating expenses	14,538	13,300	13,906	13,212	12,273	11,484	12,781	12,557
Income (loss) from operations	743	(12,977)	(13,605)	(12,918)	(12,083)	(11,464)	(12,776)	(12,523)
Interest income	95	90	110	120	118	123	75	41
Interest expense	(17)	(19)	(21)	(23)	(24)	(27)	(27)	(27)
Foreign currency exchange gain (loss)	1	3	31	(2)	(1)	3	9	28
Net income (loss)	$ 822	$ (12,903)	$ (13,485)	$ (12,823)	$ (11,990)	$ (11,365)	$ (12,719)	$ (12,481)
Basic net income (loss) per common share per common share [1]	$ 0.01	$ (0.10)	$ (0.11)	$ (0.11)	$ (0.10)	$ (0.10)	$ (0.11)	$ (0.12)
Shares used in computing basic net income (loss) per common share [1]	146,255	121,389	121,323	121,284	118,865	118,248	118,002	105,067
Diluted net income (loss) per common share per common share [1][2][3]	$ 0.01	$ (0.10)	$ (0.11)	$ (0.11)	$ (0.10)	$ (0.10)	$ (0.11)	$ (0.12)
Shares used in computing diluted net income (loss) per common share [1][2][3]	151,930	121,389	121,323	121,284	118,865	118,248	118,002	105,067
Net income (loss)	$ 822	$ (12,903)	$ (13,485)	$ (12,823)	$ (11,990)	$ (11,365)	$ (12,719)	$ (12,481)
Other comprehensive (loss) gain:								
Unrealized (loss) gain on available-for-sale securities	(16)	(13)	12	134	(107)	50	(78)	18
Comprehensive income (loss)	$ 806	$ (12,916)	$ (13,473)	$ (12,689)	$ (12,097)	$ (11,315)	$ (12,797)	$ (12,463)

(1) Computed on the basis described in Note 12 to the financial statements appearing elsewhere in this Annual Report on Form 10-K.

(2) In periods of net loss, basic shares are used in the per share calculation as including exercisable shares would be anti-dilutive.

(3) In the quarter ending December 31, 2016, shares used in computing diluted net income per share includes 1,315,000 common stock equivalents related to exercisable stock options and 4,360,000 common stock equivalents related to exercisable warrants.

Item 9. ***Changes in and Disagreements with Accountants on Accounting and Financial Disclosure.***

None.

Item 9A. ***Controls and Procedures.***

Disclosure Controls and Procedures

Our management, with the participation of our principal executive officer and principal financial officer, evaluated the effectiveness of our disclosure controls and procedures (as defined in Rules 13a-15(e) and 15d-15(e) under the Exchange Act) as of December 31, 2016. In designing and evaluating our disclosure controls and procedures, management recognizes that any controls and procedures, no matter how well designed and operated, can provide only reasonable assurance of achieving their objectives and our management necessarily applied its judgment in evaluating the cost-benefit relationship of possible controls and procedures. Based on this evaluation, our principal executive officer and principal financial officer concluded that as of December 31, 2016, our disclosure controls and procedures were (1) designed to ensure that material information relating to us is made known to our principal executive officer and principal financial officer by others, particularly during the period in which this report was prepared, and (2) effective, in that they provide reasonable assurance that information required to be disclosed by us in the reports we file or submit under the Exchange Act is recorded, processed, summarized and reported within the time periods specified in the SEC's rules and forms.

Internal Control over Financial Reporting

a) Management's Annual Report on Internal Control over Financial Reporting

Our management, with the participation of our principal executive officer and principal financial officer, is responsible for establishing and maintaining adequate internal control over financial reporting. Internal control over financial reporting is defined in Rule 13a-15(f) and 15d-15(f) promulgated under the Exchange Act as a process designed by, or under the supervision of, the Company's principal executive and principal financial officers and effected by the Company's board of directors, management and other personnel, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles and includes those policies and procedures that:

- Pertain to the maintenance of records that in reasonable detail accurately and fairly reflect the transactions and dispositions of the assets of the Company;

- Provide reasonable assurance that transactions are recorded as necessary to permit preparation of financial statements in accordance with generally accepted accounting principles, and that receipts and expenditures of the Company are being made only in accordance with authorizations of management and directors of the Company; and

- Provide reasonable assurance regarding prevention or timely detection of unauthorized acquisition, use or disposition of the Company's assets that could have a material effect on the financial statements.

Because of its inherent limitations, internal control over financial reporting may not prevent or detect misstatements. Therefore, even those systems determined to be effective can provide only reasonable assurance with respect to financial statement preparation and presentation. Projections of any evaluation of effectiveness to future periods are subject to the risk that controls may become inadequate because of changes in conditions, or that the degree of compliance with the policies or procedures may deteriorate.

Management assessed the effectiveness of our internal control over financial reporting as of December 31, 2016. In making this assessment, management used the criteria set forth by the Committee of Sponsoring Organizations of the Treadway Commission in *Internal Control — Integrated Framework* (2013).

Based on this assessment, management believes that, as of December 31, 2016, the Company's internal control over financial reporting is effective based on those criteria.

Ernst & Young LLP, our independent registered public accounting firm, has issued a report on the effectiveness of our internal control over financial reporting as of December 31, 2016. This report appears immediately below.

b) Attestation Report of the Registered Public Accounting Firm

Report of Independent Registered Public Accounting Firm

The Board of Directors and Stockholders

Idera Pharmaceuticals, Inc.

We have audited Idera Pharmaceuticals Inc.'s internal control over financial reporting as of December 31, 2016, based on criteria established in Internal Control — Integrated Framework issued by the Committee of Sponsoring Organizations of the Treadway Commission (2013 framework) (the COSO criteria). Idera Pharmaceuticals Inc.'s management is responsible for maintaining effective internal control over financial reporting, and for its assessment of the effectiveness of internal control over financial reporting included in the accompanying Management's Annual Report on Internal Control Over Financial Reporting. Our responsibility is to express an opinion on the company's internal control over financial reporting based on our audit.

We conducted our audit in accordance with the standards of the Public Company Accounting Oversight Board (United States). Those standards require that we plan and perform the audit to obtain reasonable assurance about whether effective internal control over financial reporting was maintained in all material respects. Our audit included obtaining an understanding of internal control over financial reporting, assessing the risk that a material weakness exists, testing and evaluating the design and operating effectiveness of internal control based on the assessed risk, and performing such other procedures as we considered necessary in the circumstances. We believe that our audit provides a reasonable basis for our opinion.

A company's internal control over financial reporting is a process designed to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles. A company's internal control over financial reporting includes those policies and procedures that (1) pertain to the maintenance of records that, in reasonable detail, accurately and fairly reflect the transactions and dispositions of the assets of the company; (2) provide reasonable assurance that transactions are recorded as necessary to permit preparation of financial statements in accordance with generally accepted accounting principles, and that receipts and expenditures of the company are being made only in accordance with authorizations of management and directors of the company; and (3) provide reasonable assurance regarding prevention or timely detection of unauthorized acquisition, use, or disposition of the company's assets that could have a material effect on the financial statements.

Because of its inherent limitations, internal control over financial reporting may not prevent or detect misstatements. Also, projections of any evaluation of effectiveness to future periods are subject to the risk that controls may become inadequate because of changes in conditions, or that the degree of compliance with the policies or procedures may deteriorate.

In our opinion, Idera Pharmaceuticals Inc. maintained, in all material respects, effective internal control over financial reporting as of December 31, 2016, based on the COSO criteria.

We also have audited, in accordance with the standards of the Public Company Accounting Oversight Board (United States), the balance sheets as of December 31, 2016 and 2015, and the related statements of operations and comprehensive loss, stockholders' equity, and cash flows for each of the three years in the period ended December 31, 2016 of Idera Pharmaceuticals Inc. and our report dated March 15, 2017 expressed an unqualified opinion thereon.

/s/ ERNST & YOUNG LLP

Boston, Massachusetts
March 15, 2017

c) Changes in Internal Control over Financial Reporting.

No change in our internal control over financial reporting occurred during the fourth quarter of the fiscal year ended December 31, 2016 that has materially affected, or is reasonably likely to materially affect, our internal control over financial reporting.

Item 9B. ***Other Information.***

None.

PART III.

The responses to the Part III items incorporate by reference certain sections of our Proxy Statement for our annual meeting of stockholders to be held on June 7, 2017.

Item 10. ***Directors, Executive Officers, and Corporate Governance.***

We have adopted a written code of business conduct and ethics that applies to our principal executive officer, principal financial officer, principal accounting officer or controller, or persons performing similar functions. We have posted a current copy of the Code of Business Conduct and Ethics in the "Investors — Corporate Governance" section of our website, which is located at www.iderapharma.com. We intend to satisfy the disclosure requirements under Item 5.05 of Form 8-K regarding an amendment to, or waiver from, a provision of our code of business conduct and ethics by posting such information on our website at www.iderapharma.com.

The remainder of the response to this item will be contained in the 2017 Proxy Statement under the captions "Proposal One — Election of Directors," "Section 16(a) Beneficial Ownership Reporting Compliance" and "Corporate Governance Information," which sections are incorporated herein by reference.

Item 11. ***Executive Compensation.***

The response to this item will be contained in the 2017 Proxy Statement under the captions "Corporate Governance Information — Compensation Committee Interlocks and Insider Participation" and "Executive Compensation," which sections are incorporated herein by reference.

Item 12. ***Security Ownership of Certain Beneficial Owners and Management and Related Stockholder Matters.***

The response to this item will be contained in the 2017 Proxy Statement under the caption "Security Ownership of Certain Beneficial Owners and Management," which section is incorporated herein by reference.

The disclosures required for securities authorized for issuance under equity compensation plans will be contained in the 2017 Proxy Statement under the caption "Equity Compensation Plan Information," which section is incorporated herein by reference.

Item 13. ***Certain Relationships and Related Transactions, and Director Independence.***

The response to this item will be contained in the 2017 Proxy Statement under the captions "Transactions with Related Persons" and "Corporate Governance Information — Director Independence," which sections are incorporated herein by reference.

Item 14. ***Principal Accountant Fees and Services.***

The response to this item will be contained in the 2017 Proxy Statement under the caption "Accounting Matters — Independent Registered Public Accounting Firm Fees," which section is incorporated herein by reference.

PART IV.

Item 15. ***Exhibits and Financial Statement Schedules.***

(a) (1) *Financial Statements.*

(2) We are not filing any financial statement schedules as part of this Annual Report on Form 10-K because they are not applicable or the required information is included in the financial statements or notes thereto.

(3) The list of Exhibits filed as a part of this Annual Report on Form 10-K is set forth on the Exhibit Index immediately preceding such Exhibits and is incorporated herein by this reference.

(b) The list of Exhibits filed as a part of this Annual Report on Form 10-K is set forth on the Exhibit Index immediately preceding such Exhibits and is incorporated herein by this reference.

(c) None.

Item 16. ***Form 10-K Summary.***

Not applicable.

SIGNATURES

Pursuant to the requirements of Section 13 or 15(d) of the Securities Exchange Act of 1934, as amended, the Registrant has duly caused this report to be signed on its behalf by the undersigned, thereunto duly authorized, on this 15th day of March 2017.

Idera Pharmaceuticals, Inc.

By: /S/ VINCENT J. MILANO
Vincent J. Milano
President and
Chief Executive Officer

Pursuant to the requirements of the Securities Exchange Act of 1934, as amended, this report has been signed below by the following persons on behalf of the Registrant and in the capacities and on the dates indicated.

Signature	Title	Date
/S/ VINCENT J. MILANO Vincent J. Milano	President, Chief Executive Officer and Director (Principal Executive Officer)	March 15, 2017
/S/ LOUIS J. ARCUDI III Louis J. Arcudi, III	Chief Financial Officer and Treasurer (Principal Financial and Accounting Officer)	March 15, 2017
/S/ JAMES A. GERAGHTY James A. Geraghty	Chairman of the Board of Directors	March 15, 2017
/S/ SUDHIR AGRAWAL Sudhir Agrawal, D. Phil.	Director	March 15, 2017
/S/ JULIAN C. BAKER Julian C. Baker	Director	March 15, 2017
/S/ YOUSSEF EL ZEIN Youssef El Zein	Director	March 15, 2017
/S/ MARK GOLDBERG Mark Goldberg, M.D.	Director	March 15, 2017
/S/ MAXINE GOWEN Maxine Gowen, Ph.D.	Director	March 15, 2017
/S/ KELVIN M. NEU Kelvin M. Neu, M.D.	Director	March 15, 2017
/S/ WILLIAM S. REARDON William S. Reardon, C.P.A.	Director	March 15, 2017

IDERA PHARMACEUTICALS, INC.

INDEX TO FINANCIAL STATEMENTS
December 31, 2016

REPORT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

The Board of Directors and Stockholders of Idera Pharmaceuticals, Inc.

We have audited the accompanying balance sheets of Idera Pharmaceuticals, Inc. (the Company) as of December 31, 2016 and 2015, and the related statements of operations and comprehensive loss, stockholders' equity, and cash flows for each of the three years in the period ended December 31, 2016. These financial statements are the responsibility of the Company's management. Our responsibility is to express an opinion on these financial statements based on our audits.

We conducted our audits in accordance with the standards of the Public Company Accounting Oversight Board (United States). Those standards require that we plan and perform the audit to obtain reasonable assurance about whether the financial statements are free of material misstatement. An audit includes examining, on a test basis, evidence supporting the amounts and disclosures in the financial statements. An audit also includes assessing the accounting principles used and significant estimates made by management, as well as evaluating the overall financial statement presentation. We believe that our audits provide a reasonable basis for our opinion.

In our opinion, the financial statements referred to above present fairly, in all material respects, the financial position of Idera Pharmaceuticals, Inc. at December 31, 2016 and 2015, and the results of its operations and its cash flows for each of the three years in the period ended December 31, 2016, in conformity with U.S. generally accepted accounting principles.

We also have audited, in accordance with the standards of the Public Company Accounting Oversight Board (United States), Idera Pharmaceuticals, Inc.'s internal control over financial reporting as of December 31, 2016, based on criteria established in Internal Control-Integrated Framework issued by the Committee of Sponsoring Organizations of the Treadway Commission (2013 framework) and our report dated March 15, 2017 expressed an unqualified opinion thereon.

/s/ ERNST & YOUNG LLP

Boston, Massachusetts
March 15, 2017

IDERA PHARMACEUTICALS, INC.
BALANCE SHEETS

(In thousands, except per share amounts)	December 31, 2016	December 31, 2015
ASSETS		
Current assets:		
Cash and cash equivalents	$ 80,667	$ 26,586
Short-term investments	28,347	33,574
Prepaid expenses and other current assets	2,030	3,082
Total current assets	111,044	63,242
Long-term investments	—	26,997
Property and equipment, net	1,853	1,692
Restricted cash and other assets	334	345
Total assets	$ 113,231	$ 92,276
LIABILITIES AND STOCKHOLDERS' EQUITY		
Current liabilities:		
Accounts payable	$ 556	$ 1,169
Accrued expenses	7,394	4,274
Current portion of note payable	292	261
Current portion of deferred revenue	1,111	1,111
Total current liabilities	9,353	6,815
Deferred revenue, net of current portion	152	1,262
Note payable, net of current portion	209	501
Other liabilities	168	116
Total liabilities	9,882	8,694
Commitments and contingencies		
Stockholders' equity:		
Preferred stock, $0.01 par value, Authorized — 5,000 shares:		
Series A convertible preferred stock; Designated — 1,500 shares, Issued and outstanding — 1 share	—	—
Common stock, $0.001 par value, Authorized — 280,000 shares; Issued and outstanding — 149,065 and 121,265 shares at December 31, 2016 and December 31, 2015, respectively	149	121
Additional paid-in capital	641,687	583,676
Accumulated deficit	(538,470)	(500,081)
Accumulated other comprehensive loss	(17)	(134)
Total stockholders' equity	103,349	83,582
Total liabilities and stockholders' equity	$ 113,231	$ 92,276

The accompanying notes are an integral part of these financial statements.

