CytomX Therapeutics, Inc.
Form 10-K
March 02, 2017

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 001-37587

CytomX Therapeutics, Inc.

(Exact Name of Registrant as Specified in Its Charter)

| | |
|---|---|
| Delaware | 27-3521219 |
| (State or other jurisdiction of incorporation or organization) | (I.R.S. Employer Identification No.) |
| 151 Oyster Point Boulevard, Suite 400 | |
| South San Francisco, California | 94080 |
| (Address of principal executive offices) | (Zip Code) |

(650) 515-3185

(Registrant’s telephone number, including area code)

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

| Title of each class | Name of each exchange on which registered |
|---|---|
| Common Stock, $0.00001 par value | The NASDAQ Global Select 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 Section 15(d) of the Act. Yes No

Indicate by check mark whether the issuer (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 such filing requirements for the past 90 days. Yes No

Indicate by check mark whether the registrant has submitted electronically and posted on its corporate website, 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 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 (Do not check if a smaller reporting company) | 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

As of June 30, 2016, the last business day of the registrant's most recently completed second fiscal quarter, the aggregate market value of the registrant's common stock held by non-affiliates of the registrant was approximately $197.3 million, based on the closing price of the registrant's common stock on NASDAQ Global Select Market on June 30, 2016 of $10.22 per share. Shares of the registrant's common stock held by each officer and director and each

person known to the registrant to own 10% or more of the outstanding common stock of the registrant have been excluded in that such persons may be deemed affiliates. This determination of affiliate status is not a determination for other purposes.

As of February 28, 2017, 36,518,184 shares of the registrant's common stock, $0.00001 par value per share, were outstanding.

DOCUMENTS INCORPORATED BY REFERENCE

Portions of the registrant's definitive proxy statement to be filed for its 2017 Annual Meeting of Stockholders are incorporated by reference into Part III hereof. Such proxy statement will be filed with the Securities and Exchange Commission within 120 days of the end of the fiscal year covered by this Annual Report on Form 10-K.

CYTOMX THERAPEUTICS, INC.

ANNUAL REPORT ON FORM 10-K

TABLE OF CONTENTS

Forward-Looking Statements

This Annual Report on Form 10-K contains certain forward-looking statements that involve risks and uncertainties. These forward-looking statements reflect our current views with respect to, among other things, future events and our financial performance. These statements are often, but not always, made through the use of words or phrases such as "may," "might," "should," "could," "predict," "potential," "believe," "expect," "continue," "will," "anticipate," "seek," "estima "projection," "would," "annualized" and "outlook," or the negative version of those words or other comparable words or phrases of a future or forward-looking nature. These forward-looking statements are not historical facts, and are based on current expectations, estimates and projections about our industry, management's beliefs and certain assumptions made by management, many of which, by their nature, are inherently uncertain and beyond our control. Accordingly, we caution you that any such forward-looking statements are not guarantees of future performance and are subject to risks, assumptions, estimates and uncertainties that are difficult to predict. Although we believe that the expectations reflected in these forward-looking statements are reasonable as of the date made, actual results may prove to be materially different from the results expressed or implied by the forward-looking statements.

A number of important factors could cause our actual results to differ materially from those indicated in these forward-looking statements, including those factors identified in "Risk Factors" or "Management's Discussion and Analysis of Financial Condition and Results of Operations" or the following:

- the initiation, timing, progress and results of our research and development programs, preclinical studies, any clinical trials and Investigational New Drug application ("IND"), Clinical Trial Application, New Drug Application ("NDA"), Biologics License Application ("BLA") and other regulatory submissions;
- our receipt and timing of any milestone payments or royalties under any existing or future research collaboration and license agreements or arrangements;
- our expectations regarding the activity of our product candidates once administered in a human subject;
- our expectations and beliefs regarding the evolution of the market for cancer therapies and development of the immuno-oncology industry;
- our ability to identify and develop products for novel cancer targets;
- our dependence on existing and future collaborators for developing, obtaining regulatory approval for and commercializing product candidates in the collaboration;
- our ability to identify and develop product candidates for the treatment of additional disease indications;
- our or an existing or future collaborator's ability to obtain and maintain regulatory approval of any of our product candidates;
- the rate and degree of market acceptance of any approved products candidates;
- the commercialization of any approved product candidates;
- our ability to establish and maintain collaborations and retain commercial rights for our product candidates in such collaborations;
- the implementation of our business model and strategic plans for our business, technologies and product candidates;
- our estimates of our expenses, ongoing losses, future revenue and capital requirements;
- our ability to obtain additional funds for our operations;
- our or any existing or future collaborator's ability to obtain and maintain intellectual property protection for our technologies and product candidates and our ability to operate our business without infringing the intellectual property rights of others;
- our reliance on third parties to conduct our preclinical studies or any future clinical trials;
- our reliance on third-party supply and manufacturing partners to supply the materials and components for, and manufacture, our research and development, preclinical and clinical trial product supplies;
- our ability to attract and retain qualified key management and technical personnel;
- our expectations regarding the time during which we will be an emerging growth company under the Jumpstart Our Business Startups Act of 2012;

1

- our financial performance; and
- developments relating to our competitors or our industry.

Any forward-looking statements in this Annual Report on Form 10-K reflect our current views with respect to future events or to our future financial performance and involve known and unknown risks, uncertainties and other factors that may cause our actual results, performance or achievements to be materially different from any future results, performance or achievements expressed or implied by these forward-looking statements. Factors that may cause actual results to differ materially from current expectations include, among other things, those listed under Part I, Item 1A. Risk Factors and discussed elsewhere in this Annual Report on Form 10-K. Given these uncertainties, you should not place undue reliance on these forward-looking statements. Except as required by law, we assume no obligation to update or revise these forward-looking statements for any reason, even if new information becomes available in the future.

This Annual Report on Form 10-K also contains estimates, projections and other information concerning our industry, our business and the markets for certain drugs and therapeutic biologics, including data regarding the estimated size of those markets, their projected growth rates and the incidence of certain medical conditions. Information that is based on estimates, forecasts, projections or similar methodologies is inherently subject to uncertainties and actual events or circumstances may differ materially from events and circumstances reflected in this information. Unless otherwise expressly stated, we obtained these industry, business, market and other data from reports, research surveys, studies and similar data prepared by third parties, industry, medical and general publications, government data and similar sources. In some cases, we do not expressly refer to the sources from which these data are derived.

Except where the context otherwise requires, in this Annual Report on Form 10-K, “we,” “us,” “our” and the “Company” refer to CytomX Therapeutics, Inc.

Trademarks

This Annual Report on Form 10-K includes trademarks, service marks and trade names owned by us or other companies. All trademarks, service marks and trade names included in this Annual Report on Form 10-K are the property of their respective owners.

PART I

Item 1. Business

We are a clinical-stage, oncology-focused biopharmaceutical company pioneering a novel class of investigational antibody therapeutics based on our Probody technology platform. We use our platform to create proprietary cancer immunotherapies against clinically-validated targets, as well as to develop first-in-class cancer therapeutics against difficult-to-drug targets. We believe that our Probody platform has the potential to improve the combined efficacy and safety profile of monoclonal antibody modalities, including cancer immunotherapies, antibody drug conjugates ("ADCs") and T-cell-recruiting bispecific antibodies. Our Probody therapeutics are designed to take advantage of unique conditions in the tumor microenvironment to enhance the tumor-targeting features of an antibody and reduce drug activity in healthy tissues. Our investigational Probody therapeutics address clinically-validated cancer targets in immuno-oncology, such as PD-L1, against which CX-072 is directed, as well as novel targets, such as CD-166, against which CX-2009 is directed, that may be difficult to drug without causing damage to healthy tissues. We received clearance from the United States Food and Drug Administration (the "FDA") for our IND for CX-072 in December 2016 and treated the first patient in our open-label, dose finding Phase 1/2 clinical trial in January 2017. We also expect to file an IND for CX-2009 in the first half of 2017 and initiate a Phase 1 clinical trial in 2017. In addition to our proprietary programs, we are collaborating with strategic partners including AbbVie Inc. through its subsidiary AbbVie Ireland Unlimited Company ("AbbVie"), Bristol-Myers Squibb Company ("BMS"), ImmunoGen, Inc. ("ImmunoGen"), The University of Texas MD Anderson Cancer Center ("MD Anderson"), and Pfizer Inc. ("Pfizer"). Our broad technology platform and lead product candidates are supported by more than a decade of thorough scientific research and strong intellectual property. Our vision is to transform lives with safer, more effective therapies. To realize this vision, we are executing on our mission of changing the treatment of cancer by urgently advancing our Probody pipeline.

The premise of our Probody platform is to apply the prodrug concept to create a therapeutic antibody that remains inactive until it reaches the tumor. Probody therapeutics have the potential to produce additional tumor specificity and an enhanced safety profile because they are designed to have limited interaction with their molecular targets in healthy tissue. This approach of dosing drugs in a form such that they are only activated after reaching certain tissues is called the prodrug approach, and has been used with many small molecule drugs, but has never before been effectively pursued using therapeutic antibodies.

Cancer is the second leading cause of mortality in the United States and accounts for nearly one in every five deaths. Early cancer research and treatment relied on relatively non-specific and highly toxic small molecule chemotherapies. Over the last twenty years, a new paradigm of cancer research and treatment has emerged that is focused on more targeted therapies, including monoclonal antibody modalities, which represent some of the most effective and top-selling therapies on the market today. The leading three monoclonal antibodies for cancer generated more than $20 billion in global sales in 2015. More recently, immuno-oncology has emerged as a promising new field of cancer therapy that aims to enhance anti-tumor immune responses by, for example, overcoming the suppressive mechanisms that cancer cells have developed to evade the immune system. These therapies have shown the potential to provide dramatic efficacy and to extend survival, including in cancers for which conventional therapies, such as surgery, chemotherapy and radiotherapy, have failed. In addition, new classes of monoclonal antibody modalities have also reached the market. These new classes include ADCs and bispecific antibodies, which have more potency than first-generation antibodies.

Despite these advancements, many therapeutic antibodies are limited by a suboptimal therapeutic window (the combined efficacy and safety profile of a therapeutic). For example, the targets of antibody therapies are often found not only on tumors but also on healthy tissue, leading to toxicities. Consequently, there remains a significant need for therapeutics that are more efficacious, safe and tolerable. We believe our technology has the potential to address this need and represents the next evolution of targeted monoclonal antibody cancer therapies.