IDERA PHARMACEUTICALS, INC.
STATEMENTS OF OPERATIONS AND COMPREHENSIVE LOSS

(In thousands, except per share amounts)	Year Ended December 31, 2016	2015	2014
Alliance revenue	$ 16,199	$ 249	$ 73
Operating expenses:			
Research and development	39,824	33,699	27,493
General and administrative	15,132	15,396	11,332
Total operating expenses	54,956	49,095	38,825
Loss from operations	(38,757)	(48,846)	(38,752)
Other income (expense):			
Interest income	415	357	66
Interest expense	(80)	(105)	(27)
Foreign currency exchange gain	33	39	71
Net loss	(38,389)	(48,555)	(38,642)
Loss on extinguishment of convertible preferred stock and preferred stock dividends	—	—	519
Net loss	$ (38,389)	$ (48,555)	$ (39,161)
Basic and diluted net loss per common share (Note 12)	$ (0.30)	$ (0.42)	$ (0.47)
Shares used in computing basic and diluted net loss per common share	127,597	115,092	82,827
Net loss	$ (38,389)	$ (48,555)	$ (38,642)
Other comprehensive gain (loss):			
Unrealized gain (loss) on available-for-sale securities	117	(117)	(10)
Other comprehensive gain (loss):	117	(117)	(10)
Comprehensive loss	$ (38,272)	$ (48,672)	$ (38,652)

The accompanying notes are an integral part of these financial statements.

IDERA PHARMACEUTICALS, INC.
STATEMENTS OF STOCKHOLDERS' EQUITY

(In thousands)	Series E Convertible Preferred Stock		Series D Convertible Preferred Stock		Common Stock		Additional Paid-In Capital	Accumulated Deficit	Accumulated Other Comprehensive (Loss)/Income	Total Stockholders' Equity
	Number of Shares	Amount	Number of Shares	Amount	Number of Shares	$0.001 Par Value				
Balance, December 31, 2013	424	$ 5,528	1,124	5,464	66,252	$ 66	$ 434,285	$ (412,884)	$ (7)	$ 32,452
Sale of common stock and warrants, net of issuance costs	—	—	—	—	7,867	8	37,229	—	—	37,237
Exercise of common stock options, warrants and employee stock purchases	—	—	—	—	5,932	6	8,450	—	—	8,456
Issuance of common stock for services	—	—	—	—	27	—	82	—	—	82
Non-employee stock option expense	—	—	—	—	—	—	24	—	—	24
Stock-based compensation	—	—	—	—	—		4,322	—	—	4,322
Series D convertible preferred stock dividends	—	—	—	—	—	—	(66)	—	—	(66)
Series E convertible preferred stock dividends	—	—	—	—	—	—	(453)	—	—	(453)
Unrealized loss on marketable securities	—	—	—	—	—	—		—	(10)	(10)
Conversion of Series D preferred stock to common	—	—	(1,124)	(5,464)	6,266	6	5,458	—	—	—
Conversion of Series E preferred stock to common	(424)	(5,528)	—	—	8,485	9	5,519	—	—	—
Net loss	—	—	—	—	—	—		(38,642)	—	(38,642)
Balance, December 31, 2014	—	$ —	—	$ —	94,829	$ 95	$ 494,850	$ (451,526)	$ (17)	$ 43,402
Sale of common stock, net of issuance costs	—	—	—	—	23,000	23	80,576	—	—	80,599
Exercise of common stock options, warrants and employee stock purchases	—	—	—	—	3,402	3	2,543	—	—	2,546
Issuance of common stock for services	—	—	—	—	34	—	122	—	—	122
Non-employee stock option expense	—	—	—	—	—	—	143	—	—	143
Stock-based compensation	—	—	—	—	—	—	5,442	—	—	5,442
Unrealized loss on marketable securities	—	—	—	—	—	—		—	(117)	(117)
Net loss	—	—	—	—	—	—	—	(48,555)	—	(48,555)
Balance, December 31, 2015	—	—	—	—	121,265	$ 121	$ 583,676	$ (500,081)	$ (134)	$ 83,582
Sale of common stock, net of issuance costs	—	—	—	—	26,225	26	48,822	—	—	48,848
Exercise of common stock options, warrants and employee stock purchases	—	—	—	—	1,575	2	2,342	—	—	2,344
Stock-based compensation	—	—	—	—	—	—	6,847	—	—	6,847
Unrealized gain on marketable securities	—	—	—	—	—	—	—	—	117	117
Net loss	—	—	—	—	—	—	—	(38,389)	—	(38,389)
Balance, December 31, 2016	—	—	—	—	149,065	$ 149	$ 641,687	$ (538,470)	$ (17)	$ 103,349

The accompanying notes are an integral part of these financial statements.

IDERA PHARMACEUTICALS, INC.
STATEMENTS OF CASH FLOWS

(In thousands)	Year Ended December 31, 2016	2015	2014
Cash Flows from Operating Activities:			
Net loss	$ (38,389)	$ (48,555)	$ (38,642)
Adjustments to reconcile net loss to net cash used in operating activities:			
Loss from disposition of assets	4	—	1
Non-employee stock option expense	—	143	24
Stock-based compensation	6,847	5,442	4,322
Issuance of common stock for services rendered	172	122	82
Accretion of premiums and discounts on investments	566	599	213
Depreciation and amortization expense	656	488	206
Changes in operating assets and liabilities:			
Prepaid expenses and other current assets	1,064	(1,889)	(329)
Accounts payable, accrued expenses, and other liabilities	1,988	(1,709)	2,802
Deferred revenue	(1,111)	2,373	—
Net cash used in operating activities	(28,203)	(42,986)	(31,321)
Cash Flows from Investing Activities:			
Purchases of available-for-sale securities	(2,946)	(63,106)	(23,623)
Proceeds from maturity of available-for-sale securities	32,746	29,420	4,115
Proceeds from sale of available-for-sale securities	1,974	999	—
Purchases of property and equipment	(408)	(727)	(1,093)
Net cash provided by (used in) investing activities	31,366	(33,414)	(20,601)
Cash Flows from Financing Activities:			
Sale of common stock and warrants, net of issuance costs	49,014	80,599	37,137
Proceeds from issuance of note payable	—	—	825
Proceeds from exercise of common stock warrants and options and employee stock purchases	2,172	2,546	8,456
Dividends paid	—	—	(798)
Payments on note payable	(261)	(120)	—
Payments on capital lease	(7)	(10)	(5)
Net cash provided by financing activities	50,918	83,015	45,615
Net increase (decrease) in cash and cash equivalents	54,081	6,615	(6,307)
Cash and cash equivalents, beginning of period	26,586	19,971	26,278
Cash and cash equivalents, end of period	$ 80,667	$ 26,586	$ 19,971

The accompanying notes are an integral part of these financial statements.

IDERA PHARMACEUTICALS, INC.

NOTES TO FINANCIAL STATEMENTS
December 31, 2016

1. Organization

Idera Pharmaceuticals, Inc. ("Idera" or the "Company") is a clinical-stage biopharmaceutical company focused on the discovery, development and commercialization of novel therapeutics for oncology and rare diseases. The Company uses two distinct proprietary drug discovery technology platforms to design and develop drug candidates: Toll-like receptor ("TLR") targeting technology and third-generation antisense ("3GA") technology. The Company developed these platforms based on its scientific expertise and pioneering work with synthetic oligonucleotides as therapeutic agents. Using its TLR targeting technology, the Company designs synthetic oligonucleotide-based drug candidates to modulate the activity of specific TLRs. In addition, using its 3GA technology, the Company is developing drug candidates to turn off the messenger RNA ("mRNA") associated with disease causing genes. The Company believes that its 3GA technology may potentially reduce the immunotoxicity and increase the potency of earlier generation antisense and RNA interference ("RNAi") technologies.

Idera is focused on the clinical development of drug candidates for oncology and rare diseases characterized by small, well-defined patient populations with serious unmet medical needs. The Company believes it can develop and commercialize these targeted therapies on its own. To the extent the Company seeks to develop drug candidates for broader disease indications, it may explore potential collaborative alliances to support development and commercialization.

The Company's pipeline of drug candidates includes IMO-2125, IMO-8400 and IDRA-008. TLRs are key receptors of the immune system and play a role in innate and adaptive immunity. As a result, the Company believes TLRs are potential therapeutic targets for the treatment of a broad range of diseases. Using its chemistry-based platform, the Company has designed TLR agonists and antagonists to act by modulating the activity of targeted TLRs. A TLR agonist is a compound that stimulates an immune response through the targeted TLR. A TLR antagonist is a compound that inhibits an immune response by blocking the targeted TLR.

The Company's TLR agonist lead drug candidate IMO-2125 is an agonist of TLR9. The Company is evaluating IMO-2125 for the treatment by intra-tumoral injection of multiple oncology indications both in combination with checkpoint inhibitors and as monotherapy. The Company is initially developing IMO-2125 for use in combination with checkpoint inhibitors for the treatment of patients with anti-PD1 refractory metastatic melanoma.

The Company's TLR antagonist lead drug candidate is IMO-8400, which is an antagonist of TLR7, TLR8 and TLR9. The Company is developing IMO-8400 for the treatment of a rare disease called dermatomyositis. The Company selected this indication for development based on the reported increase in TLR expression in this disease state, expression of cytokines indicative of key TLR-mediated pathways and the presence of auto-antibodies that can induce TLR-mediated immune responses.

The Company is developing its 3GA technology to "turn off" the mRNA associated with disease causing genes. The Company designed 3GA oligonucleotides to specifically address challenges associated with earlier generation antisense and RNAi technologies. Although currently used technologies to silence RNA have demonstrated the ability to inhibit the expression of disease-associated proteins, the Company believes that to reach their full therapeutic potential, gene silencing technologies need to achieve an improved therapeutic index with efficient systemic delivery, reduced immunotoxicity and increased potency. The Company has designed its 3GA oligonucleotides to provide these attributes.

As of December 31, 2016 the Company had an accumulated deficit of $538.5 million. The Company expects to incur substantial operating losses in future periods. The Company does not expect to generate significant product revenue, sales-based milestones or royalties until the Company successfully completes development and obtains marketing approval for drug candidates, either alone or in collaborations with third parties, which the Company expects will take a number of years. In order to commercialize its drug candidates, the Company needs to complete clinical development and comply with comprehensive regulatory requirements.

The Company is subject to a number of risks and uncertainties similar to those of other companies of the same size within the biotechnology industry, such as uncertainty of clinical trial outcomes, uncertainty of additional funding, and history of operating losses.

2. Summary of Significant Accounting Policies

(a) Basis of Presentation

The preparation of financial statements in conformity with accounting principles generally accepted in the United States requires management to make estimates and assumptions that affect the reported amounts of assets and liabilities and disclosure of contingent assets and liabilities at the date of the financial statements and the reported amounts of revenues and expenses during the reporting period. Actual results could differ from those estimates.

(b) Cash, Cash Equivalents and Investments

The Company considers all highly liquid investments with maturities of 90 days or less when purchased to be "cash equivalents." Cash and cash equivalents at December 31, 2016 and 2015 consisted of cash and money market funds.

Management determines the appropriate classification of marketable securities at the time of purchase. Investments that the Company does not have the positive intent to hold to maturity are classified as "available-for-sale" and reported at fair market value. Available-for-sale investments are classified as long-term if their contractual maturity is greater than one year at the balance sheet date and the Company does not have the intent to sell them in order to fund current operations. Unrealized gains and losses associated with available-for-sale investments are recorded in "Accumulated other comprehensive income" on the accompanying balance sheets. The amortization of premiums and accretion of discounts, and any realized gains and losses and declines in value judged to be other-than-temporary, and interest and dividends for all available-for-sale securities are included in "Interest income" on the accompanying statements of operations. Investments that the Company intends to hold to maturity are classified as "held-to-maturity" investments. The Company had no "held-to-maturity" investments at either December 31, 2016 or 2015. The cost of securities sold is based on the specific identification method.

The Company had no realized gains or losses from available-for-sale securities in 2016, 2015 or 2014. There were no losses or other-than-temporary declines in value included in "Interest income" for any securities for the three years ended December 31, 2016.

The Company believes that, based on its current operating plan, its existing cash, cash equivalents and investments will enable the Company to fund its operations into the second quarter of 2018. The Company has and will continue to evaluate available alternatives to extend its operations beyond the second quarter of 2018.

(c) Restricted Cash

As part of the Company's lease arrangement for its office and laboratory facility in Cambridge, Massachusetts, the Company is required to restrict cash held in a certificate of deposit securing a line of credit for the lessor. As of December 31, 2016 and 2015, the restricted cash amounted to $0.3 million held in certificates of deposit securing a line of credit for the lessor.

(d) Depreciation and Amortization

Depreciation and amortization are computed using the straight-line method based on the estimated useful lives of the related assets. Laboratory and other equipment are depreciated over three to five years. Leasehold improvements are amortized over the remaining lease term or the related useful life, if shorter.

(e) Revenue Recognition

The Company recognizes revenue in accordance with the Financial Accounting Standards Board's (FASB) Accounting Standards Codification ("ASC") Topic 605, *Revenue Recognition*. Accordingly, revenue is recognized for each unit of accounting when all of the following criteria are met:

- persuasive evidence of an arrangement exists;
- delivery has occurred or services have been rendered;
- the seller's price to the buyer is fixed or determinable; and
- collectability is reasonably assured.

Amounts received prior to satisfying the revenue recognition criteria are recognized as deferred revenue in the Company's balance sheet. Amounts expected to be recognized as revenue within the 12 months following the balance sheet date are classified as deferred revenue, current. Amounts not expected to be recognized as revenue within the 12 months following the balance sheet date are classified as deferred revenue, net of current portion.

The Company's revenues have primarily been generated through collaborative research, development and/or commercialization agreements. The terms of these agreements typically may include payment to the Company of one or more of the following: nonrefundable, up-front license fees, research, development and commercial milestone payments, other contingent payments due based on the activities of the counterparty or the reimbursement by licensees of costs associated with patent maintenance. Each of these types of revenue are recorded as Alliance revenues in the Company's statement of operations.

For each collaborative research, development and/or commercialization agreement, which results in revenues, the Company determines (i) whether multiple deliverables exist, (ii) whether the delivered elements have value to the customer on a stand-alone basis, (iii) how the deliverables should be separated or combined and (iv) how the consideration should be allocated to the deliverables.

Arrangement consideration that is fixed or determinable is allocated among the separate units of accounting using the relative selling price method. Then, the applicable revenue recognition criteria in ASC 605 are applied to each of the separate units of accounting in determining the appropriate period and pattern of recognition. The Company determines the selling price of a unit of accounting following the hierarchy of evidence prescribed by ASC 605-25. Accordingly, the Company determines the estimated selling price for units of accounting within each arrangement using vendor-specific objective evidence ("VSOE") of selling price, if available, third-party evidence ("TPE") of selling price if VSOE is not available, or best estimate of selling price ("BESP") if neither VSOE nor TPE is available. The Company typically uses BESP to estimate the selling price, since the Company generally does not have VSOE or TPE of selling price for its units of accounting. Determining the BESP for a unit of accounting requires significant judgment. In developing the BESP for a unit of accounting, the Company considers applicable market conditions and relevant entity-specific factors, including factors that were contemplated in negotiating the agreement with the customer and estimated costs. The Company validates the BESP for units of accounting by evaluating whether changes in the key assumptions used to determine the BESP will have a significant effect on the allocation of arrangement consideration between multiple units of accounting.

Options are considered substantive if, at the inception of the arrangement, this Company is at risk as to whether the collaborator will choose to exercise the option. Factors that the Company considers in evaluating whether an option is substantive include the overall objective of the arrangement, the benefit the collaborator might obtain from the arrangement without exercising the option, the cost to exercise the option and the likelihood that the option will be exercised. For arrangements under which an option is considered substantive, the Company does not consider the item underlying the option to be a deliverable at the inception of the arrangement and the associated option fees are not included in allocable arrangement consideration, assuming the option is not priced at a significant and incremental discount. Conversely, for arrangements under which an option is not considered substantive or if an option is priced at a significant and incremental discount, the Company would consider the item underlying the option to be a deliverable at the inception of the arrangement and a corresponding amount would be included in allocable arrangement consideration.

The Company recognizes arrangement consideration allocated to each unit of accounting when all of the revenue recognition criteria in ASC 605 are satisfied for that particular unit of accounting. The Company will recognize as revenue arrangement consideration attributed to licenses that have standalone value from the other deliverables to be provided in an arrangement upon delivery. The Company will recognize as revenue arrangement consideration attributed to licenses that do not have standalone value from the other deliverables to be provided in an arrangement over our estimated performance period as the arrangement would be accounted for as a single unit of accounting.

The Company's multiple element revenue arrangements may include the following:

Up-front License Fees: If a license does not have stand-alone value, the Company recognizes revenues from nonrefundable, up-front license fees on a straight-line basis over the contracted or estimated period of performance of the services under the related agreement, unless evidence suggests that revenue is earned or obligations are fulfilled in a different pattern. The Company evaluates the period of performance each reporting period and adjusts the period of performance on a prospective basis if there are changes to be made. If a license were to have stand-alone value and the other criteria of revenue recognition were satisfied, then revenue would be recognized in the period earned.

Milestone Payments: At the inception of an agreement that includes research and development milestone payments, the Company evaluates whether each milestone is substantive or represents a deliverable of the counterparty to the agreement. The Company recognized revenues related to substantive milestones in full in the period in which the substantive milestone is achieved if payment is reasonably assured. If a milestone is a deliverable of the counterparty to the agreement, it is considered contingent revenue and is recognized when the Company is informed by the counterparty that they have achieved it and such amount is reasonably assured of payment.

Research and Development Activities: If the Company is entitled to reimbursement from its collaborators for specified research and development activities or the reimbursement of costs associated with patent maintenance, the Company determines whether such funding would result in alliance revenues or an offset to research and development expenses. Reimbursement of patent maintenance costs are recognized during the period in which the related expenses are incurred as alliance revenues in the Company's statement of operations.

Royalties: If the Company is entitled to receive royalties from its collaborator for product sales, the Company will recognize royalty revenue in the period of sale of the related product(s), based on the underlying contract terms, provided that the reported sales are reliably measurable and the Company has no remaining performance obligations, assuming all other revenue recognition criteria are met.

Under the terms of the Company's exclusive license and collaboration agreement with Vivelix Pharmaceuticals, Ltd. ("Vivelix") which granted Vivelix worldwide rights to develop and market IMO-9200, an antagonist of TLR7, 8, and 9, for non-malignant gastrointestinal disorders, and certain back-up compounds to IMO-9200 (the "Vivelix Agreement"), the Company received an upfront, non-refundable fee of $15 million. In addition, the Company will be eligible for future IMO-9200 related development, regulatory and sales milestone payments totaling up to $140 million, including development and regulatory milestones totaling up to $65 million and sales milestones totaling up to $75 million, and escalating royalties ranging from the mid single-digits to low double-digits of global net sales, which percentages are subject to reduction under agreed upon circumstances. As it relates to back-up compounds, the Company will be eligible for related designation payments and development, regulatory sales and milestone payments totaling up to $52.5 million, including development and regulatory milestones totaling up to $35 million and sales milestones totaling up to $17.5 million and escalating royalties ranging from the mid single-digits to low double-digits of global net sales, which percentages are subject to reduction under agreed upon circumstances.

Under the terms of the Company's collaboration and license agreement with GlaxoSmithKline Intellectual Property Development Limited ("GSK") to license, research, develop and commercialize pharmaceutical compounds from the Company's 3GA technology for the treatment of selected targets in renal disease (the "GSK Agreement"), the Company is eligible to receive up to approximately $100 million in license, research, clinical development and commercialization milestone payments, including a $2.5 million upfront, non-refundable, non-creditable cash payment. Approximately $9 million of the milestone payments are payable by GSK upon the identification of additional targets, the completion of current and future research plans and the designation of development candidates. Approximately $89 million is payable by GSK upon the achievement of clinical milestones and commercial milestones. In addition, the Company is eligible to receive royalty payments based on net sales of licensed products following commercialization at varying rates of up to five percent on annual net sales, as defined in the GSK Agreement.

(f) Financial Instruments

The fair value of the Company's financial instruments is determined and disclosed in accordance with the three-tier fair value hierarchy specified in Note 2(m). The Company is required to disclose the estimated fair values of its financial instruments. The Company's financial instruments consist of cash, cash equivalents, available-for-sale investments, receivables and a note payable. The estimated fair values of these financial instruments approximate their carrying values as of December 31, 2016 and 2015. As of December 31, 2016 and 2015, the Company did not have any derivatives, hedging instruments or other similar financial instruments except for the note issued under the Company's loan and security agreement, which is discussed in Note 5(a), including put and call features which the Company determined are clearly and closely associated with the debt host and do not require bifurcation as a derivative liability, or the fair value of the feature is immaterial.

(g) Comprehensive Income (Loss)

Comprehensive income (loss) is defined as the change in equity of a business enterprise during a period from transactions and other events and circumstances from non-owner sources. Comprehensive income (loss) for the years ended December 31, 2016, 2015 and 2014 is comprised of reported net income (loss) and any change in net unrealized gains and losses on investments during each year, which is included in "Accumulated other comprehensive income" on the accompanying balance sheets. The Company applies Accounting Standards Update ("ASU") No. 2011-05, "Comprehensive Income" by presenting the components of net income and other comprehensive income as one continuous statement.

The following table includes the changes in the accumulated balance of the component of other comprehensive loss for the years ended December 31, 2016, 2015 and 2014:

	Year Ended December 31,		
(In thousands)	**2016**	**2015**	**2014**
Accumulated unrealized loss on available-for-sale securities at beginning of period	$ (134)	$ (17)	$ (7)
Change during the period	117	(117)	(10)
Accumulated unrealized loss on available-for-sale securities at end of period	$ (17)	$ (134)	$ (17)

(h) Net Income (Loss) per Common Share applicable to Common Stockholders

Basic and diluted net loss per common share applicable to common stockholders is computed using the weighted average number of shares of common stock outstanding during the period. Diluted net loss per common share applicable to common stockholders is the same as basic net loss per common share applicable to common stockholders for each of the three years in the period ended December 31, 2016 as the effects of the Company's potential common stock equivalents are antidilutive (see Note 12).

(i) Segment Reporting

The Company views its operations and manages its business as one operating segment. Accordingly, the Company operates in one segment, which is the business of discovering and developing novel therapeutics that modulate immune responses through TLRs. As a result, the financial information disclosed herein represents all of the material financial information related to the Company's principal operating segment. For all of the periods presented, all of the Company's revenues were generated in the United States. As of December 31, 2016 and 2015, all assets were located in the United States.

(j) Stock-Based Compensation

The Company recognizes all share-based payments to employees and directors as expense in the statements of operations and comprehensive loss based on their fair values. The Company records compensation expense over an award's requisite service period, or vesting period, based on the award's fair value at the date of grant. The Company's policy is to charge the fair value of stock options as an expense, adjusted for forfeitures, on a straight-line basis over the vesting period, which is generally four years for employees and three years for directors.

The Company recorded charges of $6.8 million, $5.4 million and $4.3 million for the years ended December 31, 2016, 2015 and 2014, respectively, for stock-based compensation expense attributable to share-based payments made to employees and directors. The 2015 charge includes approximately $0.3 million of stock-based compensation in connection with the recognition of additional expense associated with the acceleration of vesting and extension of the exercise period of a retiring director's stock options as a result of a modification to such director's stock options. The 2014 charge includes approximately $1.3 million for the recognition of amortization associated with an employee's options that were subject to accelerated vesting as a result of a modification to such employee's stock options. The fair value of each option award is estimated on the date of grant using the Black-Scholes option pricing model. The following weighted average assumptions apply to the options to purchase 3,346,250, 3,533,750, and 8,232,424 shares of common stock granted to employees and directors during the years ended December 31, 2016, 2015 and 2014, respectively:

	2016	2015	2014
Average risk free interest rate	1.4%	1.4%	1.4%
Expected dividend yield	—	—	—
Expected lives (years)	4.2	4.2	4.4
Expected volatility	93%	93%	86%
Weighted average grant date fair value of options granted during the period (per share)	$ 1.75	$ 2.51	$ 2.36
Weighted average exercise price of options granted during the period (per share)	$ 2.64	$ 3.74	$ 3.69

The expected lives of the options and the expected volatility are based on historical experience. All options granted during the three years in the period ended December 31, 2016 were granted at exercise prices equal to the fair market value of the common stock on the dates of grant**.**

The fair value of options that vested during 2016, 2015 and 2014 amounted to $6.9 million, $5.4 million and $4.2 million, respectively. There were no options exercised in 2016. The intrinsic value of options exercised amounted to $0.8 million and $0.6 million during 2015 and 2014, respectively. As of December 31, 2016, there was $13.4 million of unrecognized compensation cost related to nonvested stock-based compensation arrangements, which the Company expects to recognize over a weighted average period of 2.4 years.

(k) Research and Development Expenses

All research and development expenses, including amounts funded by research collaborations, are expensed as incurred. Research and development expenses are comprised of costs incurred in performing research and development activities, including drug development trials and studies, drug manufacturing, laboratory supplies, external research, payroll including stock-based compensation and overhead. Nonrefundable advance payments for goods or services to be received in the future for use in research and development activities are deferred and capitalized. The capitalized amounts are expensed as the related goods are accepted by the Company or the services are performed. As of December 31, 2016 and 2015, the Company recorded approximately $1.4 million and $2.3 million as prepaid research and development, respectively.

(l) Concentration of Credit Risk

Financial instruments that subject the Company to credit risk primarily consist of cash and cash equivalents and available-for-sale investments. The Company's credit risk is managed by investing its cash and cash equivalents and marketable securities in highly rated money market instruments, certificates of deposit, corporate bonds, and debt securities. Due to these factors, no significant additional credit risk is believed by management to be inherent in the Company's assets. As of December 31, 2016, all of the Company's cash, cash equivalents and investments are held at two financial institutions.

(m) Fair Value of Assets and Liabilities

The Company measures fair value at the price that would be received to sell an asset or paid to transfer a liability in an orderly transaction between market participants at the measurement date using assumptions that market participants would use in pricing the asset or liability (the "inputs") into a three-tier fair value hierarchy. This fair value hierarchy gives the highest priority (Level 1) to quoted prices in active markets for identical assets or liabilities and the lowest priority (Level 3) to unobservable inputs in which little or no market data exists, requiring companies to develop their own assumptions. Observable inputs that do not meet the criteria of Level 1, and include quoted prices for similar assets or

liabilities in active markets or quoted prices for identical assets and liabilities in markets that are not active, are categorized as Level 2. Level 3 inputs are those that reflect the Company's estimates about the assumptions market participants would use in pricing the asset or liability, based on the best information available in the circumstances. Valuation techniques for assets and liabilities measured using Level 3 inputs may include unobservable inputs such as projections, estimates and management's interpretation of current market data. These unobservable Level 3 inputs are only utilized to the extent that observable inputs are not available or cost-effective to obtain. The Company applies ASU No. 2011-04, "Fair Value Measurement (Topic 820)," in its fair value measurements and disclosures.

The table below presents the assets and liabilities measured and recorded in the financial statements at fair value on a recurring basis at December 31, 2016 and 2015 categorized by the level of inputs used in the valuation of each asset and liability.

(In thousands)	Total	Quoted Prices in Active Markets for Identical Assets or Liabilities (Level 1)	Significant Other Observable Inputs (Level 2)	Significant Unobservable Inputs (Level 3)
December 31, 2016				
Assets				
Money market funds	$ 67,580	$ 67,580	$ —	$ —
Short-term investments – corporate bonds	19,729	—	19,729	—
Short-term investments – municipal bonds	8,618	—	8,618	—
Total Assets	$ 95,927	$ 67,580	$ 28,347	$ —
Total Liabilities	$ —	$ —	$ —	$ —
December 31, 2015				
Assets				
Money market funds	$ 26,056	$ 26,056	$ —	$ —
Short-term investments – commercial paper	3,974	—	3,974	—
Short-term investments – corporate bonds	24,575	—	24,575	—
Short-term investments – municipal bonds	5,025	—	5,025	—
Long-term investments – corporate bonds	21,186	—	21,186	—
Long-term investments – municipal bonds	5,811	—	5,811	—
Total Assets	$ 86,627	$ 26,056	$ 60,571	$ —
Total Liabilities	$ —	$ —	$ —	$ —

The Level 1 assets consist of money market funds, which are actively traded daily. The Level 2 assets consist of corporate bond, commercial paper, and municipal bond investments whose fair value may not represent actual transactions of identical securities. The fair value of corporate and municipal bonds is generally determined from quoted market prices received from pricing services based upon quoted prices from active markets and/or other significant observable market transactions at fair value. The fair value of commercial paper is generally determined based on the relationship between the investment's discount rate and the discount rates of the same issuer's commercial paper available in the market which may not be actively traded daily. Since these fair values may not be based upon actual transactions of identical securities, they are classified as Level 2. Since any investments are classified as available-for-sale securities, any unrealized gains or losses are recorded in accumulated other comprehensive income or loss within stockholders' equity on the balance sheet. The Company did not elect to measure any other financial assets or liabilities at fair value at December 31, 2016 or 2015.