3

A Probody therapeutic consists of three components produced as a single protein by standard antibody production methodology: an active anti-cancer antibody, a mask for the antibody and a protease-cleavable linker. In preclinical testing, we have demonstrated the function of each of these components. The mask is a peptide designed to disguise the active binding site of the antibody to prevent the therapeutic from binding to healthy tissues. The following graphic depicts the three components of a Probody therapeutic, interacting with a protease:

When a Probody therapeutic enters a tumor, it encounters proteases, which are enzymes that cleave proteins and have increased activity in the tumor microenvironment. The proteases in the tumor cleave the linker, releasing the mask and allowing the antibody to attack the tumor. The following graphic depicts the activation of a Probody therapeutic by proteases:

Leveraging Protease Biology for our Proprietary Probody Platform

Proteases play an essential role in many aspects of normal physiology, such as digestion of food in the gastrointestinal tract, wound healing and metabolic function. However, uncontrolled protease activity can lead to destruction of essential proteins and tissues. Therefore, proteases are normally very tightly regulated by redundant mechanisms, with very little extracellular protease activity detectable in healthy tissues. In contrast, it has been well documented that proteases are not only present, but also activated, in virtually all types of tumors, playing a key role in tumor growth, invasion and metastasis. Probody therapeutics are designed to be activated in this protease-rich tumor microenvironment but not in healthy tissue where proteases are under tight control as depicted in the figure below:

Our Probody Platform

Our Probody platform utilizes active proteases in tumor tissue to allow monoclonal antibody-based therapies to be delivered in an inactive state and then to be activated at the tumor site. This approach is designed to limit toxicity that typically arises from the binding of an antibody to a target in healthy tissues while preserving biological activity in the tumor where it is desired. We have demonstrated the applicability of the Probody platform to multiple monoclonal antibody modalities, including ADCs and T-cell-recruiting bispecifics. We are also investigating the application of Probody technology to CARs, which are cell-based therapies that contain chimeric antigen receptors.

Each Probody therapeutic is recombinant; that is, it is created using molecular biology techniques so that both the binding function and the cleavable linker function are encoded in the nucleic acid sequence and expressed as a single protein, like other monoclonal antibody therapeutics.

The design of the mask peptide and protease-cleavable linker is technically challenging. Together with experts in the field, we spent the last decade conducting research to characterize protease activity and to engineer Probodies to take advantage of specific proteases. In addition, we devised criteria for identifying proteases that would work best in the context of our platform. Among these criteria, we targeted proteases that were:

- highly expressed in active form across multiple tumor types;
- either located on the outer cell surface or secreted by the cell;
- able to remove a mask from a Probody therapeutic; and
- significantly less active in normal, healthy tissues or in blood.

We have chosen and optimized protease-cleavable linkers so that any one of a number of activated proteases can cleave them. Using this approach, we believe Probody therapeutics can be cleaved and activated by at least one protease in the majority of tumors. We also developed a proprietary process to identify and optimize the mask peptides.

Key Advantages of Our Probody Platform

We believe that our Probody platform provides the following key advantages:

- A novel therapeutic antibody class enabled by our proprietary platform. We believe we have a differentiated technology platform that gives us a substantial competitive advantage supported by more than a decade of research and strong intellectual property.
- Potential to improve the therapeutic window of antibody-based therapeutics. By engineering our therapeutics to selectively activate in the tumor microenvironment, our Probody product candidates have the potential to improve safety and tolerability.
- Ability to combine more effectively with other therapies. We believe the therapeutic window and tumor specificity of our candidates have potential to reduce the dose-limiting toxicities observed in combination therapies and thus enable new combinations with other cancer therapies that are difficult or impossible to use.
- Applicability across many molecular targets. We believe that our technology addresses many different molecular targets expressed by many different kinds of tumors—including targets that are difficult to address because they are also expressed on healthy tissue—because Probody therapeutics are designed to have limited interaction with non-cancerous tissues.
- Versatility across antibody modalities. We believe that our technology can be applied to any antibody-based therapy, including novel potent modalities like ADCs, T-cell-recruiting bispecific antibodies and CARs, which are cell-based therapies that contain chimeric antigen receptors.

Cancer Remains a Major Unmet Medical Need

Cancer is the second leading cause of mortality in the United States, accounting for nearly one in every five deaths. Approximately 40% of Americans will develop cancer according to the American Cancer Society.

Cancer treatment has traditionally included chemotherapy, radiation, surgery or a combination of these approaches. Small molecule chemotherapy agents can be effective in certain types of cancer, but they can also cause toxicities that may lead to life-threatening consequences, lower quality of life or untimely termination of treatment. Furthermore, these agents offer limited efficacy in many types of cancer.

Over the last twenty years, a new paradigm of cancer research and treatment has emerged that involves more targeted therapies, including monoclonal antibodies. Monoclonal antibodies are proteins derived from living organisms that bind to targets, called antigens, on tumor cells and then inhibit tumor growth. As a drug class, monoclonal antibodies have transformed oncology treatment and represent some of the most effective and top selling therapies on the market. For example, Herceptin, Avastin and Rituxan have dominated the market with over $20 billion in annual sales in 2015. The success of conventional monoclonal antibodies has been hindered by limited efficacy and by safety and tolerability concerns. Administration of antibodies may cause systemic side effects, as well as localized, organ-specific damage. Much of this toxicity is a direct consequence of the fact that healthy tissues express the same antigens that antibodies target on cancerous cells.

More recently, immuno-oncology has emerged as a promising new field of cancer therapy that aims to enhance anti-tumor immune responses by, for example, overcoming mechanisms that cancer cells have developed to evade the immune system. Some cancer cells overly express proteins, called immune checkpoints, that apply brakes to the immune system, and enable the tumor cells to evade destruction. Immune checkpoint inhibitors, such as nivolumab, pembrolizumab, ipilimumab, and atezolizumbab, which are antibodies targeting these immune inhibitory proteins, release these brakes and allow the immune system to destroy the tumor. These drugs have shown promising efficacy in clinical trials, including long-term remission in certain patients, and have been approved for the treatment of melanoma, non-small cell lung cancer and bladder cancer. They are currently being explored for multiple other solid tumor indications. Although these drugs have demonstrated promising results, only a minority of patients receive

durable benefit from treatment with these agents alone. Most recently, combination regimens of immunotherapy agents have demonstrated signs of improved efficacy in larger numbers of patients. We believe that combination therapy will play a critical role in future cancer immunotherapy regimens. However, many of these combinations have significant toxicity and tolerability issues, due in part to the activation of the immune system in both healthy and cancerous environments. We believe these issues will likely impact further clinical and commercial advancements of combination cancer immunotherapies.

In the past decade, several new modalities of highly potent monoclonal antibody-based therapies have also emerged.

ADCs represent one such modality. These agents are comprised of two functional units chemically fused or conjugated to each other: a cytotoxic drug payload and a monoclonal antibody. ADCs combine the targeting abilities of the antibody with the cancer killing ability of cytotoxic drugs, leading to better specificity in targeting tumor cells compared to traditional chemotherapy. Ado-trastuzumab emtansine and brentuximab vedotin are ADCs that have been approved for the treatment of specific subsets of breast cancer and lymphoma, respectively. Bispecific antibodies, another class of second-generation biologics, have the ability to simultaneously bind a cancer cell and a T-cell, leading to the destruction of the cancerous cell by the T-cell. This ability improves the potency of bispecific antibodies compared to first-generation monoclonal antibodies.

Blinatumomab is an example of a T-cell-recruiting bispecific antibody that has recently been approved for the treatment of relapsed or refractory acute lymphoblastic leukemia ("ALL"). While all of these potent new therapies have shown promise, none addresses a key limitation of antibody-based therapeutics—expression of targets in healthy tissue, which leads to toxicity and limits clinical use.

Pipeline Strategies

We have three pipeline strategies that we are pursuing with our Probody platform:

- Develop a novel class of cancer immunotherapies directed against clinically-validated targets. Through our technology platform, we believe that we can expand the therapeutic window where current antibody therapies have encountered challenges with respect to safety or efficacy. For example, combination therapies in immuno-oncology have shown great promise in terms of efficacy but have been restricted by dose-limiting toxicities. Recent preclinical research has shown that localizing cancer immunotherapies to cancerous tissue has the potential to improve the therapeutic window in patients treated with the immunotherapies. We therefore see an opportunity to develop cancer immunotherapies using Probody therapeutics as the backbone for combination therapies. Our lead proprietary program for this pipeline strategy is CX-072, a Probody therapeutic candidate directed against PD-L1, a clinically-validated target in multiple tumor types including non-small cell lung cancer, bladder cancer and melanoma.
- Develop novel first-in-class therapeutics directed against difficult-to-drug targets. We believe we can create a therapeutic window in patients for targets where none exists because current approaches have not been viable as a result of toxicity concerns. Our Probody technology has the potential to address targets that are expressed in both tumor tissues and healthy tissues, which otherwise makes development of safe drugs and therapeutic biologics difficult. Given the novelty of these treatments and their potential to address unmet medical needs, we may pursue expedited review or accelerated approval paths, such as breakthrough therapy and fast-track designations, for these treatments. Furthermore, our Probody technology potentially enables us to take better advantage of the most potent modalities of monoclonal antibody therapeutics, such as ADCs and bispecific antibodies. Our lead proprietary candidate for this pipeline strategy is CX-2009, a Probody drug conjugate (a "PDC") directed against the target CD-166, which is expressed in multiple tumor types including breast, lung, colorectal and prostate cancer.
- Collaborate with leading biopharmaceutical companies to discover and develop Probody therapeutics against selected targets. Since 2013, we have entered into product-focused collaborations with AbbVie, BMS, ImmunoGen and Pfizer. These alliances are multi-target, product-focused collaborations with the objective of broadening the reach of our Probody platform. For example, we are collaborating with AbbVie to co-develop and co-commercialize PDCs directed against CD71 and with BMS on the discovery and development of a Probody version of Yervoy, an approved antibody targeting CTLA-4. Our strategy is to retain ownership of key products in our pipeline and partner selected programs. We intend to retain certain development and commercial rights for products in certain future collaborations.

Our Pipeline Strategies for Our Probody Platform

Our First Pipeline Strategy

A novel class of cancer immunotherapies directed against clinically-validated targets. Through our technology platform, we believe that we can expand the therapeutic window for clinically-validated targets where current therapies have encountered challenges with respect to safety or efficacy. We have validated this approach preclinically with multiple targets, and plan to develop multiple novel Probody therapeutics in the field of immuno-oncology to address just such issues. Our first Probody product candidate in this area, CX-072, is directed against PD-L1 and treated the first patient in our open-label, dose finding Phase 1/2 clinical trial for CX-072 in January 2017.

Opportunity for safer and more effective therapies in immuno-oncology. We believe we have multiple opportunities to enter the immuno-oncology field given the potentially enhanced safety and efficacy profiles of our Probody product candidates. In particular, therapeutic approaches already validated by current drugs offer us attractive entry points. The approaches we are targeting initially are checkpoint inhibitors, where severe dose- limiting toxicities have been observed, especially in combination therapies.

The immune system is capable of recognizing and eliminating tumor cells; however, tumors are sometimes able to block the immune response through alteration of regulatory checkpoint pathways. Tumors express proteins, called checkpoint proteins, which can apply the brakes to the immune system, preventing it from attacking the tumor. By creating a monoclonal antibody that inhibits these proteins, the brakes can be released, and the immune system can eliminate the tumor. Novel cancer therapies that target these proteins are being tested in clinical trials by others, and four antibody products, ipilimumab, pembrolizumab, atezolizumab and nivolumab, have recently been approved by the FDA.

While this approach has resulted in remarkable clinical results, including long-term remissions in patients who previously would have died, there are significant toxicities associated with these therapies. Because tumors use the same mechanisms to inhibit the immune system that the body uses to ensure that the immune system does not attack normal tissues, these therapies release the brakes not only in the tumor, but also elsewhere in the body. This can result in the immune system attacking normal tissues and cause a number of toxicities, including, for example, severe lung inflammation.

Combination therapy is the next frontier in immuno-oncology. While single-agent therapy has proven to be effective in certain patients (inducing effective, durable remissions), the oncology community is currently exploring new, more potent combinations to create longer-term and more durable responses in a larger percentage of patients. This new potency addresses the lack of response seen in the majority of patients, but it brings with it additional toxicity. Data emerging from clinical studies has suggested that some combinations may provide promising enhanced anti-tumor efficacy, but at the expense of greater toxicities that may limit their clinical utility. In a recent clinical trial, 58% of patients treated with the combination of nivolumab and ipilimumab had an objective response, 55% had adverse events in either Grades 3 or 4, and 36% had adverse events severe enough that they had to withdraw from the trial and discontinue combination therapy. That withdrawal rate compared to 8% of patients receiving nivolumab alone and 15% of patients receiving ipilimumab alone.

Our Probody therapeutic solution for immuno-oncology. Recent research results from several investigators have suggested that immunotherapy that is specifically directed to the tumor microenvironment while sparing the rest of the body may allow efficacy without the toxicities seen with systemic delivery of these drugs. For example, in a mouse model investigators have shown efficacy of antibodies targeting CTLA-4 at much lower doses when the antibody was injected directly into a tumor rather than infused into the blood stream and delivered systemically. This result suggests that there are sufficient tumor-reactive immune cells, called T-cells, activated by the antibodies targeting CTLA-4 within the tumor to elicit an anti-tumor response, and that activation of T-cells outside of the tumor is not required to get the desired therapeutic effect. Therefore, local activation of immuno-oncology agents, such as checkpoint inhibitors, in the tumor microenvironment may yield efficacy while minimizing systemic exposure that may lead to toxicity.

Based on these results and our own research, we believe that employing Probody technology to inhibit the checkpoints on T-cells locally, rather than systemically, has the potential to significantly reduce toxicities and increase the tolerability of these types of cancer immunotherapies, especially in combination with other therapies. We believe that the challenges faced by combinations, including combinations with PD-L1 checkpoint inhibitors, will be observed across many classes of immuno-oncology therapeutics and other cancer therapeutics. We believe that Probody therapeutics represent an attractive way to limit or avoid the toxicities that are observed in these approaches, leading to better efficacy and safety. We believe that CX-072, our PD-L1 Probody therapeutic and follow-on product candidates against other immuno-oncology targets, for example, PD-1, have the potential to become a new backbone of the combination therapy in immuno-oncology.

Our Second Pipeline Strategy

Novel first-in-class therapeutics directed against difficult-to-drug targets. We believe we can create a therapeutic window in patients where current approaches have not been viable or are not expected to be viable because of toxicity concerns. Furthermore, our Probody technology potentially enables us to take better advantage of the most potent modalities of monoclonal antibody therapeutics such as ADCs and bispecific antibodies, which can be too toxic to use in some settings. We have validated this approach with multiple preclinical Probody therapeutics. Our first Probody product candidate in this area is CX-2009, a PDC directed against CD-166.

Opportunity for therapies against difficult-to-drug targets. We are addressing targets that are difficult to drug, in a way that we believe will make these targets useful for cancer therapies for the first time. The development of oncology therapeutics has traditionally been hindered by the need to find “druggable” targets, that is, proteins that not only can be biologically affected by therapeutics, but also are found in abundance on tumor cells and less abundantly on normal cells. Based on the conventional paradigm, a druggable target must be expressed at very low levels, or be absent, on healthy cells or there will likely be indiscriminate cell killing and toxicities as a result. Further, the target should be expressed at high levels in tumors to allow delivery of high levels of cytotoxic drug to the tumor. As a consequence, only a small number of targets have an expression profile that is suitable for developing effective oncology drugs and avoiding toxicity in normal tissues. This is especially the case for the new generation of highly potent antibody-based therapies, such as ADCs, T-cell- recruiting bispecific antibodies, and others, whose extreme potency typically demands even more stringent target selection.

Accordingly, targets that are difficult to drug due to their wide expression represent a very attractive new space for cancer drug development that we believe we have an advantage in pursuing. Given our Probody technology, we believe we are in a position to address many new targets in previously untapped areas and open up a greater portion of tumor biology to therapeutic intervention.

Our Probody solution to difficult-to-drug targets. To be effective therapeutics, ADCs must bind to highly expressed tumor targets to enable the delivery of enough cytotoxic payload to kill tumor cells, yet bind at low levels to normal tissues. We have systemically surveyed the human genome to identify targets for PDCs that are highly expressed in tumor tissue but that have not been pursued by other companies, likely because of the concern of toxicity due to healthy tissue expression. Our Probody therapeutics have the potential to deliver more payload to tumor tissue but not significantly bind normal tissues, thereby creating products with viable therapeutic windows in patients. We have identified and are pursuing a number of such targets, such as CD-166. CD-166 is expressed at high levels in tumor cells, which may allow delivery of high levels of cytotoxin and therefore enable efficient tumor killing. Further, unlike conventional ADC targets, which are found in only a small number of tumor types because of their requirements for low normal tissue expression, PDC targets can be found in many different tumor types, suggesting that these product candidates could address very large markets.

Our Third Pipeline Strategy

Collaborations with leading biopharmaceutical companies to advance Probody product candidates. We believe that the Probody platform has broad applicability across a number of targets and antibody formats. We have leveraged strategic partnering to extend the reach of our therapeutic opportunity. Since the beginning of 2013, we have entered into product-focused collaborations with AbbVie, BMS, ImmunoGen and Pfizer to enable development of certain Probody therapeutics. In constructing each of these collaborations, our primary objectives were to collaborate with leading biopharmaceutical players to validate the potential of Probody therapeutics, to gain meaningful near-term funding and/or technology access to enable advancement of CytomX’s wholly owned Probody therapeutics pipeline, and to retain significant milestones and royalties for long term upside. The details of our four existing collaborations are as follows:

- AbbVie PDC collaborations. In April 2016, we entered into a collaboration with AbbVie to co-develop and co-commercialize PDCs against CD71. Under the terms of the agreement, we will co-develop a PDC against CD71 with AbbVie, with CytomX leading pre-clinical and early clinical development. AbbVie will lead later development and commercialization, with global late-stage development costs shared between the two companies. We received an upfront payment of $20 million and are eligible to receive up to $470 million in development, regulatory and commercial milestones and royalties on ex-US sales in the high teens to low twenties if we participate in the co-development of a CD71 licensed product subject to a reduction in such royalties if we opt-out from the co-development of the CD71 PDC. AbbVie and CytomX will share 65% and 35%, respectively, of the net profits or

net losses from the co-development of the CD71 PDC. We have selected a clinical candidate, CX-2029, that is currently in IND-enabling studies.

We also entered into a second collaboration with AbbVie in April 2016 pursuant to which AbbVie has exclusive worldwide rights to develop and commercialize Probody drug conjugates against up to two undetermined targets. We received an upfront payment of $10 million pursuant to the agreement and are eligible to receive up to $275 million in target nominations, development, regulatory and commercial milestones and royalties in the high single to low teens from commercial sales of any resulting PDCs. Pursuant to the agreement, AbbVie has the right to select a total of up to two targets under this collaboration and we will collaborate with AbbVie in the research and development of Probodies against selected targets. AbbVie has not yet selected any target.

- BMS Probody therapeutic collaboration. In May 2014, we entered into a collaboration with BMS for up to four targets. The initial focus of this collaboration is to develop Probody therapeutics against certain immunotherapy targets. We chose to form a collaboration with BMS because we believe that they have industry leading capabilities in immunotherapy, including approved products such as Yervoy, targeting CTLA-4, and Opdivo, targeting PD-1. The BMS collaboration provides us with a $50 million upfront payment, $25 million in target nomination fees for the two targets BMS selected in January and December 2016, provides research funding, and may provide up to $1,192 million in development, regulatory, and commercial milestones and mid-single digit to low-teen royalties on net sales of products arising from this collaboration. Our collaboration is structured such that we are responsible for generating Probody therapeutics against selected BMS targets. BMS is responsible for development and commercialization for each of the four product candidates and bears all such costs in the collaboration. BMS has selected all four of the targets in this collaboration. The most advanced product candidate in this collaboration is our CTLA-4 Probody product candidate, which is currently in IND enabling studies. In preclinical models, our CTLA-4 Probody candidate has demonstrated in vivo efficacy with reduced systemic T-cell activation as compared to the underlying CTLA-4 antibody. Given their success with Yervoy, an antibody that targets CTLA-4, we believe that BMS is the optimal partner to advance a Probody therapeutic against this clinically-validated target.
- ImmunoGen PDC collaboration. In January 2014, we entered into a collaboration with ImmunoGen in which we gained limited access to ImmunoGen's drug conjugate technology in exchange for granting ImmunoGen limited access to our Probody platform. We chose to form a collaboration with ImmunoGen because they have drug conjugate technology that has been clinically-validated for multiple antibody products targeting solid tumor indications, including Kadcyla and mirvetuximab soravtansine. Our collaboration is structured so that we have access to ImmunoGen's toxins and related linkers for one of our PDC targets. We have elected to utilize this license to enable our CD-166 PDC program. ImmunoGen is responsible for conjugating our Probody product candidate with their proprietary toxins and related linkers to create the PDC for our research and preclinical development. We have selected CX-2009 as the proprietary candidate for our CD-166 PDC program. In February 2016, we exercised our option under the collaboration agreement with ImmunoGen and obtained a development and commercial license for this product. Under the license agreement, we will pay ImmunoGen up to $60 million in development and regulatory milestones, up to $100 million in sales milestones, and tiered mid to high single digit royalties. We granted ImmunoGen access to our Probody platform for two targets, which they have already nominated. We are responsible for generating Probody therapeutics against these ImmunoGen targets and ImmunoGen is responsible for conjugating these targets using their proprietary toxins and related linkers to create the PDCs. ImmunoGen retains full development and commercial rights for these products, and if ImmunoGen exercise its option(s) to obtain a commercial license, it will owe us up to $30 million in development and regulatory milestones, $50 million in sales milestones, and mid-single digit royalties per program. The most advanced ImmunoGen product is currently at discovery stage.
- Pfizer PDC collaboration. In May 2013, we entered into a collaboration with Pfizer for up to four targets. We chose to form a collaboration with Pfizer because we believe that they have industry leading capabilities in ADCs, including access to proprietary drug conjugate linkers and toxins. Pfizer nominated three research targets pursuant to the agreement but did not select the fourth target before the option lapsed in May 2016. We continue to work with Pfizer on two of the three targets they selected under the collaboration. The most advanced programs in the collaboration are in the lead optimization stage. To date, we have received a total of $7.5 million in upfront and target nomination payments pursuant to the Pfizer collaboration. The Pfizer collaboration also provides us with up to $19 million in regulatory milestone payments per collaboration target and $110 million in sales milestone payments as well as tiered mid-single digit royalties on potential future sales per collaboration target. Our collaboration is structured such that we are responsible for generating Probody therapeutics against Pfizer-selected targets and Pfizer is responsible for conjugating the Probody therapeutics with their proprietary toxins and related linkers to create PDCs. If Pfizer exercises its option for a commercial license, it would be responsible for development and commercialization for each of the four product candidates and would bear all costs in the collaboration.