(n) New Accounting Pronouncements — Recently Issued

In May 2014, the Financial Accounting Standards Board (the "FASB") issued Accounting Standards Update ("ASU") No. 2014-09, Revenue from Contracts with Customers (Topic 606), which was amended by ASU No. 2015-14. ASU No. 2014-09, as amended by ASU No. 2015-14, requires an entity to recognize revenue from the transfer of promised goods or services to customers in an amount that reflects the consideration to which the entity expects to be entitled in exchange for those goods or services. In particular, this ASU addresses contracts with more than one performance obligation, as well as the accounting for some costs to obtain or fulfill a contract with a customer, and provides for additional disclosures with respect to revenues and cash flows arising from contracts with customers. This ASU will be

effective for fiscal years beginning after December 15, 2017, including interim periods within that fiscal year. Early adoption of this ASU is permitted only for fiscal years beginning after December 15, 2016, including interim periods within that fiscal year. The Company expects to adopt ASU 2014-09 in the first quarter of 2018 and is currently determining the transition method it will adopt. The adoption of ASU 2014-09 may have a material effect on our financial statements, including the footnote disclosures. To date, we have derived our revenues from a limited number of license and collaboration agreements. The consideration we are eligible to receive under these agreements includes upfront payments, research and development funding, contingent revenues in the form of commercial and development milestones and option payments and royalties. Each of our license and collaboration agreements has unique terms that will need to be evaluated separately under the new standard. We have started our preliminary assessment of our active license and collaboration agreements. ASU 2014-09 differs from the current accounting standard in many respects, such as in the accounting for variable consideration, including milestone payments. Accordingly, we expect that our evaluation of the accounting for collaboration agreements under the new revenue standard could identify material changes from the current accounting treatment. In addition, the current accounting standards include a presumption that revenue from upfront non-refundable fees are recognized ratably over the performance period, unless another attribution method is determined to more closely approximate the delivery of the goods or services to the customer. The new accounting standard will require entities to determine an appropriate attribution method using either output or input methods and does not include a presumption that entities would default to a ratable attribution approach. These factors could materially impact the amount and timing of our revenue recognition from our license and collaboration agreements under the new revenue standard.

In August 2014, the FASB issued ASU No. 2014-15, Disclosure of Uncertainties about an Entity's Ability to Continue as a Going Concern. ASU 2014-15 amends FASB ASC 205-40, Presentation of Financial Statements – Going Concern, by providing guidance on determining when and how reporting entities must disclose going-concern uncertainties in their financial statements, including requiring management to perform interim and annual assessments of an entity's ability to continue as a going concern within one year of the date of issuance of the entity's financial statements and providing certain disclosures if there is substantial doubt about the entity's ability to continue as a going concern. ASU 2014-15 will be effective for fiscal years ending after December 15, 2016 and for interim periods thereafter. Early adoption of ASU 2014-15 is permitted. The Company has adopted this standard, which has not had a material impact on its financial statements.

In January 2016, the FASB issued ASU No. 2016-01, Recognition and Measurement of Financial Assets and Financial Liabilities. The amendments in ASU 2016-01 address certain aspects of recognition, measurement, presentation and disclosure of financial instruments. ASU 2016-01 will be effective for fiscal years beginning after December 15, 2017, including interim periods within those fiscal years. Early adoption of some of the amendments included in ASU 2016-01 for financial statements of fiscal years or interim periods that have not yet been issued is permitted as of the beginning of the fiscal year of adoption. The Company is currently evaluating the effect that the adoption of ASU 2016-01 will have on its financial statements.

In February 2016, the FASB issued ASU No. 2016-02, Leases. The amendments in ASU 2016-02 will require organizations that lease assets, with lease terms of more than 12 months, to recognize on the balance sheet the assets and liabilities for the rights and obligations created by those leases. Consistent with current U.S. Generally Accepted Accounting Principles ("U.S. GAAP"), the recognition, measurement, and presentation of expenses and cash flows arising from a lease by a lessee primarily will depend on its classification as a finance or operating lease. However, unlike current U.S. GAAP which requires only capital leases to be recognized on the balance sheet, ASU No. 2016-02 will require both types of leases to be recognized on the balance sheet. ASU 2016-02 will be effective for fiscal years beginning after December 15, 2018, including interim periods within those fiscal years. Early adoption is permitted. The Company is currently evaluating the effect that the adoption of ASU 2016-02 will have on its financial statements.

In March 2016, the FASB issued ASU No. 2016-09, Compensation – Stock Compensation (Topic 718). ASU 2016-09 will require organizations to recognize all income tax effects of awards in the statement of operations when the awards vest or are settled. ASU 2016-09 will also allow organizations to repurchase more shares from employees than they could previously purchase for tax withholding purposes without triggering liability accounting and to make a policy election to account for forfeitures as they occur. ASU 2016-09 will be effective for fiscal years beginning after December 15, 2016, and interim periods within those fiscal years. Early adoption is permitted in any interim or annual period. The Company is currently evaluating the effect that the adoption of ASU 2016-09 will have on its financial statements.

3. Investments

The Company's available-for-sale investments at fair value consisted of the following at December 31, 2016 and 2015:

	December 31, 2016			
	Cost	Gross Unrealized (Losses)	Gross Unrealized Gain	Estimated Fair Value
	(In thousands)			
Short-term investments – corporate bonds	$ 19,740	$ (11)	$ —	$ 19,729
Short-term investments – municipal bonds	8,624	(6)	—	8,618
Total short-term investments	28,364	(17)	—	28,347
Total investments	$ 28,364	$ (17)	$ —	$ 28,347

	December 31, 2015			
	Cost	Gross Unrealized (Losses)	Gross Unrealized Gains	Estimated Fair Value
	(In thousands)			
Short-term investments – commercial paper	$ 3,973	$ —	$ 1	$ 3,974
Short-term investments – corporate bonds	24,600	(25)	—	24,575
Short-term investments – municipal bonds	5,025	—	—	5,025
Total short-term investments	33,598	(25)	1	33,574
Long-term investments – corporate bonds	21,289	(103)	—	21,186
Long-term investments – municipal bonds	5,818	(9)	2	5,811
Total long-term investments	27,107	(112)	2	26,997
Total investments	$ 60,705	$ (137)	$ 3	$ 60,571

The Company had no realized gains or losses from available-for-sale securities in 2016, 2015 or 2014. There were no losses or other-than-temporary declines in value included in "Interest income" for any securities for the three years ended December 31, 2016. The Company had no auction rate securities as of December 31, 2016 and 2015. See Notes 2(f) and 2(m).

4. Property and Equipment

At December 31, 2016 and 2015, net property and equipment at cost consisted of the following:

	December 31,	
(In thousands)	2016	2015
Leasehold improvements	$ 671	$ 603
Laboratory equipment and other	5,127	4,543
Total property and equipment, at cost	5,798	5,146
Less: Accumulated depreciation and amortization	3,945	3,454
Property and equipment, net	$ 1,853	$ 1,692

Depreciation and amortization expense on Property and equipment was approximately $0.6 million, $0.5 million and $0.2 million in 2016, 2015 and 2014, respectively. As of December 31, 2016, Property and equipment includes $0.4 million of equipment that was received in December 2016, but was not in service as of December 31, 2016. As this equipment was unpaid at December 31, 2016, the $0.4 million payment due is reported in Accrued expenses.

5. Note Payable and Accrued Expenses

(a) Note Payable

On September 30, 2014, the Company executed a loan and security agreement with Oxford Finance LLC ("Oxford"). Under the agreement, Oxford committed to lend the Company up to an aggregate principal amount of $3 million, through December 31, 2015, in one or more advances each of which is to be evidenced by a promissory note. The

Company's obligations to Oxford are secured by the specific laboratory, manufacturing, office or computer equipment financed under the agreement. Each equipment advance includes interest at a fixed interest rate equal to the greater of 7.50% per annum and 7.27% plus the three-month U.S. Libor Rate per annum, set at the time of funding. The principal amount of each equipment advance will be repaid in 36 monthly installments commencing on the applicable amortization date, which was July 1, 2015 for any equipment advance made on or before June 30, 2015. Monthly installments payable prior to July 1, 2015 consisted of interest only and monthly installments payable on or after July 1, 2015 consist of principal and accrued interest.

The Company is required to pay a final payment in an amount equal to 5.7% of the aggregate advanced amount under each equipment advance at the time that the final monthly installment is due or such earlier date as specified in the loan and security agreement. The final payments will be accrued as interest expense over the term of each equipment advance using the effective interest method. The weighted average annual effective interest rate on the notes payable based on the amount advanced through December 31, 2015, including accrual of the final payment, is 11.1%. If the Company prepays all or a portion of the principal amount of any equipment advance prior to maturity, it will be required to pay Oxford a prepayment fee of between 1% and 3% of the principal amount of such equipment advance.

As of December 31, 2016, the Company had received approximately $0.9 million in advances under the loan and security agreement and additional advances were not available under the agreement because the draw down period had expired. Aggregate future minimum payments, reflecting payments on outstanding principal plus interest, due under the loan and security agreement as of December 31, 2016, were as follows (in thousands):

Year Ended December 31,	
2017	$ 333
2018	219
Total minimum payments	552
Less amount representing interest	(80)
Notes payable, gross	472
Unamortized facility fee	(7)
Accrual of final payment	36
Notes payable, balance	501
Less current portion of notes payable	(292)
Non-current portion of notes payable	$ 209

The loan and security agreement includes standard affirmative and restrictive covenants, but does not include any covenants to attain or maintain any financial metrics, and also includes standard events of default, including payment defaults, breaches of covenants following any applicable cure period, a material impairment in the perfection or priority of Oxford's security interest or in the value of the collateral, a material impairment of the prospect of repayment of the loans and a material adverse change in the business, operations or conditions of the Company. Upon the occurrence of an event of default and following any applicable cure periods, a default interest rate of an additional 5% may be applied to the outstanding loan balances, and Oxford may declare all outstanding obligations immediately due and payable and take such other actions as set forth in the loan and security agreement.

The Company assessed all terms and features of the note that the Company issued under its loan and security agreement in order to identify any potential embedded features that would require bifurcation. As part of this analysis, the Company assessed the economic characteristics and risks of the note, including put and call features. The Company determined that all features of the note are clearly and closely associated with a debt host and do not require bifurcation as a derivative liability, or the fair value of the feature is immaterial. The Company will continue to reassess the features to determine if they require separate accounting on a quarterly basis.

(b) Accrued Expenses

At December 31, 2016 and 2015, accrued expenses consisted of the following:

	December 31,	
	2016	2015
	(In thousands)	
Payroll and related costs	$ 2,498	$ 2,325
Clinical and nonclinical trial expenses	3,577	1,339
Professional and consulting fees	840	425
Equipment purchase	368	—
Other	111	185
	$ 7,394	$ 4,274

The Equipment purchase relates to equipment received by the Company that was not in service and unpaid as of December 31, 2016.

6. Collaboration and License Agreements

(a) Collaboration with Vivelix

In November 2016, the Company entered into the Vivelix Agreement. Under the terms of the agreement, the Company granted Vivelix worldwide rights to develop and market IMO-9200 and certain back-up compounds to IMO-9200. Vivelix is solely responsible for the development and commercialization of IMO-9200 and any designated back-up compounds. In connection with the Vivelix Agreement, Idera also transferred certain drug material to Vivelix for Vivelix's use in its development activities.

In accordance with the Vivelix Agreement, a Joint Research Committee ("JRC") was formed with equal representation from Idera and Vivelix. The responsibilities of the JRC, include, but are not limited to monitoring the progress of the research program, advising on the designation of back-up compounds, sharing information between the parties and dealing with disputes that may arise between the parties. If a dispute cannot be resolved by the JRC, Vivelix has final decision making authority.

If requested by Vivelix pursuant to the Vivelix Agreement, Idera will create, characterize and perform research on back-up compounds. Such activity is to be mutually agreed upon and moderated by the JRC. The research period commenced with the execution of the agreement and will last for one year. Vivelix may extend the research period by up to two one year periods. During the research period, the parties will agree on the number of full time equivalents to work on the program. Vivelix will reimburse Idera at an annual market rate for the services rendered.

Vivelix has certain rights under the agreement whereby it may (i) exercise the right of first refusal, (ii) the right of first negotiation to obtain an exclusive license for any compound controlled by Idera that has activity in the field of inflammatory bowel disease and (iii) the right to request an expanded Field beyond the GI Field. The Company has determined that these rights are substantive options.

Under the terms of the Vivelix Agreement, the Company received an upfront, non-refundable fee of $15 million. In addition, the Company will be eligible for future IMO-9200 related development, regulatory and sales milestone payments totaling up to $140 million, including development and regulatory milestones totaling up to $65 million and sales milestones totaling up to $75 million, and escalating royalties ranging from the mid single-digits to low double-digits of global net sales, which percentages are subject to reduction under agreed upon circumstances. As it relates to back-up compounds, the Company will be eligible for related designation payments and development, regulatory sales and milestone payments totaling up to $52.5 million, including development and regulatory milestones totaling up to $35 million and sales milestones totaling up to $17.5 million and escalating royalties ranging from the mid single-digits to low double-digits of global net sales, which percentages are subject to reduction under agreed upon circumstances. Under the terms of the agreement and if requested by and at Vivelix's expense, the Company is responsible for performing research services related to the back-up compounds.

At the effective date of the Vivelix Agreement and as of December 31, 2016, Baker Bros. Advisors LP and certain of its affiliated funds ("Baker Brothers") beneficially owned approximately 7.0% of the Company's outstanding common stock. Baker Brothers also owned a controlling financial interest of Vivelix at the effective date of the Vivelix Agreement and as of December 31, 2016. Baker Brothers holds two of the four board seats on the Board of Directors of Vivelix and two of the nine board seats on the Board of Directors of the Company. However, the Boards of the Company and Vivelix share no individual common Board members.

Accounting Analysis

The Company evaluated the Vivelix Agreement in accordance with the provisions of ASC 605-25. The Vivelix Agreement contains the following initial deliverables: (i) a research and commercialization license for IMO-9200 and back-up compounds to IMO-9200 (the "IMO-9200 License"), (ii) drug materials transferred, and (iii) participation in the JRC (the "JRC Deliverable").

The Company has determined that Vivelix's right of first refusal, the right of first negotiation and the right to request an expanded field are substantive options. Vivelix is not contractually obligated to exercise the options and Idera is not contractually obligated to perform. Accordingly, the substantive options are not considered deliverables at the inception of the arrangement and the associated payments are not accounted for at inception of the agreement.

The Company concluded that the IMO-9200 License has standalone value from the undelivered elements as Vivelix could benefit from the IMO-9200 License on a standalone basis as they would be able to sell the compound in the market without any additional involvement or participation from Idera. Idera has no further obligations related to the IMO-9200 License. In the event that Vivelix does not make a designated compound payment, the license to back-up compounds reverts back to Idera at the end of the research term at no cost or payment by either party. The research and development services in the Vivelix Agreement relate to the back-up compounds and Vivelix would be able to conduct research and development activities with external third parties, as IMO-9200 is at an advanced enough stage where Idera's expertise would not be required. Accordingly, the IMO-9200 License is a separate unit of accounting.

The Company concluded that the materials transferred identified at the inception and the JRC Deliverable of the Vivelix Agreement also have standalone value from the other deliverables based on their nature. In the case of the materials transferred, it was noted that Vivelix would not be able to realize any of the value associated without the IMO-9200 License; however, the IMO-9200 License was provided at the inception of the arrangement and therefore, this determination is not relevant.

Therefore, the Company has identified three units of accounting in connection with its initial deliverables under the Vivelix Agreement as follows: (i) the IMO-9200 License, (ii) drug materials transferred, and (iii) the JRC Deliverable.

Allocable arrangement consideration at inception of the Vivelix Agreement is comprised of the up-front payment of $15 million. The $15 million was allocated based on the relative values of the best estimate of selling price of the units of accounting. Allocated revenue associated with the IMO-9200 License was recognized at the inception of the Vivelix Agreement in the fourth quarter of 2016 as Vivelix was granted an exclusive, perpetual license to develop and commercialize IMO-9200 and certain back-up compounds to IMO-9200, subject to certain designation milestone and royalty payments, and the performance obligations of Idera under the agreement are extinguished at that point. Allocable revenue associated with drug materials transferred shortly after the inception of the agreement was recognized upon delivery, in the fourth quarter of 2016. The JRC deliverable was deemed to be de minimus and no amount separately accounted for.

The development and commercial milestones provided for in the Vivelix Agreement are all performance obligations of Vivelix occurring after the Company has completed its obligations. As a result, they represent contingent revenue to the Company and will be accounted for at the time the contingencies are resolved.

The Company will recognize royalty revenue in the period of sale of the related product(s), based on the underlying contract terms, provided that the reported sales are reliably measurable and the Company has no remaining performance obligations, assuming all other revenue recognition criteria are met.

The Company recognized as Alliance revenue $15.0 million in the Statement of Operations for the year ended December 31, 2016.

(b) Collaboration with GSK

In November 2015, the Company entered into the GSK Agreement. The initial collaboration term is currently anticipated to last between two and four years. In connection with the GSK Agreement, GSK identified an initial target for the Company to attempt to identify a potential population of development candidates to address such target under a mutually agreed upon research plan, currently estimated to take 27 months to complete. From the population of identified development candidates, GSK may designate one development candidate in its sole discretion to move forward into clinical development. Once GSK designates a development candidate, GSK would be solely responsible for the development and commercialization activities for that designated development candidate.

At any time during the first two years of the GSK Agreement, GSK has the option to select up to two additional targets, for further research under mutually agreed upon research plans. GSK may then designate one development candidate for each additional target, at which time GSK would have sole responsibility to develop and commercialize each such designated development candidate.

In accordance with the GSK Agreement, a Joint Steering Committee ("JSC") was formed with equal representation from Idera and GSK. The responsibilities of the JSC, include, but are not limited to monitoring the progress of the collaboration, reviewing research plans and dealing with disputes that may arise between the parties. If a dispute cannot be resolved by the JSC, GSK has final decision making authority.

Under the terms of the GSK Agreement, the Company received a $2.5 million upfront, non-refundable, non-creditable cash payment upon the execution of the GSK Agreement. The Company is eligible to receive up to approximately $100 million in license, research, clinical development and commercialization milestone payments. Approximately $9 million of these milestone payments are payable by GSK upon the identification of the additional targets, the completion of current and future research plans and the designation of development candidates. Approximately $89 million is payable by GSK upon the achievement of clinical milestones and commercial milestones. In addition, the Company is eligible to receive royalty payments based on net sales upon licensed products following commercialization at varying rates of up to five percent on annual net sales, as defined in the GSK Agreement.

Accounting Analysis

The Company evaluated the GSK Agreement in accordance with the provisions of ASC 605-25. The GSK Agreement contains the following initial deliverables: (i) a collaboration license for Idera's proprietary technology related to the initial target (the "Collaboration License"), (ii) research services (the "Research Services"), and (iii) participation in the JSC (the "JSC Deliverable").

The Company has determined that GSK's options to choose up to two additional targets and to purchase additional collaboration licenses for the Company's proprietary technology related to each additional target are substantive options. GSK is not contractually obligated to exercise the options. Moreover, as a result of the uncertain outcome of the research activities, there is significant uncertainty as to whether GSK will decide to exercise its options for any additional targets. Consequently, the Company is at risk with regard to whether GSK will exercise the options. The Company has determined that GSK's options to choose up to two additional targets and to purchase additional collaboration licenses for the Company's proprietary technology related to each additional target are not priced at a significant and incremental discount.

The Company has concluded that the Collaboration License does not qualify for separation from the Research Services. As it relates to the assessment of standalone value, the Company has determined that GSK cannot fully exploit the value of the Collaboration License without receipt of the Research Services from the Company. The Research Services involve unique skills and specialized expertise, particularly as it relates to the Company's proprietary technology, which is not available in the marketplace. Accordingly, GSK must obtain the Research Services from the Company which significantly limits the ability for GSK to utilize the Collaboration License for its intended purpose on a standalone basis. Therefore, the Collaboration License does not have standalone value from the Research Services. As a result, the Collaboration License and the Research Services have been combined as a single unit of accounting (the R&D Services Unit of Accounting). The Company has concluded that the JSC Deliverable identified at the inception of the arrangement has standalone value from the other deliverables noted based on its nature. Factors considered in this determination included, among other things, the capabilities of the collaborator, whether any other vendor sells the item separately, whether the value of the deliverable is dependent on the other elements in the arrangement, whether there are other vendors

that can provide the items and if the customer could use the item for its intended purpose without the other deliverables in the arrangement.

Therefore, the Company has identified two units of accounting in connection with its initial deliverables under the GSK Agreement as follows: (i) R&D Services Unit of Accounting, and (ii) JSC Deliverable.

Allocable arrangement consideration at inception of the GSK Agreement is comprised of the up-front payment of $2.5 million, which was allocated to the R&D Services Unit of Accounting. No amount was allocated to the JSC Deliverable because the related best estimate of selling price was determined to be de minimis. The $2.5 million was recorded as deferred revenue in the Company's balance sheet and is being recognized as revenue on a straight line basis as the Research Services are delivered over the estimated 27 month research plan period.

Payments to be received in connection with GSK's identification of additional targets and designation of development candidates are considered substantive options as a result of the uncertainties related to the research, development and commercialization activities, and the uncertainty as to whether GSK will exercise the options. The substantive options are not priced at a significant incremental discount. Accordingly, the substantive options are not considered deliverables at the inception of the arrangement and the associated option exercise payments are not accounted for at inception of the agreement.

The clinical and commercial milestones provided for in the GSK Agreement are all performance obligations of GSK occurring after the Company has completed its obligations. As a result, they represent contingent revenue to the Company and will be accounted for at the time the contingencies are resolved.

The Company will recognize royalty revenue in the period of sale of the related product(s), based on the underlying contract terms, provided that the reported sales are reliably measurable and the Company has no remaining performance obligations, assuming all other revenue recognition criteria are met.

The Company recognized as revenue approximately $1.1 million and $0.1 million of deferred revenue related to the GSK Agreement during the years ended December 31, 2016 and 2015, respectively. This revenue is classified as alliance revenue in the accompanying statements of operations and comprehensive loss. There was approximately $1.3 million of deferred revenue related to the GSK Agreement at December 31, 2016, including approximately $1.1 million classified as current portion of deferred revenue in the accompanying balance sheet.

(c) Collaboration with Abbott Molecular Inc.

In May 2014, the Company entered into a development and commercialization agreement with Abbott Molecular, Inc. ("Abbott Molecular") for the development of an in vitro companion diagnostic for use in the Company's clinical development programs to treat certain genetically defined forms of B-cell lymphoma with IMO-8400, the Company's TLR antagonist lead drug candidate. The agreement provides for the development and subsequent commercialization by Abbott Molecular of a companion diagnostic test utilizing polymerase chain reaction technology to identify with high sensitivity and specificity the presence in tumor biopsy samples of the oncogenic mutation referred to scientifically as MYD88 L265P. Under the agreement, Abbott Molecular is primarily responsible for developing and obtaining regulatory approvals for the companion diagnostic in accordance with an agreed development plan and regulatory plan and for making the companion diagnostic test commercially available in accordance with an agreed commercialization plan. Abbott Molecular will retain all proceeds from commercialization of the companion diagnostic test. Subject to the terms of the agreement, the Company will pay Abbott Molecular fees and fund Abbott Molecular's development of the companion diagnostic test in an approximate aggregate amount of $6.7 million over an approximately five year development period, which includes clinical trial site costs and Abbott Molecular's costs of preparation and filing fees for regulatory submissions for the companion diagnostic with the U.S. Food and Drug Administration ("FDA"). This amount is subject to increase if Abbott Molecular incurs additional expenses in order to meet unexpected material requirements or obligations not included in the agreement or if the Company is required to conduct additional or different clinical trials which result in Abbott Molecular incurring additional costs. The Company incurred approximately $0.4 million, $0.9 million and $2.2 million in expenses under the Abbott Molecular agreement during the years ended December 31, 2016, 2015 and 2014, respectively.

(d) Collaboration and License Agreement with Merck & Co.

In April 2014, the Company entered into an amendment of its December 2006 exclusive, worldwide license and research collaboration agreement with Merck & Co. to research, develop, and commercialize vaccine products containing the Company's TLR7, TLR8, and TLR9 agonists in the fields of cancer, infectious diseases, and Alzheimer's disease. As a result of this amendment, Merck & Co.'s rights to a number of the Company's TLR7, TLR8 and TLR9 agonists under the agreement have been limited to specified TLR7, TLR8, and TLR9 agonists that Merck & Co. selected in January 2012, and the Company regained the rights to pursue its other independently discovered TLR7, TLR8, and TLR9 agonists for use as vaccine adjuvants in the fields of cancer, infectious diseases and Alzheimer's disease so that it now has the right to pursue its TLR7, TLR8, and TLR9 agonists for use as vaccine adjuvants in all fields. Merck & Co.'s obligations under the agreement to pay the Company milestone payments and royalties continue in effect with respect to the specified TLR7, TLR8, and TLR9 agonists. However, in connection with this amendment, the Company agreed that, to the extent that the Company licenses to third parties any TLR7, TLR8, and TLR9 agonists for use as vaccine adjuvants in the fields of cancer, infectious diseases and Alzheimer's disease and receives income under such licenses, Merck & Co. may credit against any milestone payments and royalties it owes to the Company an amount equal to 15% of the license income received by the Company under the third-party licenses, up to a maximum of $60.0 million in credits.

(e) Other License Agreements

The Company has out-licensed and in-licensed therapies related to antisense technology.

In 2001, Idera entered into an agreement with Ionis Pharmaceuticals, Inc. ("Ionis"), formerly Isis Pharmaceuticals, Inc., under which the Company granted Ionis a license (with the right to sublicense) to its second-generation antisense chemistry and delivery patents and patent applications, but the Company retained the right to use these patents and applications in its own drug discovery and development efforts and in collaborations with third parties.

7. Stockholders' Equity

(a) Common Stock

Pursuant to the terms of a unit purchase agreement dated as of May 5, 1998, the Company issued and sold a total of 1,199,684 shares of common stock (the "Put Shares") at a price of $16.00 per share. Under the terms of the unit purchase agreement, the initial purchasers (the "Put Holders") of the Put Shares have the right (the "Put Right") to require the Company to repurchase the Put Shares. The Put Right may not be exercised by any Put Holder unless: (1) the Company liquidates, dissolves or winds up its affairs pursuant to applicable bankruptcy law, whether voluntarily or involuntarily; (2) all of the Company's indebtedness and obligations, including without limitation the indebtedness under the Company's then outstanding notes, has been paid in full; and (3) all rights of the holders of any series or class of capital stock ranking prior and senior to the common stock with respect to liquidation, including without limitation the Series A convertible preferred stock, have been satisfied in full. The Company may terminate the Put Right upon written notice to the Put Holders if the closing sales price of its common stock exceeds $32.00 per share for the twenty consecutive trading days prior to the date of notice of termination. Because the Put Right is not transferable, in the event that a Put Holder has transferred Put Shares since May 5, 1998, the Put Right with respect to those shares has terminated. As a consequence of the Put Right, in the event the Company is liquidated, holders of shares of common stock that do not have Put Rights with respect to such shares may receive smaller distributions per share upon the liquidation than if there were no Put Rights outstanding.

As of December 31, 2016, the Company has repurchased or received documentation of the transfer of 399,950 Put Shares and 35,780 of the Put Shares continued to be held in the name of Put Holders. The Company cannot determine at this time what portion of the Put Rights of the remaining 763,954 Put Shares have terminated.

As of December 31, 2016, the Company had 76,137,792 shares reserved for issuance upon the exercise of outstanding warrants and options to purchase common stock, employee and director stock purchases, conversion of Series A convertible preferred stock, and additional shares available for grant under the 2013 Stock Incentive Plan.

(b) Warrants

The Company has the following warrants outstanding and exercisable for the purchase of common stock at December 31, 2016:

Expiration Date	Shares	Weighted Average Exercise Price Per Share
November 9, 2017	7,252,081	$ 0.70
May 7, 2018	22,306,327	0.47
May 7, 2020	15,816,327	0.01
September 30, 2020	4,175,975	0.01
February 10, 2021	2,158,750	0.01
Total	51,709,460	$ 0.31

(c) Stock Options

Under the Company's 2013 Stock Incentive Plan (the "2013 Stock Incentive Plan"), the Company may grant options to purchase common stock, stock appreciation rights, restricted stock awards and other forms of stock-based compensation. Stock options generally vest over three to four years, and expire no later than 10 years from the date of grant. A total of 15,224,460 shares of common stock, plus such additional number of shares of common stock (up to 6,946,975) as is equal to the number of shares of common stock subject to awards granted under the Company's 2005 Stock Incentive Plan or 2008 Stock Incentive Plan which awards expire, terminate or are otherwise surrendered, cancelled, forfeited or repurchased by the Company at their original issuance price pursuant to a contractual repurchase right may be issued pursuant to awards granted under the 2013 Stock Incentive Plan subject to reduction in the event that there are any "full-value awards," as defined in the plan. The maximum number of shares of common stock with respect to which awards may be granted to any participant under the plan is 1,500,000 per calendar year. The compensation committee of the board of directors has the authority to select the employees to whom options are granted and determine the terms of each option, including (i) the number of shares of common stock subject to the option; (ii) when the option becomes exercisable, which generally may be no earlier than the first anniversary of the date of grant; (iii) the option exercise price, which must be at least 100% of the fair market value of the common stock as of the date of grant; and (iv) the duration of the option, which may not exceed 10 years. Stock options may not be re-priced without shareholder approval. Discretionary awards to non-employee directors are granted and administered by a committee comprised of independent directors. As of December 31, 2016, options to purchase a total of 10,235,083 shares of common stock were outstanding under the 2013 Stock Incentive Plan. As of December 31, 2016, 6,275,852 shares of common stock remain available for grant under the 2013 Stock Incentive Plan.

The Company is no longer granting stock options or other awards pursuant to the share-based compensation plans that were utilized prior to the approval of the 2013 Stock Incentive Plan. Under these earlier plans, stock options generally vested over three to four years and expired no later than 10 years from the date of grant. As of December 31, 2016, options to purchase a total of 4,616,437 shares of common stock were outstanding under these earlier plans. During 2015, the Company also granted as inducement grants non-statutory stock options to purchase an aggregate of 1,150,000 shares of common stock. The inducement grant awards were made outside of the 2013 Stock Incentive Plan pursuant to the NASDAQ inducement grant exception as a material component of new hires' employment compensation. Options to purchase 3,150,000 shares as inducement grants remained outstanding at December 31, 2016. The balance of the inducement options were forfeited.