CX-072, PD-L1 Probody Therapeutic

CX-072 is a wholly-owned PD-L1 targeting Probody therapeutic for the treatment of cancer. In December 2016, we received clearance from the FDA for our Investigational New Drug ("IND") application for CX-072. In January 2017, we treated the first patient in our open-label, dose finding Phase 1/2 clinical trial evaluating CX-072 as monotherapy and in combination with Yervoy® (ipilimumab) or Zelboraf®(vemurafenib) in patients with metastatic or locally advanced unresectable solid tumors or lymphomas. Our aim is to achieve three goals as part of the clinical trial:

- Tolerability: Demonstrate that CX-072 is well tolerated in patients and potentially improves safety, particularly in the combination setting.
- Anti-cancer activity: Demonstrate initial evidence of CX-072's anti-cancer activity as monotherapy and in combination.
- Translational program and Probody platform proof-of-concept: Explore mechanistic aspects of Probody activity in patients.

We have designed an international umbrella program, PROCLAIM (Probody Clinical Assessment In Man) ("PROCLAM"), to evaluate our Probody therapeutics. Our CX-072 clinical study is the first module to be initiated under PROCLAIM as PROCLAIM-072 ("PROCLAIM-072"). Clinical data from PROCLAIM-072 is expected to begin to emerge in late 2017 and throughout 2018.

CX-2009, CD-166 Probody Therapeutic

CX-2009, is a first-in-class Probody drug conjugate targeting CD166. CX-2009 utilizes ImmunoGen, Inc. drug conjugate technology. CD166 is highly and homogeneously expressed in the majority of patients with a variety of solid tumors. Despite high expression of CD166 in normal tissues, our Probody technology is designed to concentrate CX-2009 only in tumor tissue. As such, we believe that CX-2009 is uniquely positioned to deliver on the promise of CD166 as a target. We anticipate filing our IND for CX-2009 in the first half of 2017 and initiate a Phase 1 clinical trial in 2017.

Other Product Candidates in Preclinical Development

We are actively pursuing the application of our Probody technology to multiple other product candidates. These include other product candidates directed against other immunotherapy targets, and other first-in-class PDC product candidates. We have applied our technology and are advancing product candidates based on T-cell-recruiting bispecific antibodies. We also recognize that new immunocellular therapies such as CAR-T therapies rely on recognition of tumor antigens using molecular components that may be synthesized as Probody constructs. We believe that our technology has the potential to enhance the therapeutic window of CAR-T therapies enabling them to translate their remarkable clinical responses in hematological tumors to solid tumors.

CX-2029, CD71, Probody Drug Conjugates in Collaboration with AbbVie

CD71, also known as transferrin receptor 1 (“TfR1”), is a protein that is essential for iron uptake in dividing cells, is highly expressed in a number of solid and hematologic cancers and has attractive molecular properties for efficient delivery of cytotoxic payloads to tumor cells. The combination of high expression in tumors and ubiquitous expression in normal tissues makes CD-71 a difficult target for conventional ADCs and an ideal candidate for development of PDCs. We have shown that CD71 PDCs are as efficacious as CD71 ADCs in multiple xenograph models at the expected human therapeutic dose. We have also investigated the tolerability of CD71 ADCs and PDCs in non-human primates. We noted life threatening toxicity for the ADCs whereas the PDCs were tolerated at the expected human therapeutic dose.

In April 2016, we entered into a collaboration to co-develop and co-commercialize Probody Drug Conjugates against CD71 with AbbVie. Our lead clinical candidate under this program, CX-2029, is currently in IND-enabling phase.

CTLA-4 Probody Product Candidate in Collaboration with BMS

We are developing a CTLA-4 Probody therapeutic with BMS. Published data in mouse models have demonstrated the potential value of localized intratumoral delivery of CTLA-4 antibodies to maintain efficacy while limiting toxicity. We believe that our CTLA-4 Probody therapeutic can effectively localize CTLA-4 antibody activity to the tumor while allowing systemic dosing, thereby limiting systemic toxicities normally seen with Yervoy. We believe that BMS is the optimal strategic partner for our CTLA-4 Probody therapeutic given their expertise in cancer immunotherapy and their success with Yervoy.

CTLA-4 is an immune checkpoint involved in regulating T-cell activation. BMS is currently marketing a CTLA-4 monoclonal antibody, Yervoy, that has been approved for unresectable or metastatic melanoma. CTLA-4 antibodies lead to T-cell activation for a wide range of antigens, including tumor antigens, which is the basis for its anti-tumor effect, and self-antigens, which may be the basis for the autoimmune toxicities associated with CTLA-4 antibodies therapies. In partnership with BMS, we are developing a CTLA-4 Probody therapeutic. The FDA approval for ipilimumab comes with a black box warning about potential severe and fatal immune-related adverse events. While the toxicities associated with ipilimumab can be successfully managed in many patients, up to 27% of patients in a phase 2 trial discontinued treatment due to adverse events. The use of ipilimumab in combination therapy with nivolumab, a PD-1 checkpoint inhibitor, led to increased rates of serious adverse events with 55% of patients with a severity of grade 3 or 4 events in patients treated with both drugs compared to 27% in the ipilimumab-treated patients and 16% in the nivolumab treated-patients.

We believe the systemic toxicity associated with CTLA-4 directed therapy might be reduced by local delivery of CTLA-4 antibodies to the tumor. In previous experiments with a MC-38 xenograft mouse model, investigators have shown local infusion of small doses of the antibody directly into the tumor resulted in an anti- tumor response and increased survival while lowering the systemic levels of the CTLA-4 antibody by approximately 1,000 fold. In MC-38

xenograft preclinical models, our CTLA-4 Probody candidate has demonstrated in vivo efficacy with reduced activity on peripheral T-cells as compared to CTLA-4 antibody. We believe that our CTLA-4 Probody therapeutic can be dosed systemically, achieve localized tumor-specific activation, and thus achieve a clinically important improvement in safety. This program is currently in IND-enabling phase.

CX-188, PD-1 Probody Therapeutic

PD-1 is the receptor for the PD-L1 ligand responsible for inhibiting T-cell activation. It is the target for various immuno-oncology products including nivolumab and pembrolizumab, which have been approved for melanoma. Because, like PD-L1, inhibiting PD-1 is associated with immune attack on normal cells, PD-1 therapy has been associated with significant toxicities, especially when used in combination with ipilimumab, another immunotherapy. We are developing a PD-1 Probody therapeutic, CX-188, as an additional approach to block the PD-L1/PD-1 pathway. This program is currently in IND-enabling phase.

Our Business Strategy

We are utilizing our innovative Probody platform to build a long-term, multiproduct company focused on the development of new cancer treatments. Our vision is to transform lives with safer, more effective therapies. To realize this vision, we are executing on our mission of changing the treatment of cancer by urgently advancing our Probody pipeline.

Manufacturing

Our Probody candidates are designed to be produced as fully recombinant antibody prodrugs. Our Probody candidates are also designed to maintain the manufacturability benefits of antibodies and leverage well established technologies used for antibody production. We have significant expertise in the production of therapeutic biologics. We conduct cell line development and process development both in-house and in collaboration with contract manufacturing organizations ("CMOs"). CMOs are responsible for manufacturing of drug substance and clinical drug product materials.

Our process development and manufacturing strategies are tailored to rapidly advance our two lead programs and we employ multiple complementary approaches to ensure successful execution. Our lead Chinese hamster ovary cell line has been successfully used for manufacturing several antibodies and requires minimal process optimization to establish a process to support early phase manufacturing. We utilize well established production steps typically part of a platform manufacturing process for antibodies. The CMO we have selected has a strong track record in manufacturing therapeutic biologics, including antibodies. All activities from cell line development to formulated drug product are performed at one location to maintain aggressive timelines and minimize delays that can result from engaging multiple parties for manufacturing. Similarly, for our PDC projects we have selected CMOs with strong expertise in clinical/commercial drug conjugate manufacturing and with capabilities for toxin conjugation and fill-finish. Furthermore, our two lead PDC programs incorporates toxin payloads that have an established clinical and regulatory history.

Competition

The biotechnology and biopharmaceutical industries, and the immuno-oncology subsector, are characterized by rapid evolution of technologies, fierce competition and strong defense of intellectual property. Any product candidates that we successfully develop and commercialize will have to compete with existing therapies and new therapies that may become available in the future. While we believe that our proprietary Probody platform and scientific expertise in the field of biologics and immuno-oncology provide us with competitive advantages, a wide variety of institutions, including large biopharmaceutical companies, specialty biotechnology companies, academic research departments and public and private research institutions, are actively developing potentially competitive products and technologies. We face substantial competition from biotechnology and biopharmaceutical companies developing products in immuno-oncology. These competitors generally fall within the following categories:

Cancer immunotherapies: AstraZeneca PLC, BMS, GlaxoSmithKline plc, Merck & Co., Inc., Novartis AG, Pfizer, Roche Holding Ltd, Sanofi SA and numerous small companies.

Antibody drug conjugates: ImmunoGen and Seattle Genetics, Inc.

Many of our competitors, either alone or with strategic partners, have substantially greater financial, technical and human resources than we do. Accordingly, our competitors may be more successful than us in obtaining approval for treatments and achieving widespread market acceptance, rendering our treatments obsolete or non-competitive. Accelerated merger and acquisition activity in the biotechnology and biopharmaceutical industries may result in even

more resources being concentrated among a smaller number of our competitors. These companies also compete with us in recruiting and retaining qualified scientific and management personnel, establishing clinical study sites and patient registration for clinical studies and acquiring technologies complementary to, or necessary for, our programs. Smaller or early-stage companies may also prove to be significant competitors, particularly through collaborative arrangements with large and established companies. Our commercial opportunity could be substantially limited in the event that our competitors develop and commercialize products that are more effective, safer, less toxic, more convenient or less expensive than our comparable products. In geographies that are critical to our commercial success, competitors may also obtain regulatory approvals before us, resulting in our competitors building a strong market position in advance of our products' entry. We believe the factors determining the success of our programs will be the efficacy, safety and convenience of our product candidates.

Intellectual Property

We strive to protect and enhance the proprietary technology, inventions, and improvements that are commercially important to our business, including seeking, maintaining, and defending patent rights, whether developed internally or licensed from third parties. Our policy is to seek to protect our proprietary position by, among other methods, pursuing and obtaining patent protection in the United States and in jurisdictions outside of the United States related to our proprietary technology, inventions, improvements, platforms and product candidates that are important to the development and implementation of our business. Our patent portfolio is intended to cover, but is not limited to, our technology platforms, our product candidates and components thereof, their methods of use and processes for their manufacture, our proprietary reagents and assays, and any other inventions that are commercially important to our business. We also rely on trade secret protection of our confidential information and know-how relating to our proprietary technology, platforms and product candidates, continuing innovation, and in-licensing opportunities to develop, strengthen, and maintain our proprietary position in our Probody platform and product candidates. We expect to rely on data exclusivity, market exclusivity, patent term adjustment and patent term extensions when available. Our commercial success may depend in part on our ability to obtain and maintain patent and other proprietary protection for our technology, inventions, and improvements; to preserve the confidentiality of our trade secrets; to maintain our licenses to use intellectual property owned or controlled by third parties; to defend and enforce our proprietary rights, including our patents; to defend against and challenge the assertion by third parties of their purported intellectual property rights; and to operate without the unauthorized infringement on the valid and enforceable patents and other proprietary rights of third parties.

We believe that we have a strong global intellectual property position and substantial know-how and trade secrets relating to our Probody technology, platform and product candidates. Our patent portfolio as of February 15, 2017 contained 13 United States ("U.S.") issued patents and four non-U.S. issued patents owned solely by CytomX and four U.S. issued patents and two non-U.S. issued patents that we co-own with the University of Santa Barbara ("UCSB"). We also have 23 U.S. pending applications as well as 121 non-U.S. pending applications owned solely by CytomX, as well as one U.S. pending applications and six non-U.S. pending applications that we co-own with UCSB. We have exclusively licensed UCSB's rights in the co-owned issued and pending patents. We also co-own one U.S. issued patent and one U.S. pending application with the University of California, San Francisco ("UCSF"). These patents and patent applications include claims directed to:

- Probody platform and PDC platform;
- Other pro-protein platforms;
- Probody conjugates and conjugation methods to produce PDCs;
- Bispecific and other multispecific Probody therapeutics, including T-cell-recruiting bispecific Probody therapeutics;
- Protease-cleavable linkers, e.g., serine protease- or MMP-cleavable linkers;
- Improved display systems for peptide display, e.g., to identify masks, substrates, and other proteins;
- Cancer immunotherapy Probody therapeutics, e.g., PD-L1, PD-1, and CTLA-4 Probody therapeutics, as well as related novel antibodies and combination therapies;
- PDCs, e.g., CD-166, CD-71 (transferrin receptor), and CD49c (integrin alpha 3) PDCs, as well as related Probody therapeutics, novel antibodies and ADCs;
- Probody therapeutics to other targets, e.g., EGFR, Jagged, and IL6R Probody therapeutics, as well as related PDCs, novel antibodies and ADCs;
- Antibodies that bind Probody therapeutics, e.g., anti-mask and anti-Probody antibodies; and
- Antibodies that bind the active site of uPA protease.

In addition, we have exclusively licensed the following patent portfolio from UCSB: nine U.S. issued patents; six non-U.S. issued patents; three U.S. pending applications; and five non-U.S. pending applications. This patent portfolio covers compositions and methods related to screening and identification of masks and protease-cleavable linkers that

we incorporate into our Probody therapeutics.

As for the Probody platform, product candidates and processes we develop and commercialize, in the normal course of business, we intend to pursue, where appropriate, patent protection or trade secret protection relating to compositions, methods of manufacture, assay methods, methods of use, treatment of indications, dosing and formulations. We may also pursue patent protection with respect to product development processes and technology.

We continually assess and refine our intellectual property strategy as we develop new platform technologies and product candidates. To that end, we are prepared to file additional patent applications if our intellectual property strategy requires such filings, or where we seek to adapt to competition or seize business opportunities. Further, we are prepared to file patent applications, as we consider appropriate under the circumstances, relating to the new technologies that we develop. In addition to filing and prosecuting patent applications in the United States, we often file counterpart patent applications in the European Union and in additional countries where we believe such foreign filing is likely to be beneficial, including but not limited to any or all of Australia, Brazil, Canada, China, Hong Kong, India, Israel, Japan, Mexico, New Zealand, Russia, South Africa and South Korea.

The term of individual patents depends upon the laws of the countries in which they are obtained. In most countries in which we file, the patent term is 20 years from the earliest date of filing of a non-provisional patent application. However, the term of United States patents may be extended for delays incurred due to compliance with FDA requirements or by delays encountered during prosecution that are caused by the United States Patent and Trademark Office (the "USPTO"). For example, the Hatch-Waxman Act permits a patent term extension for FDA-approved drugs of up to five years beyond the expiration of the patent. The length of the patent term extension is related to the length of time the drug is under regulatory review. Patent extension cannot extend the remaining term of a patent beyond a total of 14 years from the date of product approval and only one patent applicable to an approved drug may be extended. Similar provisions are available in Europe and other jurisdictions to extend the term of a patent that covers an approved drug. In the future, if and when our biopharmaceutical product candidates receive FDA approval, we expect to apply for patent term extensions on patents covering those product candidates. We intend to seek patent term extensions to any of our issued patents in any jurisdiction where these are available; however there is no guarantee that the applicable authorities, including the FDA in the United States, will agree with our assessment of whether such extensions should be granted, and even if granted, the length of such extensions. Our currently issued patents will likely expire on dates ranging from 2028 to 2035, unless we receive patent term extension or adjustment. If patents are issued on our pending patent applications, the resulting patents are projected to expire on dates ranging from 2028 to 2037, unless we receive patent term extension or adjustment. However, the actual protection afforded by a patent varies on a product-by-product basis, from country-to-country, and depends upon many factors, including the type of patent, the scope of its coverage, the availability of regulatory-related extensions, the availability of legal remedies in a particular country, and the validity and enforceability of the patent.

The patent positions of companies like ours are generally uncertain and involve complex legal and factual questions. No consistent policy regarding the scope of claims allowable in patents in the field of immunotherapy has emerged in the U.S. The patent situation outside of the United States is even more uncertain. Changes in the patent laws and rules, either by legislation, judicial decisions, or regulatory interpretation in the U.S. and other countries may diminish our ability to protect our inventions and enforce our intellectual property rights, and more generally could affect the value of our intellectual property. In particular, our ability to stop third parties from making, using, selling, offering to sell, or importing any of our patented inventions, either directly or indirectly, will depend in part on our success in obtaining, defending, and enforcing patent claims that cover our technology, inventions, and improvements. With respect to both licensed and company-owned intellectual property, we cannot be sure that patents will be granted with respect to any of our pending patent applications or with respect to any patent applications filed by us in the future, nor can we be sure that any of our existing patents or any patents that may be granted to us in the future will be commercially useful in protecting our platforms and product candidates and the methods used to manufacture those platforms and product candidates. Moreover, even our issued patents do not guarantee us the right to practice our technology in relation to the commercialization of our platform's product candidates. However, the area of patent and other intellectual property rights in biotechnology is an evolving one with many risks and uncertainties, and third parties may have blocking patents that could be used to prevent us from commercializing our patented Probody technology, platforms and product candidates and practicing our proprietary technology. Our issued patents and those that may issue in the future may be challenged, invalidated, or circumvented, which could limit our ability to stop competitors from marketing related platforms or product candidates or limit the length of the term of patent protection

that we may have for our Probody technology, platforms, and product candidates. In addition, the rights granted under any issued patents may not provide us with protection or competitive advantages against competitors with similar technology. Furthermore, our competitors may independently develop similar technologies. For these reasons, we may have competition for our Probody technology, platforms and product candidates. Moreover, because of the extensive time required for development, testing and regulatory review of a potential product, it is possible that, before any particular product candidate can be commercialized, any related patent may expire or remain in force for only a short period following commercialization, thereby reducing any advantage of the patent. For this and more comprehensive risks related to our proprietary technology, inventions, improvements, platforms and product candidates, please see the section entitled “Risk Factors—Risks Related to Intellectual Property.”

We intend to file applications for trademark registrations in connection with our product candidates in various jurisdictions, including the U.S. The USPTO previously accepted the PROBODY mark under an intent-to-use trademark application. Because we were unable to show use for that mark within three years of acceptance, the mark became abandoned. We have re-filed for trademark protection of the PROBODY mark with the USPTO. We also have filed for trademark protection of the IHZ mark with the USPTO. Both the PROBODY and IHZ marks were allowed by the USPTO in 2016.

We also rely on trade secret protection for our confidential and proprietary information. Although we take steps to protect our confidential and proprietary information as trade secrets, including through contractual means with our employees and consultants, third parties may independently develop substantially equivalent proprietary information and techniques or otherwise gain access to our trade secrets or disclose our technology. Thus, we may not be able to meaningfully protect our trade secrets. It is our policy to require our employees, consultants, outside scientific collaborators, sponsored researchers and other advisors to execute confidentiality agreements upon the commencement of employment or consulting relationships with us. These agreements provide that all confidential information concerning our business or financial affairs developed or made known to the individual during the course of the individual's relationship with us is to be kept confidential and not disclosed to third parties except in specific circumstances. In the case of employees, the agreements provide that all inventions conceived by the individual, and which are related to our current or planned business or research and development or made during normal working hours, on our premises or using our equipment or proprietary information, are our exclusive property. In many cases our confidentiality and other agreements with consultants, outside scientific collaborators, sponsored researchers and other advisors require them to assign or grant us licenses to inventions they invent as a result of the work or services they render under such agreements or grant us an option to negotiate a license to use such inventions.

We also seek to preserve the integrity and confidentiality of our proprietary technology and processes by maintaining physical security of our premises and physical and electronic security of our information technology systems. Although we have confidence in these individuals, organizations, and systems, agreements or security measures may be breached and we may not have adequate remedies for any breach. To the extent that our employees, contractors, consultants, collaborators, and advisors use intellectual property owned by others in their work for us, disputes may arise as to the rights in related or resulting know-how and inventions.

In-Licenses

License from UCSB

In August 2010, we entered into an agreement with Regents of the University of California ("UC"), acting through its Santa Barbara campus, that grants us an exclusive license, with the right to sublicense, under the patent rights owned by UC covering mask and screening technologies in the field of identification and discovery of pro-protein biologics, including masks and substrates, for the identification of pro-proteins. The agreement also grants us an exclusive license, with the right to sublicense, under the patent rights co-owned by UC with us covering Probody antibodies and other pro-proteins in the fields of therapeutics, diagnostics, in vivo imaging and prophylactics.

We had no upfront payment obligations under the agreement. We are required to make milestone payments to UC on the accomplishment of certain regulatory milestones, including a $300,000 payment due upon the first patient enrollment in the first Phase 3 clinical trial and a $500,000 payment due upon approval of the first NDA by the FDA for each of the first two indications for each licensed product consisting of a molecule or compound covered by the licensed patent rights. We have paid minimum annual royalties in increasing amounts to UC since 2011 in the aggregate amount of $555,000 through December 31, 2016, and, beginning in 2016, annual minimum royalties of $150,000 that will continue for the term of the agreement. In addition, the agreement provides that we are required to pay to UC running royalties on net sales in the low single-digits. The agreement with UC requires us to meet specified due diligence product development milestones. We did not meet the milestones in 2013, 2014, 2015 and 2016, and we paid an extension fee of $25,000 in 2013, $50,000 in each of 2014 and 2015 and $25,000 in 2016 to maintain the license.

License from ImmunoGen

In February 2016, we exercised our option to obtain a worldwide, exclusive, sublicensable license from ImmunoGen for development and commercialization of products directed against the target selected by us under our research collaboration agreement with ImmunoGen. See the description of the license agreement set forth under the caption "Collaborations—ImmunoGen" in this Item 1 of this Annual Report on Form 10-K.

Government Regulation and Product Approval

Governmental authorities in the U.S., at the federal, state and local level, and other countries extensively regulate, among other things, the research, development, testing, manufacture, labeling, packaging, promotion, storage, advertising, distribution, marketing and export and import of products such as those we are developing. Our therapeutic candidates must be approved by the FDA through the NDA or BLA process before they may be legally marketed in the U.S. and will be subject to similar requirements in other countries prior to marketing in those countries. The process of obtaining regulatory approvals and the subsequent compliance with applicable federal, state, local and foreign statutes and regulations require the expenditure of substantial time and financial resources.

U.S. Government Regulation

In the U.S., the FDA regulates drugs under the Federal Food, Drug, and Cosmetic Act ("FDCA") and, in the case of therapeutic biologics, the Public Health Services Act ("PHSA"), and implementing regulations. Failure to comply with the applicable U.S. requirements at any time during the product development or approval process, or after approval, may subject an applicant to administrative or judicial sanctions, any of which could have a material adverse effect on us. These sanctions could include:

- refusal to approve pending applications;
- withdrawal of an approval;
- imposition of a clinical hold;
- warning or untitled letters;
- seizures or administrative detention of product;
- total or partial suspension of production or distribution; or
- injunctions, fines, disgorgement, or civil or criminal penalties.