The following table summarizes information related to the outstanding and exercisable options during 2016 (in thousands, except per share amounts and years):

	Stock Options	Weighted-Average Exercise Price	Weighted-Average Remaining Contractual Life (in years)	Aggregate Intrinsic Value
Outstanding at December 31, 2015	16,261	$ 3.45		
Granted	3,346	2.64		
Exercised	—	—		
Forfeited	(878)	3.15		
Expired	(727)	3.85		
Outstanding at December 31, 2016	18,002	3.30	7.14	$ 1,648
Exercisable at December 31, 2016	10,522	3.41	6.18	1,536
Total exercisable or expected to vest	17,283	3.31	7.08	1,637

(d) Employee Stock Purchase Plan

The Company's 1995 Employee Stock Purchase Plan (the "Stock Purchase Plan"), as amended, provides for the issuance of up to 500,000 shares of common stock to participating employees of the Company or its subsidiaries. Participation is limited to employees that would not own 5% or more of the total combined voting power or value of the stock of the Company after the grant.

Under the Stock Purchase Plan, on the first day of a designated payroll deduction period, the "Offering Period," the Company will grant to each eligible employee who has elected to participate in the Stock Purchase Plan an option to purchase shares of common stock as follows: the employee may authorize an amount, a whole percentage from 1% to 10% of such employee's regular pay, to be deducted by the Company from such pay during the Offering Period. On the last day of the Offering Period, the employee is deemed to have exercised the option, at the option exercise price, to the extent of accumulated payroll deductions. Under the terms of the Stock Purchase Plan, the option price is an amount equal to 85% of the fair market value per share of the common stock on either the first day or the last day of the Offering Period, whichever is lower. In no event may an employee purchase in any one Offering Period a number of shares that is more than 15% of the employee's annualized base pay divided by 85% of the market value of a share of common stock on the commencement date of the Offering Period. The compensation committee may, in its discretion, choose an Offering Period of 12 months or less for each of the Offerings and choose a different Offering Period for each Offering.

Offering periods are three months in duration and commence on March 1, June 1, September 1, and December 1. In 2016, 2015, and 2014, the Company issued 121,460, 27,951, and 13,844 shares of common stock, respectively, under the Stock Purchase Plan.

(e) Preferred Stock

The Restated Certificate of Incorporation of the Company permits its board of directors to issue up to 5,000,000 shares of preferred stock, par value $0.01 per share, in one or more series, to designate the number of shares constituting such series, and fix by resolution, the powers, privileges, preferences and relative, optional or special rights thereof, including liquidation preferences and dividends, and conversion and redemption rights of each such series. As of December 31, 2016, the Company has designated 1,500,000 shares as Series A convertible preferred stock.

(f) Series A Convertible Preferred Stock

The dividends on the Series A convertible preferred stock are payable semi-annually in arrears at the rate of 1% per annum, at the election of the Company, either in cash or additional duly designated, fully paid and nonassessable shares of Series A preferred stock. The Company paid dividends in stock until 2004 when it elected to pay further dividends in cash. In the event of liquidation, dissolution or winding up of the Company, after payment of debts and other liabilities of the Company, the holders of the Series A convertible preferred stock then outstanding will be entitled to a distribution of $1 per share out of any assets available to shareholders. The Series A preferred stock is non-voting. All remaining shares of Series A preferred stock rank as to payment upon the occurrence of any liquidation event senior to the common stock. Shares of Series A preferred stock are convertible, in whole or in part, at the option of the holder into fully paid and

nonassessable shares of common stock at $34.00 per share, subject to adjustment. As of December 31, 2016 and 2015, there were 655 shares of Series A convertible preferred stock outstanding.

(g) Series D Convertible Preferred Stock

On January 10, 2014, the Company notified Pillar Pharmaceuticals I, L.P. ("Pillar I"), an investment partnership managed by one of the Company's directors and significant stockholders and the holder of all 1,124,260 shares of the Company's issued and outstanding Series D redeemable convertible preferred stock ("Series D preferred stock"), of its intention to redeem the Series D preferred stock on February 10, 2014 in accordance with the terms of the Certificate of Designations, Preference and Rights of Series D Preferred Stock of the Company (the "Series D Certificate of Designations"). On February 6, 2014, Pillar I converted such shares into 6,266,175 shares of the Company's common stock in accordance with the terms of the Series D Certificate of Designations. As a result of the conversion, no shares of the Company's Series D preferred stock remain outstanding.

On March 28, 2014, the Company filed a Certificate of Elimination of Number of Shares of Preferred Stock Designated as Series D Convertible Preferred Stock with the State of Delaware Secretary of State which eliminated the designation of the shares of Series D preferred stock.

(h) Series E Convertible Preferred Stock

In December 2014, the holders of all of the 424,242 shares of Series E convertible preferred stock ("Series E preferred stock") converted such shares into 8,484,840 shares of common stock in accordance with the terms of the Certificate of Designations, Preferences and Rights of Series E Preferred Stock (the "Series E Certificate of Designations"). As a result of this conversion, no shares of Series E preferred stock remain outstanding.

On March 12, 2015, the Company filed a Certificate of Elimination of Number of Shares of Preferred Stock Designated as Series E Convertible Preferred Stock with the State of Delaware Secretary of State which eliminated the designation of the shares of Series E preferred stock.

8. Common Stock Warrant and Option Exercises and Employee Stock Purchases

The Company issued 1,491,000, 3,402,000, and 5,932,000 shares of common stock and received total proceeds of $2.2 million, $2.5 million, and $8.5 million for warrant and stock option exercises and employee stock purchases under the Stock Purchase Plan during the years ended December 31, 2016, 2015 and 2014, respectively, as follows:

	2016		2015		2014	
(In thousands)	**Shares**	**Proceeds**	**Shares**	**Proceeds**	**Shares**	**Proceeds**
Warrant exercises	1,370	$ 2,000	2,968	$ 1,888	5,544	$ 7,534
Stock option exercises	—	—	406	584	374	890
Employee stock purchases	121	172	28	74	14	32
Total	1,491	$ 2,172	3,402	$ 2,546	5,932	$ 8,456

9. Commitments and Contingencies

(a) Lease Commitments

The Company leases its facilities in Cambridge, Massachusetts and Exton, Pennsylvania. During 2016, 2015 and 2014, rent expense, including real estate taxes, was $1.9 million, $1.7 million and $1.7 million, respectively. As part of the Cambridge facility lease, the Company is required to restrict approximately $0.3 million of cash for a security deposit as of December 31, 2016 and 2015. The leases are classified as operating leases. Future minimum commitments as of December 31, 2016 under the Company's lease agreements are approximately:

December 31,	Operating Lease (In thousands)
2017	$ 1,842
2018	2,024
2019	2,084
2020	2,018
2021	1,984
Thereafter	1,348
	$ 11,300

The Cambridge facility lease was amended on November 17, 2016 to, among other things, extend the expiration date to August 31, 2022 subject to a five-year renewal option exercisable by the Company. The Cambridge facility lease amendment includes certain lease incentives in the form of premises improvement allowance of up to $0.3 million. Amounts will be recorded in future periods when such premises improvements are made. The Company entered into the Exton facility lease on April 1, 2015 and amended it on September 23, 2015 to include additional space. The Exton facility lease term ends on May 31, 2020 subject to a three-year renewal option exercisable by the Company.

(c) Contract Obligations

The Company has employment agreements with its executive officers that include future minimum commitments of approximately $2.7 million per year.

In the normal course of business, the Company enters into contracts with clinical research organizations, drug manufacturers and other vendors for preclinical and clinical research studies, research and development supplies and other services and products for operating purposes. These contracts generally provide for termination on notice, and therefore are cancellable contracts and not included in contract obligations.

(d) Related-Party Transactions

In November 2011, the Company issued and sold, for an aggregate purchase price of $9.5 million, 1,124,260 shares of Series D preferred stock and warrants to purchase 2,810,650 shares of its common stock with an exercise price of $1.63 per share ("Series D warrants") pursuant to a Convertible Preferred Stock and Warrant Purchase Agreement with Pillar I, an investment partnership managed by one of the Company's current directors and significant shareholders. The Series D warrants expired on November 4, 2016. As a result of an anti-dilution adjustment triggered by the sale of the Company's Series E preferred stock in November, 2012, the exercise price of the Series D warrants was reduced to $1.46 per share. As discussed in Note 7(g), all shares of Series D preferred stock were converted to 6,266,175 shares of common stock in February, 2014. In November 2012, the Company issued and sold, for an aggregate purchase price of $7.0 million, 424,242 shares of Series E preferred stock and warrants to purchase 8,484,840 shares of its common stock with an exercise price of $0.70 per share ("Series E warrants") pursuant to a Convertible Preferred Stock and Warrant Purchase Agreement with Pillar Pharmaceuticals II, L.P. ("Pillar II"), an investment partnership managed by two of the Company's directors (one of the Company's current directors) and one of its significant shareholders and an entity affiliated with Pillar II (together with Pillar II, the "Pillar II Entities"). The Series E warrants expire on November 9, 2017. As discussed in Note 7(h), all shares of Series E preferred stock were converted to 8,484,840 shares of common stock in December 2014.

In connection with the Company's follow-on underwritten public offering on May 7, 2013, the Company sold 5,000,000 shares of common stock and warrants to purchase 5,000,000 shares of common stock at $0.47 per share for an aggregate purchase price of $2,500,000 to Pillar Pharmaceuticals III, L.P. ("Pillar III") and an entity affiliated with Pillar III (together with Pillar III, the "Pillar III Entities"), which is described in Note 14. In connection with the Company's follow-on underwritten public offering on September 30, 2013, the Company sold 1,774,193 shares of common stock for an aggregate purchase price of $2,750,000 to Pillar Pharmaceuticals IV, L.P. ("Pillar IV") and an entity affiliated with Pillar IV (together with Pillar IV, the "Pillar IV Entities"), which is described in Note 14.

Youssef El Zein, a member of the Company's board of directors, is a director and controlling stockholder of Pillar Invest Corporation ("Pillar Invest"), which is the general partner of Pillar I, Pillar II, Pillar III and Pillar IV. Mr. El Zein has voting and investment control over the securities beneficially owned by the Pillar III Entities and the Pillar IV Entities.

In addition, Abdul-Wahab Umari, who was also a member of the Company's board of directors until June 2014, is a managing partner of Pillar Invest.

During 2016, the Pillar I exercised 1,370,000 warrants to purchase common stock at a total exercise price of $2,000,200. The warrant exercise prices had been established at the time that the warrants were purchased.

During 2015, the Pillar II Entities exercised 232,759 warrants to purchase common stock at a total exercise price of $163,000 and the Pillar III Entities exercised 2,600,000 warrants to purchase common stock at a total exercise price of $1,222,000. The warrant exercise prices had been established at the time that the warrants were purchased.

During 2014, Pillar I exercised 1,575,758 warrants to purchase common stock at a total exercise price of $1,065,000, the Pillar II Entities exercised 1,424,242 warrants to purchase common stock at a total exercise price of $1,035,000 and the Pillar III Entities exercised 500,000 warrants to purchase common stock at a total exercise price of $235,000. The warrant exercise prices had been established at the time that the warrants were purchased.

The Company issued common stock in lieu of director board and committee fees of approximately $172,000, $122,000, and $82,000 during 2016, 2015 and 2014, respectively. Such shares were issued at the market closing price on the purchase date.

Additional information on related party transactions associated with the April 2013 agreements between the Company and the Pillar Entities (as defined in Note 14) is included in Note 14.

See also Note 6, "Collaboration and License Agreements" and Note 14, "Financings," for additional information on related party transactions.

10. Income Taxes

The Tax Reform Act of 1986 contains provisions that limit the amount of net operating loss carryforwards ("NOLs") and tax credit carryforwards that companies may utilize in any one year in the event of cumulative changes in ownership over a three-year period in excess of 50%. The Company has completed several financings since the effective date of the Tax Reform Act of 1986, which as of December 31, 2016, have resulted in ownership changes in excess of 50% that will significantly limit the Company's ability to utilize its NOL and tax credit carryforwards. In December, 2014, the Company completed a study which determined that a cumulative three-year ownership change in excess of 50% had occurred in November 2012. The 2016 and 2015 federal and state NOLs, tax credit carryforwards and related deferred tax assets shown below have been adjusted to reflect the ownership change limitations that resulted from this study. The Company has entered into additional equity transactions since November 2012 that could result in ownership changes that further limit its ability to utilize its NOL and tax credit carryforwards. The Company has not determined whether any additional ownership change limitations have resulted from equity transactions that have occurred after November 2012.

As of December 31, 2016, the Company had cumulative federal and state NOLs of approximately $149.3 million and $138.2 million available to reduce federal and state taxable income, respectively. These NOLs expire through 2036. In addition, at December 31, 2016, the Company had cumulative federal and state tax credit carryforwards of $8.4 million and $1.6 million, respectively, available to reduce federal and state income taxes, respectively, which expire through 2036 and 2031, respectively. The federal and state NOLs include approximately $1.0 million and $0.7 million, respectively, of deductions related to the exercise of stock options subsequent to the adoption of ASC 718, "Stock Compensation." These amounts represent excess tax benefits as defined under ASC 718 and have not been included in the gross deferred tax asset reflected for NOLs. However, the Company intends to adopt ASU 2016-09, Improvements to Employee Share-Based Payment Accounting, during the quarter ended March 31, 2017. As a result of the adoption, it is anticipated that the net operating losses deferred tax assets will increase by $1.4 million and will be offset by a corresponding increase in the valuation allowance. The Company does not anticipate that the adoption of ASU 2016-09 will have an impact on the Company's Financial statements.

As of December 31, 2016 and 2015, the components of the deferred tax assets are approximately as follows:

	2016	2015
	(In thousands)	
Operating loss carryforwards	$ 56,832	$ 46,432
Tax credit carryforwards	9,428	5,627
Other	7,710	5,698
	73,970	57,757
Valuation allowance	(73,970)	(57,757)
	$ —	$ —

The Company has provided a valuation allowance for its deferred tax asset due to the uncertainty surrounding the ability to realize this asset.

The difference between the 34% U.S. federal corporate tax rate and the Company's effective tax rate is as follows for the years ended December 31, 2016, 2015 and 2014:

	2016	2015	2014
Expected federal income tax rate	(34.0)%	(34.0)%	(34.0)%
Expiring credits and NOLs	—	—	—
Change in valuation allowance	42.2	39.8	(115.3)
Federal and state credits	(9.9)	(7.4)	(4.0)
State income taxes, net of federal benefit	(3.7)	(4.5)	(5.1)
Permanent differences	3.5	2.4	0.8
Section 382 limitation	—	—	157.5
Other	1.9	3.7	0.1
Effective tax rate	0.0 %	0.0 %	0.0 %

The Company applies ASC 740-10, "Accounting for Uncertainty in Income Taxes, an interpretation of ASC 740." ASC 740-10 clarifies the accounting for uncertainty in income taxes recognized in financial statements and requires the impact of a tax position to be recognized in the financial statements if that position is more likely than not of being sustained by the taxing authority. The Company had no unrecognized tax benefits resulting from uncertain tax positions at December 31, 2016 and 2015.