NDA and BLA approval processes

The process required by the FDA before a therapeutic may be marketed in the U.S. generally involves the following:

- completion of nonclinical laboratory tests, animal studies and formulation studies conducted according to good laboratory practices ("GLPs"), and other applicable regulations;
- submission to the FDA of an IND, which must become effective before human clinical trials may begin;
- performance of adequate and well-controlled human clinical trials according to good clinical practices ("GCPs"), to establish the safety and efficacy of the product candidate for its intended use;
- submission to the FDA of an NDA or BLA;
- satisfactory completion of an FDA inspection of the manufacturing facility or facilities at which the product candidate is produced to assess readiness for commercial manufacturing and conformance to the manufacturing-related elements of the application, to conduct a data integrity audit, and to assess compliance with current good manufacturing practices ("cGMPs") to assure that the facilities, methods and controls are adequate to preserve the product candidate's identity, strength, quality and purity; and
- FDA review and approval of the NDA or BLA.

Once a biopharmaceutical candidate is identified for development, it enters the preclinical or nonclinical testing stage. Nonclinical tests include laboratory evaluations of product chemistry, toxicity and formulation, as well as animal studies. An IND sponsor must submit the results of the nonclinical tests, together with manufacturing information and analytical data, to the FDA as part of the IND. Some nonclinical testing may continue even after the IND is submitted. In addition to including the results of the nonclinical studies, the IND will also include a protocol detailing, among other things, the objectives of the clinical trial, the parameters to be used in monitoring safety and the effectiveness criteria to be evaluated if the first phase lends itself to an efficacy determination. The IND automatically becomes effective 30 days after receipt by the FDA, unless the FDA, within the 30-day time period, places the IND on clinical hold. In such a case, the IND sponsor and the FDA must resolve any outstanding concerns before clinical trials can begin. A clinical hold may occur at any time during the life of an IND and may affect one or more specific studies or all studies conducted under the IND.

All clinical trials must be conducted under the supervision of one or more qualified investigators in accordance with GCPs. They must be conducted under protocols detailing the objectives of the trial, dosing procedures, research subject selection and exclusion criteria and the safety and effectiveness criteria to be evaluated. Each protocol, and any subsequent material amendment to the protocol, must be submitted to the FDA as part of the IND, and progress reports detailing the status of the clinical trials must be submitted to the FDA annually. Sponsors also must report to the FDA serious and unexpected adverse reactions in a timely manner, any clinically important increase in the rate of

a serious suspected adverse reaction over that listed in the protocol or investigation brochure or any findings from other studies or animal or in vitro testing that suggest a significant risk in humans exposed to the product candidate. An institutional review board ("IRB") at each institution participating in the clinical trial must review and approve the protocol before a clinical trial commences at that institution and must also approve the information regarding the trial and the consent form that must be provided to each research subject or the subject's legal representative, monitor the study until completed and otherwise comply with IRB regulations. There are also requirements governing the reporting of ongoing clinical trials and completed clinical trial results to public registries.

Human clinical trials are typically conducted in three sequential phases that may overlap or be combined.

- Phase 1—The product candidate is initially introduced into healthy human subjects and tested for safety, dosage tolerance, absorption, metabolism, distribution and elimination. In the case of some therapeutic candidates for severe or life-threatening diseases, such as cancer, especially when the product candidate may be inherently too toxic to ethically administer to healthy volunteers, the initial human testing is often conducted in patients.
- Phase 2—Clinical trials are performed on a limited patient population intended 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—Clinical trials are undertaken to further evaluate dosage, clinical efficacy and safety in an expanded patient population at geographically dispersed clinical study sites. These studies are intended to establish the overall risk-benefit ratio of the product and provide an adequate basis for product labeling.

A pivotal study is a clinical study that adequately meets regulatory agency requirements for the evaluation of a product candidate's efficacy and safety such that it can be used to justify the approval of the product. Generally, pivotal studies are also Phase 3 studies but may be Phase 2 studies if the trial design provides a reliable assessment of clinical benefit, particularly in situations where there is an unmet medical need. Human clinical trials are inherently uncertain and Phase 1, Phase 2 and Phase 3 testing may not be successfully completed. The FDA or the sponsor may suspend a clinical trial at any time for a variety of reasons, including a finding that the research subjects or patients are being exposed to an unacceptable health risk. Similarly, an IRB can suspend or terminate approval of a clinical trial at its institution if the clinical trial is not being conducted in accordance with the IRB's requirements or if the product candidate has been associated with unexpected serious harm to patients.

During the development of a new product candidate, sponsors are given opportunities to meet with the FDA at certain points; specifically, prior to the submission of an IND, at the end of Phase 2 and before a BLA or NDA is submitted. Meetings at other times may be requested. These meetings can provide an opportunity for the sponsor to share information about the data gathered to date and for the FDA to provide advice on the next phase of development. Sponsors typically use the meeting at the end of Phase 2 to discuss their Phase 2 clinical results and present their plans for the pivotal Phase 3 clinical trial that they believe will support the approval of the new therapeutic. If a Phase 3 clinical trial is the subject of discussion at the end of Phase 2 meeting with the FDA, a sponsor may be able to request a Special Protocol Assessment ("SPA"), the purpose of which is to reach agreement with the FDA on the Phase 3 clinical trial protocol design and analysis that will form the primary basis of an efficacy claim.

Post-approval trials, sometimes referred to as "Phase 4" clinical trials, may be conducted after initial marketing approval. These trials are used to gain additional experience from the treatment of patients in the intended therapeutic indication. In certain instances, FDA may mandate the performance of such "Phase 4" clinical trials.

According to published guidance on the SPA process, a sponsor that meets the prerequisites may make a specific request for a SPA and provide information regarding the design and size of the proposed clinical trial. The FDA is supposed to evaluate the protocol within 45 days of the request to assess whether the proposed trial is adequate, which evaluation may result in discussions and a request for additional information. A SPA request must be made before the proposed trial begins, and all open issues must be resolved before the trial begins. Although the FDA will assess protocols that have already begun, these assessments will not be subject to the 45-day review applicable to SPAs. If a written agreement is reached, it will be documented and made part of the record. The agreement will be binding on the FDA and may not be changed by the sponsor or the FDA after the trial begins except with the written agreement of the sponsor and the FDA or if the FDA determines that a substantial scientific issue essential to determining the safety or efficacy of the product candidate was identified after the testing began.

Concurrent with clinical trials, sponsors usually complete additional animal safety studies, develop additional information about the chemistry and physical characteristics of the product candidate and finalize a process for

manufacturing commercial quantities of the product candidate in accordance with cGMP requirements. The manufacturing process must be capable of consistently producing quality batches of the product candidate and the manufacturer must develop methods for testing the quality, purity and potency of the product candidate. To help reduce the risk of the introduction of adventitious agents with use of biological products, the PHSA emphasizes the importance of manufacturing control for products whose attributes cannot be precisely defined. The manufacturing process must be capable of consistently producing quality batches of the product candidate and, among other criteria, the sponsor must develop methods for testing the identity, strength, quality, potency and purity of the final biological product. Additionally, appropriate packaging must be selected and tested, and stability studies must be conducted to demonstrate that the biological product candidate does not undergo unacceptable deterioration over its shelf life. Additionally, for both NDA and BLA products, appropriate packaging must be selected and tested and stability studies must be conducted to demonstrate that the product candidate does not undergo unacceptable deterioration over its proposed shelf-life.

The results of product development, nonclinical studies and clinical trials, along with descriptions of the manufacturing process, analytical tests and other control mechanisms, proposed labeling and other relevant information are submitted to the FDA as part of an NDA or BLA requesting approval to market the product.

Under the Prescription Drug User Fee Act ("PDUFA") as amended, each BLA or NDA must be accompanied by a significant user fee. The FDA adjusts the PDUFA user fees on an annual basis. PDUFA also imposes an annual product fee for products and an annual establishment fee on facilities used to manufacture prescription biological or drug products. Fee waivers or reductions are available in certain circumstances, such as where a waiver is necessary to protect the public health, where the fee would present a significant barrier to innovation, or where the applicant is a small business submitting its first human therapeutic application for review.

Within 60 days following submission of the application, the FDA reviews a BLA or NDA submitted to determine if it is substantially complete before the agency accepts it for filing. The FDA may refuse to file any BLA or NDA that it deems incomplete or not properly reviewable at the time of submission, and may request additional information. In this event, the BLA or NDA must be resubmitted with the additional information. The resubmitted application also is 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 of the BLA or NDA. The FDA reviews the BLA to determine, among other things, whether the proposed product is safe, potent, and/or effective for its intended use, and has an acceptable purity profile, and in the case of an NDA, whether the product is safe and effective for its intended use, and in each case, whether the product is being manufactured in accordance with cGMP. The FDA may refer applications for novel products or products that present difficult questions of safety or efficacy to an advisory committee, typically a panel that includes clinicians and other experts, for review, evaluation and 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.

During the product approval process, the FDA also will determine whether a risk evaluation and mitigation strategies ("REMS") plan is necessary to assure the safe use of the product. If the FDA concludes a REMS plan is needed, the sponsor of the BLA or NDA must submit a proposed REMS plan. The FDA will not approve a BLA or NDA without a REMS plan, if required. The FDA has authority to require a REMS plan under the Food and Drug Administration Amendments Act of 2007 (the "FDAAA") when necessary to ensure that the benefits of a drug or therapeutic biologic outweigh the risks. In determining whether a REMS plan is necessary, the FDA must consider the size of the population likely to use the drug or therapeutic biologic, the seriousness of the disease or condition to be treated, the expected benefit of the drug or therapeutic biologic, the duration of treatment, the seriousness of known or potential adverse events, and whether the drug or therapeutic biologic is a new molecular entity. A REMS plan may be required to include various elements, such as a medication guide or patient package insert, a communication plan to educate health care providers of the risks, limitations on who may prescribe or dispense the drug or therapeutic biologic, or other measures that the FDA deems necessary to assure the safe use of the drug or therapeutic biologic. In addition, the REMS plan must include a timetable to assess the strategy at 18 months, three years, and seven years after the strategy's approval.

The FDA may also require a REMS plan for a drug or therapeutic biologic that is already on the market if it determines, based on new safety information, that a REMS plan is necessary to ensure that the product's benefits outweigh its risks.

Before approving a BLA or NDA, the FDA will inspect the facilities at which the product is manufactured. The FDA will not approve the product 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 a BLA or NDA, the FDA will typically inspect one or more clinical sites to assure that the clinical trials were conducted in compliance with IND trial requirements and GCP requirements. To assure cGMP

and GCP compliance, an applicant must incur significant expenditure of time, money and effort in the areas of training, record keeping, production and quality control.

Notwithstanding the submission of relevant data and information, the FDA may ultimately decide that the BLA or NDA does not satisfy its regulatory criteria for approval and deny approval. Data obtained from clinical trials are not always conclusive and the FDA may interpret data differently than we interpret the same data. If the agency decides not to approve the BLA or NDA in its present form, the FDA will issue a complete response letter that describes all of the specific deficiencies in the BLA or NDA identified by the FDA. The deficiencies identified may be minor, for example, requiring labeling changes, or major, for example, requiring additional clinical trials. Additionally, the complete response letter may include recommended actions that the applicant might take to place the application in a condition for approval. If a complete response letter is issued, the applicant may either resubmit the BLA or NDA, addressing all of the deficiencies identified in the letter, or withdraw the application.

Even if a product receives regulatory approval, the approval may be significantly limited to specific indications and dosages or the indications for use may otherwise be limited, which could restrict the commercial value of the product. Further, the FDA may require that certain contraindications, warnings or precautions be included in the product labeling. The FDA may impose restrictions and conditions on product distribution, prescribing, or dispensing in the form of a risk management plan, or otherwise limit the scope of any approval. In addition, the FDA may require post marketing clinical trials, sometimes referred to as "Phase 4" clinical trials, designed to further assess a biological product's safety and effectiveness, and testing and surveillance programs to monitor the safety of approved products that have been commercialized.

Companion Diagnostics

The FDA issued a final guidance document in July 2014 addressing agency policy in relation to in vitro companion diagnostic tests. The guidance explains that for some drugs and therapeutic biologics, the use of a companion diagnostic test is essential for the safe and effective use of the product, such as when the use of a product is limited to a specific patient subpopulation that can be identified by using the test. According to the guidance, the FDA generally will not approve such a product if the companion diagnostic is not also approved or cleared for the appropriate indication, and accordingly the therapeutic product and the companion diagnostic should be developed and approved or cleared contemporaneously. However, the FDA may decide that it is appropriate to approve such a product without an approved or cleared in vitro companion diagnostic device when the drug or therapeutic biologic is intended to treat a serious or life-threatening condition for which no satisfactory alternative treatment exists and the FDA determines that the benefits from the use of a product with an unapproved or uncleared in vitro companion diagnostic device are so pronounced as to outweigh the risks from the lack of an approved or cleared in vitro companion diagnostic device. The FDA encourages sponsors considering developing a therapeutic product that requires a companion diagnostic to request a meeting with both relevant device and therapeutic product review divisions to ensure that the product development plan will product sufficient data to establish the safety and effectiveness of both the therapeutic product and the companion diagnostic. Because the FDA's policy on companion diagnostics is set forth only in guidance, this policy is subject to change and is not legally binding.

Expedited Review and Approval

The FDA has various programs, including Fast Track, priority review, accelerated approval and breakthrough therapy designation, which are intended to expedite or simplify the process for reviewing therapeutic candidates, or provide for the approval of a product candidate on the basis of a surrogate endpoint. Even if a product candidate qualifies for one or more of these programs, the FDA may later decide that the product candidate no longer meets the conditions for qualification or that the time period for FDA review or approval will be lengthened. Generally, therapeutic candidates that are eligible for these programs are those for serious or life-threatening conditions, those with the potential to address unmet medical needs and those that offer meaningful benefits over existing treatments. For example, Fast Track is a process designed to facilitate the development and expedite the review of therapeutic candidates to treat serious or life-threatening diseases or conditions and fill unmet medical needs. Priority review is designed to give therapeutic candidates that offer major advances in treatment or provide a treatment where no adequate therapy exists an initial review within eight months as compared to a standard review time of twelve months.

Although Fast Track and priority review do not affect the standards for approval, the FDA will attempt to facilitate early and frequent meetings with a sponsor of a Fast Track designated product candidate and expedite review of the application for a product candidate designated for priority review. Accelerated approval, which is described in Subpart H of 21 CFR Part 314, provides for an earlier approval for a new product candidate that is (1) intended to treat a serious or life-threatening disease or condition; (2) generally provides a meaningful advantage over available therapies; and (3) demonstrates an effect on either a surrogate endpoint that is reasonably likely to predict clinical benefit or on a clinical endpoint that can be measured earlier than irreversible morbidity or mortality ("IMM") and is

reasonably likely to predict an effect on IMM or other clinical benefit, taking into account the severity, rarity or prevalence of the condition and the availability or lack of alternative treatments. A surrogate endpoint is a laboratory measurement or physical sign used as an indirect or substitute measurement representing a clinically meaningful outcome. As a condition of approval, the FDA may require that a sponsor of a product candidate receiving accelerated approval perform post-marketing studies to verify and describe the predicted effect on irreversible morbidity or mortality or other clinical endpoint, and the product may be subject to accelerated withdrawal procedures.

In the Food and Drug Administration Safety and Innovation Act (the "FDASIA"), which was signed into law in July 2012, the U.S. Congress encouraged the FDA to utilize innovative and flexible approaches to the assessment of therapeutic candidates under accelerated approval. The law required the FDA to issue related guidance and also promulgate confirming regulatory changes. In May 2014, the FDA published a final Guidance for Industry titled "Expedited Programs for Serious Conditions—Drugs and Biologics," which provides guidance on FDA programs that are intended to facilitate and expedite development and review of new therapeutic candidates as well as threshold criteria generally applicable to concluding that a product candidate is a candidate for these expedited development and review programs.

In addition to the Fast Track, accelerated approval and priority review programs discussed above, the FDA's "Expedited Programs" guidance also describes the Breakthrough Therapy designation. The FDA defines a Breakthrough Therapy as a therapeutic that is intended, alone or in combination with one or more other therapeutics, to treat a serious or life-threatening disease or condition, and preliminary clinical evidence indicates that the therapeutic may demonstrate substantial improvement over existing therapies on one or more clinically significant endpoints, such as substantial treatment effects observed early in clinical development. A therapeutic designated as a Breakthrough Therapy is eligible for accelerated approval. The FDA must take certain actions, such as holding timely meetings and providing advice, intended to expedite the development and review of an application for approval of a Breakthrough Therapy. Even if a product qualifies for one or more of these programs, the FDA may later decide that the product no longer meets the conditions for qualification or decide that the time period for FDA review or approval will not be shortened. A request for Breakthrough Therapy designation should be submitted concurrently with, or as an amendment to, an IND, but ideally no later than the end of Phase 2 meeting.

Patent Term Restoration and Marketing Exclusivity

Depending upon the timing, duration and specifics of FDA approval of the use of our therapeutic candidates, some of our U.S. patents may be eligible for limited patent term extension under the Drug Price Competition and Patent Term Restoration Act of 1984, referred to as the Hatch-Waxman Act. The Hatch-Waxman Act permits a patent restoration term of up to five years as compensation for patent term lost during product development and the FDA regulatory review process. However, patent term restoration cannot extend the remaining term of a patent beyond a total of 14 years from the product candidate's approval date. The patent term restoration period is generally one half of 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 approval of that application, except that the review period is reduced by any time during which the applicant failed to exercise due diligence. Only one patent applicable to an approved product candidate is eligible for the extension and the application for extension must be made prior to expiration of the patent. The USPTO, in consultation with the FDA, reviews and approves the application for any patent term extension or restoration. In the future, we intend to apply for restorations of patent term for some of our currently owned or licensed patents to add patent life beyond their current expiration date, depending on the expected length of clinical trials and other factors involved in the submission of the relevant NDA.

Market exclusivity provisions under the FDCA also can delay the submission or the approval of certain applications. The FDCA provides a five-year period of non-patent marketing exclusivity within the U.S. to the first applicant to gain approval of an NDA for a new chemical entity. A product candidate is a new chemical entity if the FDA has not previously approved any other new product candidate containing the same active moiety, which is the molecule or ion responsible for the action of the product candidate substance. During the exclusivity period, the FDA may not accept for review an abbreviated new drug application (an "ANDA"), or a 505(b)(2) NDA submitted by another company for another version of such product candidate where the applicant does not own or have a legal right of reference to all the data required for approval. However, an application may be submitted after four years if it contains a certification of patent invalidity or non-infringement of one of the patents listed with the FDA by the innovator NDA holder. The FDCA also provides three years of marketing exclusivity for an NDA, or supplement to an existing NDA, if new clinical investigations, other than bioavailability studies, that were conducted or sponsored by the applicant are deemed by the FDA to be essential to the approval of the application. Examples of such new clinical investigations include those with respect to new indications, dosages or strengths of an existing product candidate. This three-year exclusivity covers only the modification for which the product received approval on the basis of the new clinical investigations and does not prohibit the FDA from approving ANDAs for product candidates containing the active agent for the original indication or condition of use. Five-year exclusivity will not delay the submission or approval of another company's full NDA. However, an applicant submitting a full NDA would be required to conduct or obtain a right of reference to all of the preclinical studies and adequate and well-controlled clinical trials necessary to demonstrate safety and effectiveness.

The Biologics Price Competition and Innovation Act (the "BPCIA") amended the PHSA to authorize the FDA to approve similar versions of innovative biologics, commonly known as biosimilars. A competitor seeking approval of a biosimilar must file an application to establish its molecule as highly similar to an approved innovator biologic, among other requirements. The BPCIA, however, bars the FDA from approving biosimilar applications for 12 years after an innovator biological product receives initial marketing approval.

Orphan Drug Designation

Under the Orphan Drug Act, the FDA may grant Orphan Drug Designation to therapeutic candidates intended to treat a rare disease or condition, which is generally a disease or condition that affects either (1) fewer than 200,000 individuals in the U.S., or (2) more than 200,000 individuals in the U.S. and for which there is no reasonable expectation that the cost of developing and making available in the U.S. a product candidate for this type of disease or condition will be recovered from sales in the U.S. for that product candidate. Orphan Drug Designation must be requested before submitting an NDA. After the FDA grants Orphan Drug Designation, the identity of the therapeutic agent and its potential orphan use are disclosed publicly by the FDA. Orphan Drug Designation does not convey any advantage in or shorten the duration of the regulatory review and approval process.

If a product candidate that has Orphan Drug Designation subsequently receives the first FDA approval for the disease for which it has such designation, the product candidate is entitled to orphan product exclusivity, which means that the FDA may not approve any other applications to market the same product candidate for the same indication, except under limited circumstances, for seven years. Orphan drug exclusivity, however, could also block the approval of one of our therapeutic candidates for seven years if a competitor obtains approval of the same product candidate as defined by the FDA or if our product candidate is determined to be contained within the competitor's product candidate for the same indication or disease.

Pediatric Exclusivity and Pediatric Use

Under the Best Pharmaceuticals for Children Act (the "BPCA"), certain therapeutic candidates may obtain an additional six months of exclusivity if the sponsor submits information requested in writing by the FDA, referred to as a Written Request, relating to the use of the active moiety of the product candidate in children. Although the FDA may issue a Written Request for studies on either approved or unapproved indications, it may only do so where it determines that information relating to that use of a product candidate in a pediatric population, or part of the pediatric population, may produce health benefits in that population.

In addition, the Pediatric Research Equity Act ("PREA"), requires a sponsor to conduct pediatric studies for most therapeutic candidates and biologics, for a new active ingredient, new indication, new dosage form, new dosing regimen or new route of administration. Under PREA, original NDAs, BLAs and supplements thereto must contain a pediatric assessment unless the sponsor has received a deferral or waiver. The required assessment must assess the safety and effectiveness of the product candidate for the claimed indications in all relevant pediatric subpopulations and support dosing and administration for each pediatric subpopulation for which the product candidate is safe and effective. The sponsor or FDA may request a deferral of pediatric studies for some or all of the pediatric subpopulations. A deferral may be granted for several reasons, including a finding that the product candidate or biologic is ready for approval for use in adults before pediatric studies are complete or that additional safety or effectiveness data needs to be collected before the pediatric studies begin. The law requires the FDA to send a PREA Non-Compliance letter to sponsors who have failed to submit their pediatric assessments required under PREA, have failed to seek or obtain a deferral or deferral extension or have failed to request approval for a required pediatric formulation. It further requires the FDA to post the PREA Non- Compliance letter and sponsor's response.