The Company has not, as of yet, conducted a study of its research and development credit carryforwards. Such a study might result in an adjustment to the Company's research and development credit carryforwards, however, until a study is completed and any adjustment is known, no amounts are being presented as an uncertain tax position under ASC 740-10. A full valuation allowance has been provided against the Company's research and development credits and, if an adjustment is required, this adjustment would be offset by an adjustment to the valuation allowance. Thus, there would be no impact to the statements of operations and comprehensive loss if an adjustment was required.

The Company files income tax returns in the U.S. federal and Massachusetts jurisdictions. The Company is no longer subject to tax examinations for years before 2013, except to the extent that it utilizes NOLs or tax credit carryforwards that originated before 2013. The Company does not believe there will be any material changes in its unrecognized tax positions over the next 12 months. The Company has not incurred any interest or penalties. In the event that the Company is assessed interest or penalties at some point in the future, they will be classified in the Statement of Operations and comprehensive loss as general and administrative expense.

In November 2015, the FASB released ASU No. 2015-17, Balance Sheet Classification of Deferred Taxes. ASU No. 2015-17 requires that all deferred income tax assets, liabilities and valuation allowances applicable to the same taxing jurisdiction be presented as noncurrent in a classified statement of financial position. ASU No. 2015-17 permits early application on a prospective or retrospective basis. The Company elected to early adopt ASU No. 2015-17 on a prospective basis in its 2015 financial statements because this change in accounting principal will allow the Company to benefit from the simplified presentation of deferred income taxes. Prior period financial statements have not been retrospectively adjusted to reflect the adoption of ASU No. 2015-17.

11. Employee Benefit Plan

The Company has an employee benefit plan under Section 401(k) of the Internal Revenue Code. The plan allows employees to make contributions up to a specified percentage of their compensation. Under the plan, the Company matches a portion of the employees' contributions up to a defined maximum. The Company is currently contributing up to 3% of employee base salary, by matching 50% of the first 6% of annual base salary contributed by each employee. Approximately $0.3 million, $0.2 million and $0.1 million of 401(k) benefits were charged to operating expenses during 2016, 2015 and 2014, respectively.

12. Net Loss per Common Share Applicable to Common Stockholders

For the years ended December 31, 2016, 2015 and 2014, basic and diluted net loss per common share applicable to common stockholders is computed using the weighted average number of shares of common stock outstanding during the period. Diluted net loss per common share applicable to common stockholders is the same as basic net loss per common share applicable to common stockholders as the effects of the Company's potential common stock equivalents are antidilutive. Total antidilutive securities were 69,712,906, 70,782,788 and 74,640,383 at December 31, 2016, 2015 and 2014, respectively, and consisted of stock options, preferred stock and warrants.

13. Supplemental Disclosure of Cash Flow Information

Supplemental disclosure of cash flow information for the periods presented is as follows:

	Year Ended December 31,		
	2016	2015	2014
	(In thousands)		
Supplemental disclosure of cash flow information:			
Cash paid for interest	$ 72	$ 93	$ 49
Supplemental disclosure of non-cash financing and investing activities:			
Conversion of Series D preferred stock to common stock	$ —	$ —	$ 5,464
Conversion of Series E preferred stock to common stock	$ —	$ —	$ 5,528
Non-cash property additions	$ 425	$ 123	$ 324
Accrued 2016 financing transaction costs paid in 2017	$ 166	$ —	$ —

14. April 2013 Pillar Agreements

In April 2013, the Company entered into two agreements (the "Pillar Agreements") with Pillar I, Pillar II and an entity affiliated with Pillar I and Pillar II (together with Pillar I and Pillar II, the "Pillar Entities"). The agreements, including the Company's obligations to issue the warrants under the Pillar Agreements, became effective upon the consummation of the follow-on underwritten public offering of the Company's securities on May 7, 2013. Mr. El Zein, a member of the Company's board of directors, is a director and controlling stockholder of Pillar Invest, which is the general partner of Pillar I and Pillar II, and is a limited partner of Pillar I and Pillar II. Mr. El Zein has voting and investment control over the securities beneficially owned by the Pillar Entities. In addition, Mr. Umari, who was also a member of the Company's board of directors until June 2014, is a managing partner of Pillar Invest.

Under the first agreement entered into with Pillar I and Pillar II (the "April 22, 2013 Pillar Agreement"), Pillar I, as the sole holder of the Company's Series D preferred stock, irrevocably waived and agreed to not exercise the rights, powers, preferences and other terms of the Series D preferred stock under Section 6 of the Series D Certificate of Designations, including without limitation the right to require the Company to purchase all or any portion of the shares of its Series D preferred stock at a price equal to the original Series D preferred stock purchase price per share plus all accrued or declared but unpaid dividends thereon upon the occurrence of specified fundamental changes such as mergers, consolidations, business combinations, stock purchases or similar transactions resulting in a person or group unaffiliated with any holder of Series D preferred stock owning 66.67% or more of the outstanding voting securities of the Company or successor entity (the "Series D Redemption Rights").

Under the April 22, 2013 Pillar Agreement, the Company agreed to seek approval and each of Pillar I and Pillar II agreed to vote in favor, of the following proposals at the Company's 2013 annual meeting of stockholders held on July 26, 2013 ("Annual Meeting"):

- amendments to the Series D Certificate of Designations for the Series D preferred stock to:
  - modify the dividend provisions of the Series D Certificate of Designations to change the date after which the Company may elect to pay dividends in shares of its common stock from December 31, 2014 to October 1, 2013, and to allow for the payment of such dividends in shares of a to-be-created new series of non-voting preferred stock in the event that payment of such dividends may not be made in shares of its common stock as a result of the application of the beneficial ownership and voting power limitations set forth the Series D Certificate of Designations; and
  - modify the Series D Certificate of Designations to provide, in the event of a sale of the Company, for the distribution of any assets that remain available for distribution to its stockholders, after payment to the holders of its Series A convertible preferred stock and any other class of its capital stock that ranks senior to its Series D preferred stock, to the holders of the Company's Series D preferred stock on a pro rata basis with the holders of its common stock, Series E preferred stock and such new series of non-voting preferred stock; and
- amendments to the Series E Certificate of Designations to:
  - modify the dividend provisions of the Series E Certificate of Designations to allow for the payment of dividends in shares of its common stock commencing October 1, 2013; and
  - allow for the payment of dividends in shares of a to-be-created new series of non-voting preferred stock in the event that payment of such dividends may not be made in shares of its common stock as a result of the application of the beneficial ownership and voting power limitations set forth in the Series E Certificate of Designations.

Under the second agreement with the Pillar Entities (the "April 30, 2013 Pillar Agreement"), Pillar I irrevocably waived the right of the holders of the Series D preferred stock under Section 2.1 of the Series D Certificate of Designations to receive, in the event of a voluntary or involuntary liquidation, dissolution or winding up of the Company (a "Liquidation"), an amount per share of Series D preferred stock equal to the original issue price of such share of Series D preferred stock plus any dividends accrued or declared but unpaid thereon to the extent such amount is greater than the amount that would have been payable with respect to such share had all shares of Series D preferred stock been converted into shares of the Company's common stock immediately prior to such Liquidation, and that upon a Liquidation the holders of the Series D preferred stock will receive an amount per share of Series D preferred stock equal to the amount that would be payable with respect to such share had all shares of Series D preferred stock been converted into shares of common stock immediately prior to such Liquidation.

In addition, under the April 30, 2013 Pillar Agreement, Pillar II and the entity affiliated with Pillar I and Pillar II, as the holders of 100% of the Company's Series E preferred stock, irrevocably waived the right of the holders of the Series E preferred stock under Section 2.1.1 of the Series E Certificate of Designations to receive, in the event of a Liquidation, an amount per share of Series E preferred stock equal to the original issue price of such share of Series E preferred stock plus any dividends accrued or declared but unpaid thereon to the extent such amount is greater than the amount that would have been payable with respect to such share had all shares of Series E preferred stock been converted into shares of common stock immediately prior to such Liquidation, and that upon a Liquidation the holders of the Series E preferred stock will receive under Section 2.1 of the Series E Certificate of Designations an amount per share of Series E preferred stock equal to the amount that would be payable with respect to such share had all shares of Series E preferred stock been converted into shares of common stock immediately prior to such Liquidation.

In accordance with the terms of the Pillar Agreements, the Company sought approval from its stockholders of amendments to the Series D Certificate of Designations and Series E Certificate of Designations to effect the changes described above to the dividend and liquidation provisions of the Company's Series D preferred stock and Series E preferred stock, the redemption rights of the holders of its Series D preferred stock and the rights of the holders of its

Series D preferred stock to distributions in the event of a sale of the Company. These matters were approved at the 2013 Annual Meeting.

Under the April 22, 2013 Pillar Agreement, in consideration of the agreements of Pillar I and II under the April 22, 2013 Pillar Agreement and the delivery of the waiver by Pillar I, and for no additional cash consideration, the Company issued to Pillar I warrants, the "Pillar I Warrants," to purchase up to 1,000,000 shares of the Company's common stock at an exercise price of $0.61 per share.

In addition, under the April 30, 2013 Pillar Agreement, in consideration of the agreements of the Pillar Entities under the April 30, 2013 Pillar Agreement and the delivery of the waivers by the Pillar Entities, and for no additional cash consideration, the Company issued to the Pillar Entities warrants (the "Additional Pillar Warrants," and together with the Pillar I Warrants, the "Pillar Warrants"), to purchase up to an aggregate of 1,000,000 shares of the Company's common stock at an exercise price of $0.79 per share.

The Pillar Warrants became exercisable immediately upon issuance. The Pillar I Warrants will expire if not exercised on or prior to the fifth anniversary from the date of issuance and the Additional Pillar Warrants will expire if not exercised on or prior to June 1, 2014. The Pillar I Warrants provide that, after the second anniversary of the date of issuance, the Company may redeem such Pillar I Warrants for $0.01 per share of common stock issuable on exercise of such Pillar I Warrants following notice to the holder thereof if the closing price of its common stock for 20 or more trading days in a period of 30 consecutive trading days is greater than or equal to $2.80 per share.

In connection with the Pillar Agreements, the Company filed a registration statement that became effective on July 10, 2013, registering the resale of the shares of common stock issuable upon exercise of the Pillar Warrants. All of the Pillar I Warrants and the Additional Pillar Warrants were exercised during 2014.

The amendments to the Series D Certificate of Designations and Series E Certificate of Designations did not become effective until the amendments were approved by the Company's stockholders at the 2013 Annual Meeting. As discussed in Note 7(g), all shares of Series D preferred stock were converted to common stock in February, 2014. As discussed in Note 7(h), all shares of Series E preferred stock were converted to common stock in December 2014.

Since Pillar I irrevocably waived and agreed to not exercise the Series D Redemption Rights, the Company reassessed its accounting in May 2013 for the Series D preferred stock, which had been classified as temporary equity in the Company's condensed balance sheet because the Series D Redemption Rights represented a contingent put feature that was outside the Company's control. Upon effectiveness of this waiver, the contingent put feature ceased to exist.

In addition, the Pillar Entities irrevocably waived the liquidation preferences of both the Series D preferred stock and the Series E preferred stock. The Company concluded that these irrevocable waivers of the Series D Redemption Rights and the Series D and Series E liquidation preferences, which became effective on May 7, 2013, represented changes to the fundamental terms of both the Series D preferred stock and the Series E preferred stock. As a result, the Company has accounted for these irrevocable waivers as an extinguishment of the Series D preferred stock and the Series E preferred stock and changed the classification of the Series D preferred stock from temporary equity to permanent equity. The Company compared (1) the sum of the fair values of the Series D preferred stock, the Series E preferred stock and the Pillar Warrants immediately after the effectiveness of the waivers to (2) the sum of the carrying values of the Series D preferred stock and Series E preferred stock immediately prior to the effectiveness of the waivers on May 7, 2013. The Company recorded the excess of the aggregate fair value of the preferred stock plus the Pillar Warrants immediately after the effectiveness of the waivers over the aggregate carrying value of the preferred stock immediately prior to May 7, 2013 as a loss on extinguishment and classified the fair values, immediately after the effectiveness of the waivers, of the Series D preferred stock, the Series E preferred stock and the Pillar Warrants within permanent equity on its balance sheet.

The effect of this extinguishment accounting on the Company's financial statements was to (1) remove the $5,921,000 carrying value of the Series D preferred stock immediately prior to the extinguishment from temporary equity; (2) record the $5,464,000 fair value of the Series D preferred stock immediately after the extinguishment in permanent equity ("equity"); (3) remove the $3,701,000 carrying value of the Series E preferred stock immediately prior to the extinguishment from equity; (4) record the $5,528,000 fair value of the Series E preferred stock immediately after the extinguishment in equity; (5) record the $380,000 fair value of the Pillar Warrants in equity; and (6) record a $1,750,000 extinguishment loss to net loss applicable to common stockholders. These accounting entries resulted in a $5,921,000 net increase in stockholders' equity on its balance sheet.

The Company determined the fair value of the Series D preferred stock and the Series E preferred stock as of May 7, 2013, the date the above described waivers became effective, based on the Option Pricing Method ("OPM") which is a market based approach to imply the aggregate equity value of the Company by using the closing price of the Company's publicly traded common stock as of the May 7, 2013 valuation date. Under the OPM, the fair value of preferred stock and common stock are determined based on the net value of a series of call options representing the present value of the expected future returns to each shareholder class. Essentially, the rights of the common stock are equivalent to a call option on any value of the Company above any cumulative preferred stock liquidation preference. The analysis involves calculating the equity value breakeven points at which the various equity classes would participate, or convert in the case of preferred stock, or exercise in the case of stock options and warrants.

The Company used the Black-Scholes option pricing model to compute the fair value of the Pillar Warrants as of the May 7, 2013 effective date on which the Pillar Warrants were issued based on the following assumptions and other inputs:

	Pillar I Warrants	Additional Pillar Warrants
Common stock price	$ 0.57	$ 0.57
Warrant exercise price	$ 0.61	$ 0.79
Term of warrant (years)	5.0	1.1
Expected volatility	62 %	67 %
Average risk free interest rate	0.8 %	0.1 %
Expected dividend yield	—	—
Expected percentage of warrants to be exercised	100 %	100 %

The closing price of the Company's common stock is readily determinable since it is publicly traded. The warrant exercise prices and the warrant terms are readily determinable from the warrant agreements. The expected volatility is based on the actual stock-price volatility over a period equal to the greater of the term of the warrant or three years. The assumed risk-free interest rate is based on the U.S. Treasury security rate with a term equal to the term of the warrant. The assumed dividend yield of zero is based on the fact that the Company has never paid cash dividends to common stockholders and has no present intention to pay cash dividends to common stockholders. The Company assumed that future financings would dilute the warrant holder's ownership in the Company such that the 19.99% ownership limitation would not prevent the warrant holder from exercising all of the warrants during the term of the warrants.

15. Financings

October 13, 2016 Follow-on Underwritten Public Offering

On October 13, 2016, the Company closed a follow-on underwritten public offering, in which it sold 25,000,000 shares of common stock at a price to the public of $2.00 per share for aggregate gross proceeds of $50.0 million. On October 28, 2016, the Company sold an additional 1,225,243 shares of common stock pursuant to the underwriters' 30-day option to purchase additional shares at the public offering price less the underwriting discount. The net proceeds to the Company from the offering, including the exercise by the underwriters of their option to purchase additional shares and after deducting underwriters' discounts and commissions and other offering costs and expenses, were approximately $48.8 million. Investment funds affiliated with Baker Brothers and Pillar Invest Corporation, two of the Company's principal stockholders, and certain members of the Company's board of directors, purchased 5,125,000 shares in this offering at the $2.00 per share purchase price.

February 19, 2015 Follow-on Underwritten Public Offering

On February 19, 2015, the Company closed a follow-on underwritten public offering, in which it sold 23,000,000 shares of common stock at a price to the public of $3.75 per share for aggregate gross proceeds of $86.3 million. The net proceeds to the Company from the offering, after deducting underwriters' discounts and commissions and other offering costs and expenses, were $80.6 million. Investment funds affiliated with Baker Brothers and two members of the Company's board of directors purchased 5,333,333 shares in this offering at the $3.75 per share purchase price.

On February 19, 2015, Baker Brothers held 6,965,432 shares of the Company's common stock, warrants to purchase up to 20,316,327 shares of the Company's common stock at an exercise price of $0.47 per share and pre-funded warrants to purchase up to 22,151,052 shares of the Company's common stock at an exercise price of $0.01 per share.

February 10, 2014 Follow-on Underwritten Public Offering

On February 10, 2014, the Company closed a follow-on underwritten public offering, in which it sold 7,867,438 shares of common stock at a price to the public of $4.00 per share and pre-funded warrants to purchase up to 2,158,750 shares of common stock at a price to the public of $3.99 per share for aggregate gross proceeds of $40.1 million. The pre-funded warrants have an exercise price of $0.01 per share and will expire if not exercised by February 10, 2021. The net proceeds to the Company from the offering, after deducting underwriters' discounts and commissions and other offering costs and expenses and excluding the proceeds of the exercise of the warrants, if any, were approximately $37.2 million.

16. Subsequent Event

The Company considers events or transactions that occur after the balance sheet date but prior to the issuance of the financial statements to provide additional evidence relative to certain estimates or to identify matters that require additional disclosure.

Exhibit Index

Exhibit Number	Description	Filed Herewith	Incorporated by Reference to		
			Form	Filing Date	SEC File No.
3.1	Restated Certificate of Incorporation of Idera Pharmaceuticals, Inc., as amended.		10-Q	August 6, 2015	001-31918
3.2	Amended and Restated Bylaws of Idera Pharmaceuticals, Inc.		S-1	November 6, 1995	33-99024
4.1	Specimen Certificate for shares of Common Stock, $.001 par value, of Idera Pharmaceuticals, Inc.		S-1	December 8, 1995	33-99024
10.1††	2008 Stock Incentive Plan, as amended		8-K	June 17, 2011	001-31918
10.2††	2005 Stock Incentive Plan, as amended		10-Q	August 14, 2006	001-31918
10.3††	Amended and Restated 1997 Stock Incentive Plan.		10-Q	May 15, 2001	000-27352
10.4††	1995 Director Stock Option Plan.		8-K	June 10, 2008	001-31918
10.5††	1995 Employee Stock Purchase Plan, as amended.		8-K	June 17, 2011	001-31918
10.6††	Non-Employee Director Nonstatutory Stock Option Agreement Granted under 1997 Stock Incentive Plan.		10-K	March 25, 2005	001-31918
10.7††	Form of Incentive Stock Option Agreement Granted Under the 2005 Stock Incentive Plan.		8-K	June 21, 2005	001-31918
10.8††	Form of Nonstatutory Stock Option Agreement Granted Under the 2005 Stock Incentive Plan.		8-K	June 21, 2005	001-31918
10.9††	Form of Incentive Stock Option Agreement Granted Under the 2008 Stock Incentive Plan.		8-K	June 10, 2008	001-31918
10.10††	Form of Nonstatutory Stock Option Agreement Granted Under the 2008 Stock Incentive Plan.		8-K	June 10, 2008	001-31918
10.11††	Form of Nonstatutory Stock Option Agreement (Non-Employee Directors) Granted Under the 2008 Stock Incentive Plan.		8-K	June 10, 2008	001-31918
10.12††	Form of Restricted Stock Agreement Under the 2008 Stock Incentive Plan.		8-K	June 10, 2008	001-31918

Exhibit Number	Description	Filed Herewith	Incorporated by Reference to		
			Form	Filing Date	SEC File No.
10.13††	Policy on Treatment of Stock Options in the Event of Retirement, approved April 28, 2014.		10-Q	August 12, 2014	001-31918
10.14††	Employment Agreement dated October 19, 2005 between Idera Pharmaceuticals, Inc. and Dr. Sudhir Agrawal		10-Q	November 9, 2005	001-31918
10.15††	Amendment dated December 17, 2008 to Employment Agreement by and between Idera Pharmaceuticals, Inc. and Dr. Sudhir Agrawal dated October 19, 2005.		8-K	December 18, 2008	001-31918
10.16††	Amended and Restated Employment Letter Agreement by and between Idera Pharmaceuticals, Inc. and Louis J. Arcudi, III, Dated December 2, 2011.		10-K	March 13, 2012	001-31918
10.17††	Director Compensation Program		10-Q	May 12, 2014	001-31918
10.18	First Amendment dated February 21, 2014 to Lease Agreement dated October 31, 2006 between Idera Pharmaceuticals, Inc. and ARE-MA-Region No. 23, LLC.		10-Q	May 12, 2014	001-31918
10.19†	Development and Commercialization Agreement, dated May 1, 2014, by and between Abbott Molecular Inc. and Idera Pharmaceuticals, Inc.		10-Q	August 12, 2014	001-31918
10.20††	Employment Letter Agreement, dated December 1, 2014, by and between Idera Pharmaceuticals, Inc. and Vincent Milano.		10-K	March 12, 2015	001-31918
10.21	Unit Purchase Agreement by and among Idera Pharmaceuticals, Inc. and certain persons and entities listed therein, dated April 1, 1998.		10-K	April 1, 2002	000-27352
10.22	Registration Rights Agreement dated as of May 20, 2005 by and among Idera Pharmaceuticals, Inc., Purchasers and Pillar Investment Limited.		10-Q	August 9, 2005	001-31918
10.23	Registration Rights Agreement, dated March 24, 2006, by and among Idera Pharmaceuticals, Inc. and the Investors named therein.		8-K	March 29, 2006	001-31918
10.24	Registration Rights Agreement, dated March 24, 2006, by and among Idera Pharmaceuticals, Inc., Biotech Shares Ltd. and Youssef El Zein.		8-K	March 29, 2006	001-31918

Exhibit Number	Description	Filed Herewith	Incorporated by Reference to		
			Form	Filing Date	SEC File No.
10.25	Amendment No. 1 to the Registration Rights Agreement dated March 24, 2006, by and among Idera Pharmaceuticals, Inc. and Biotech Shares Ltd.		10-Q	August 14, 2006	001-31918
10.26	Form of Warrant issued to Investors in Idera Pharmaceuticals, Inc.'s August 5, 2010 Financing.		10-Q	November 4, 2010	001-31918
10.27††	Second Amendment dated December 1, 2014 to Employment Agreement by and between Idera Pharmaceuticals, Inc. and Dr. Sudhir Agrawal dated October 19, 2005.		10-K	March 12, 2015	001-31918
10.28††	Employment Letter, dated December 12, 2014, by and between Idera Pharmaceuticals, Inc. and J. Peter Wolf, III.		10-K	March 12, 2015	001-31918
10.29	Form of Pre-Funded Warrant issued to purchasers in Idera Pharmaceuticals, Inc.'s registered public offering on Idera Pharmaceuticals, Inc.'s registration statement on Form S-3 (File No. 333-191073).		8-K	September 26,2013	001-31918
10.30	Form of Pre-Funded Warrant issued to purchasers in Idera Pharmaceuticals, Inc.'s registered public offering on Idera Pharmaceuticals, Inc.'s registration statement on Form S-3 (File No. 333-191073).		8-K	February 5, 2014	001-31918
10.31	Convertible Preferred Stock and Warrant Purchase Agreement, dated November 4, 2011, between Idera Pharmaceuticals, Inc. and the Purchaser named therein.		8-K	November 10, 2011	001-31918
10.32	Amendment No. 1, dated November 9, 2012, to Convertible Preferred Stock and Warrant Purchase Agreement, dated November 4, 2011, between Idera Pharmaceuticals, Inc. and the Purchaser named therein.		8-K	November 14, 2012	001-31918
10.33	Registration Rights Agreement, November 4, 2011, between Idera Pharmaceuticals, Inc. and the Purchaser named therein.		8-K	November 10, 2011	001-31918
10.34	Form of Warrant issued to Purchaser pursuant to Convertible Preferred Stock and Warrant Purchase Agreement, dated November 4, 2011, between Idera Pharmaceuticals, Inc. and the Purchaser named therein.		8-K	November 10, 2011	001-31918

Exhibit Number	Description	Filed Herewith	Incorporated by Reference to		
			Form	Filing Date	SEC File No.
10.35	Amendment No. 1, dated November 9, 2012, to Warrant, dated November 4, 2011, between Idera Pharmaceuticals, Inc. and the Registered Holder named therein.		8-K	November 14, 2012	001-31918
10.36	Convertible Preferred Stock and Warrant Purchase Agreement, dated November 9, 2012, among Idera Pharmaceuticals, Inc. and the Purchasers named therein.		8-K	November 14, 2012	001-31918
10.37	Registration Rights Agreement, November 9, 2012, among Idera Pharmaceuticals, Inc. and the Purchasers named therein.		8-K	November 14, 2012	001-31918
10.38	Form of Warrant issued to each Purchaser pursuant to Convertible Preferred Stock and Warrant Purchase Agreement, dated November 9, 2012, among Idera Pharmaceuticals, Inc. and the Purchasers named therein.		8-K	November 14, 2012	001-31918
10.39††	Employment Letter Agreement by and between Idera Pharmaceuticals, Inc. and Louis Brenner, dated January 3, 2014.		10-K	March 13, 2014	001-31918
10.40	Lease Agreement dated October 31, 2006 between Idera Pharmaceuticals, Inc. and ARE-MA-Region No. 23, LLC.		10-K/A	May 8, 2007	001-31918
10.41	Agreement, dated April 22, 2013, among Idera Pharmaceuticals, Inc., Pillar Pharmaceuticals I, L.P. and Pillar Pharmaceuticals II, L.P.		8-K	April 23, 2013	001-31918
10.42	Agreement, dated April 30, 2013, among Idera Pharmaceuticals, Inc., Pillar Pharmaceuticals I, L.P., Pillar Pharmaceuticals II, L.P. and Participations Besancon.		S-1/A	May 1, 2013	333-187155
10.43	Form of Warrant issued to purchasers in Idera Pharmaceuticals, Inc.'s registered public offering on Idera Pharmaceuticals, Inc.'s registration statement on Form S-1 (File No. 333-187155).		10-Q	May 15, 2013	001-31918
10.44	Form of Warrant issued to entities affiliated with Pillar Invest Corporation in Idera Pharmaceuticals, Inc.'s registered public offering on Idera Pharmaceuticals, Inc.'s registration statement on Form S-1 (File No. 333-187155).		10-Q	May 15, 2013	001-31918

Exhibit Number	Description	Filed Herewith	Incorporated by Reference to		
			Form	Filing Date	SEC File No.
10.45	Form of Pre-Funded Warrant issued to purchasers in Idera Pharmaceuticals, Inc.'s registered public offering on Idera Pharmaceuticals, Inc.'s registration statement on Form S-1 (File No. 333-187155).		10-Q	May 15, 2013	001-31918
10.46††	2013 Stock Incentive Plan, as amended.		8-K	June 13, 2014	001-31918
10.47††	Form of Incentive Stock Option Agreement granted under the 2013 Stock Incentive Plan.		8-K	July 29, 2013	001-31918
10.48††	Form of Nonstatutory Stock Option Agreement granted under the 2013 Stock Incentive Plan.		8-K	July 29, 2013	001-31918
10.49††	Form of Nonstatutory Stock Option Agreement (Non-Employee Directors) granted under the 2013 Stock Incentive Plan.		8-K	July 29, 2013	001-31918
10.50††	Employment Letter, dated January 26, 2015, by and between Idera Pharmaceuticals, Inc. and Clayton Fletcher.		10-Q	May 11, 2015	001-31918
10.51††	Consulting Agreement, dated January 30, 2015, by and between Idera Pharmaceuticals, Inc. and Robert D. Arbeit, M.D.		10-Q	May 11, 2015	001-31918
10.52	Registration Rights Agreement, dated February 9, 2015, among Idera Pharmaceuticals, Inc. and the Selling Stockholders named therein.		8-K	February 9, 2015	001-31918
10.53††	Amendment to 2013 Stock Incentive Plan, as amended.		8-K	June 11, 2015	001-31918
10.54††	Form of Inducement Stock Option Award – Nonstatutory Stock Option Agreement.		10-Q	November 6, 2015	001-31918
10.55††	Employment Letter, dated June 5, 2015, by and between Idera Pharmaceuticals, Inc. and Mark J. Casey.		10-Q	May 9, 2016	001-31918
10.56*	License Agreement, dated November 28, 2016, by and between Idera Pharmaceuticals, Inc. and Vivelix Pharmaceuticals, Ltd.	X			
10.57	Second Amendment dated November 17, 2016 to Lease Agreement dated October 31, 2006 between Idera Pharmaceuticals, Inc. and ARE-MA-Region No. 23, LLC.	X			
23.1	Consent of Independent Registered Public Accounting Firm	X			
31.1	Certification of Chief Executive Officer pursuant to Exchange Act Rules 13a-14 and 15d-14, as adopted pursuant to Section 302 of Sarbanes-Oxley Act of 2002.	X			
31.2	Certification of Chief Financial Officer pursuant to Exchange Act Rules 13a-14 and 15d-14, as adopted pursuant to Section 302 of Sarbanes-Oxley Act of 2002.	X			
32.1	Certification of Chief Executive Officer pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002.	X			

Exhibit Number	Description	Filed Herewith	Incorporated by Reference to		
			Form	Filing Date	SEC File No.
32.2	Certification of Chief Financial Officer pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002.	X			
101.INS	XBRL Instance Document	X			
101.SCH	XBRL Taxonomy Extension Schema	X			
101.CAL	XBRL Taxonomy Extension Calculation Linkbase Document	X			
101.DEF	XBRL Taxonomy Extension Definition Linkbase Document	X			
101.LAB	XBRL Taxonomy Extension Labels Linkbase Document	X			
101.PRE	XBRL Taxonomy Extension Presentation Linkbase Document	X			

† Confidential treatment granted as to certain portions, which are omitted and filed separately with the Commission.

†† Management contract or compensatory plan or arrangement required to be filed as an Exhibit to the Annual Report on Form 10-K.

* Confidential treatment requested as to certain portions, which portions are omitted and filed separately with the Commission.