As part of the FDASIA, the U.S. Congress made a few revisions to the BPCA and PREA, which were slated to expire on September 30, 2012, and made both laws permanent.

Post-Approval Requirements

Once an approval is granted, the FDA may withdraw the approval if compliance with regulatory requirements is not maintained or if problems occur after the product candidate reaches the market. Later discovery of previously

unknown problems with a product candidate may result in restrictions on the product candidate or even complete withdrawal of the product candidate from the market. After approval, some types of changes to the approved product candidate, such as adding new indications, manufacturing changes and additional labeling claims, are subject to further FDA review and approval. In addition, the FDA may under some circumstances require testing and surveillance programs to monitor the effect of approved therapeutic candidates that have been commercialized, and the FDA under some circumstances has the power to prevent or limit further marketing of a product candidate based on the results of these post-marketing programs.

Any therapeutic candidates manufactured or distributed by us pursuant to FDA approvals are subject to continuing regulation by the FDA, including, among other things:

- record-keeping requirements;
- reporting of adverse experiences with the product candidate;
- providing the FDA with updated safety and efficacy information;

- product sampling and distribution requirements;
- notifying the FDA and gaining its approval of specified manufacturing or labeling changes; and
- complying with FDA promotion and advertising requirements, which include, among other things, standards for direct-to-consumer advertising, restrictions on promoting products for uses or in patient populations that are not described in the product's approved labeling, limitations on industry-sponsored scientific and educational activities and requirements for promotional activities involving the internet.

Therapeutic manufacturers and other entities involved in the manufacture and distribution of approved therapeutic products are required to register their establishments with the FDA and certain state agencies and are subject to periodic unannounced inspections by the FDA and some state agencies for compliance with cGMPs and other laws. The FDA periodically inspects manufacturing facilities to assess compliance with cGMP, which imposes extensive procedural, substantive and record-keeping requirements. In addition, changes to the manufacturing process are strictly regulated, and, depending on the significance of the change, may require FDA approval before being implemented. FDA regulations would also require investigation and correction of any deviations from cGMP and impose reporting and documentation requirements upon us and any third-party manufacturers that we may decide to use if our product candidates are approved. Accordingly, manufacturers must continue to expend time, money and effort in the area of production and quality control to maintain compliance with cGMP and other aspects of regulatory compliance.

New Legislation and Regulations

From time to time, legislation is drafted, introduced and passed in Congress that could significantly change the statutory provisions governing the testing, approval, manufacturing and marketing of products regulated by the FDA. In addition to new legislation, FDA regulations and policies are often revised or interpreted by the agency in ways that may significantly affect our business and our products. It is impossible to predict whether further legislative changes will be enacted or whether FDA regulations, guidance, policies or interpretations changed or what the effect of such changes, if any, may be.

Regulation Outside of the U.S.

In addition to regulations in the U.S., we will be subject to regulations of other jurisdictions governing any clinical trials and commercial sales and distribution of our therapeutic candidates. Whether or not we obtain FDA approval for a product, we must obtain approval by the comparable regulatory authorities of countries outside of the U.S. before we can commence clinical trials in such countries and approval of the regulators of such countries or economic areas, such as the European Union, before we may market products in those countries or areas. The approval process and requirements governing the conduct of clinical trials, product licensing, pricing and reimbursement vary greatly from place to place, and the time may be longer or shorter than that required for FDA approval.

Under European Union regulatory systems, a company can consider applying for marketing authorization in several European Union member states by submitting its marketing authorization application(s) under a centralized, decentralized or mutual recognition procedure. The centralized procedure provides for the grant of a single marketing authorization that is valid for all European Union member states. The centralized procedure is compulsory for medicines derived from biotechnology, orphan medicinal products, or those medicines with an active substance not authorized in the European Union on or before May 20, 2004 intended to treat acquired immune deficiency syndrome ("AIDS"), cancer, neurodegenerative disorders or diabetes and optional for those medicines containing a new active substance not authorized in the European Union on or before May 20, 2004, medicines which are highly innovative, or medicines to which the granting of a marketing authorization under the centralized procedure would be in the interest of patients at the European Union-level.. The decentralized procedure provides for recognition by European Union national authorities of a first assessment performed by one member state. Under this procedure, an identical application for marketing authorization is submitted simultaneously to the national authorities of several European

Union member states, one of them being chosen as the “Reference Member State”, and the remaining being the “Concerned Member States”. The Reference Member State must prepare and send drafts of an assessment report, summary of product characteristics and the labelling and package leaflet within 120 days after receipt of a valid marketing authorization application to the Concerned Member States, which must decide within 90 days whether to recognize approval. If any Concerned Member State does not recognize the marketing authorization on the grounds of potential serious risk to public health, the disputed points are eventually referred to the European Commission, whose decision is binding on all member states. The mutual recognition procedure is similar to the decentralized procedure except that a medicine must have already received a marketing authorization in at least one member state, and that member state acts as the Reference Member State.

As in the U.S., we may apply for designation of a product candidate as an orphan drug for the treatment of a specific indication in the European Union before the application for marketing authorization is made.

Orphan drugs in the European Union enjoy economic and marketing benefits, including up to ten years of market exclusivity for the approved indication unless another applicant can show that its product is safer, more effective or otherwise clinically superior to the orphan-designated product, the marketing authorization holder is unable to supply sufficient quantity of the medicinal product or the marketing authorization holder has given its consent.

Coverage and Reimbursement

Sales of our products will depend, in part, on the extent to which our products will be covered by third-party payors, such as government health programs, commercial insurance and managed healthcare organizations. These third-party payors are increasingly reducing reimbursements for medical products and services. Additionally, the containment of healthcare costs has become a priority of federal and state governments and the prices of therapeutics have been a focus in this effort. The U.S. government, state legislatures and foreign 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 our net revenue and results. If these third- party payors do not consider our products to be cost-effective compared to other therapies, they may not cover our products after approval as a benefit under their plans or, if they do, the level of payment may not be sufficient to allow us to sell our products on a profitable basis.

The American Recovery and Reinvestment Act of 2009 provides funding for the federal government to compare the effectiveness of different treatments for the same illness. The plan for the research was published in 2012 by the Department of Health and Human Services, the Agency for Healthcare Research and Quality and the National Institutes for Health, and periodic reports on the status of the research and related expenditures will be made to the U.S. Congress. Although the results of the comparative effectiveness studies are not intended to mandate coverage policies for public or private payors, it is not clear what effect, if any, the research will have on the sales of our product candidates, if any such product or the condition that it is intended to treat is the subject of a study. It is also possible that comparative effectiveness research demonstrating benefits in a competitor’s product could adversely affect the sales of our product candidates. If third-party payors do not consider our products to be cost-effective compared to other available therapies, they may not cover our products after approval as a benefit under their plans or, if they do, the level of payment may not be sufficient to allow us to sell our products on a profitable basis.

The Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act (together, the “ACA”) has had a significant impact on the health care industry. The ACA expanded coverage for the uninsured while at the same time containing overall healthcare costs. With regard to biopharmaceutical products, the ACA, among other things, 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, increased the minimum Medicaid rebates owed by manufacturers under the Medicaid Drug Rebate Program and extended the rebate program to individuals enrolled in Medicaid managed care organizations, established annual fees and taxes on manufacturers of certain branded prescription drugs, and 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 drugs to eligible beneficiaries during their coverage gap period, as a condition for the manufacturer’s outpatient drugs to be covered under Medicare Part D.

In addition, other legislative changes have been proposed and adopted in the United States since the ACA was enacted that impact payment methodologies and reimbursement amounts. On August 2, 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 2013 through 2021, was unable to reach required goals, thereby triggering the legislation’s automatic reduction to several government programs. This includes aggregate reductions to Medicare payments to providers of 2% per fiscal year,

started in April 2013, and, due to subsequent legislative amendments, will stay in effect through 2025 unless additional Congressional action is taken. On January 2, 2013, President Obama signed into law the American Taxpayer Relief Act of 2012 (the “ATRA”) which among other things, also reduced Medicare payments types of 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. Recently, there has been heightened governmental scrutiny over the manner in which manufacturers set prices for their marketed products, which has resulted in several Congressional inquiries and proposed bills designed to, among other things, bring more transparency to product pricing, review the relationship between pricing and manufacturer patient programs, and reform government program reimbursement methodologies for drug products. For example, the 21st Century Cures Act changed the reimbursement methodology for infusion drugs and biologics furnished through durable medical equipment in an attempt to remedy over- and underpayment of certain products.

We expect that the new presidential administration and U.S. Congress will seek to modify, repeal, or otherwise invalidate all, or certain provisions of, the ACA. Since taking office, President Trump has continued to support the repeal of all or portions of the ACA. In January 2017, the House and Senate passed a budget resolution that authorizes congressional committees to draft legislation to repeal all or portions of the ACA and permits such legislation to pass with a majority vote in the Senate. President Trump has also recently issued an executive order in which he stated that it is his administration's policy to seek the prompt repeal of the ACA and directed executive departments and federal agencies to waive, defer, grant exemptions from, or delay the implementation of the provisions of the ACA to the maximum extent permitted by law. There is still uncertainty with respect to the impact President Trump's administration and the U.S. Congress may have, if any, and any changes will likely take time to unfold, and could have an impact on coverage and reimbursement for healthcare items and services covered by plans that were authorized by the ACA. However, we cannot predict the ultimate content, timing or effect of any healthcare reform legislation or the impact of potential legislation on us.

Finally, in some foreign countries, the proposed pricing for a product candidate must be approved before it may be lawfully marketed. The requirements governing therapeutic pricing vary widely from country to country. For example, the European Union provides options for its member states to restrict the range of medicinal products for which their national health insurance systems provide reimbursement and to control the prices of medicinal products for human use. A member state may approve a specific price for the medicinal product or it may instead adopt a system of direct or indirect controls on the profitability of the Company placing the medicinal product on the market. There can be no assurance that any country that has price controls or reimbursement limitations for pharmaceutical products will allow favorable reimbursement and pricing arrangements for any of our product candidates. Historically, therapeutic candidates launched in the European Union do not follow price structures of the U.S. and generally tend to be significantly lower.

Other Healthcare Laws

We may also be subject to healthcare regulation and enforcement by the federal government and the states and foreign governments where we may market our product candidates, if approved. These laws include, without limitation, state and federal anti-kickback, fraud and abuse, false claims, privacy and security, physician sunshine and drug pricing transparency laws and regulations.

The federal Anti-Kickback Statute prohibits, among other things, any person from knowingly and willfully offering, soliciting, receiving or providing remuneration, directly or indirectly, to induce either the referral of an individual, for an item or service or the purchasing or ordering of a good or service, for which payment may be made under federal healthcare programs such as the Medicare and Medicaid programs. The Anti-Kickback Statute is subject to evolving interpretations. In the past, the government has enforced the Anti-Kickback Statute to reach large settlements with healthcare companies based on sham consulting and other financial arrangements with physicians. A person or entity does not need to have actual knowledge of the statute or specific intent to violate it in order to have committed a violation. In addition, the government may assert that a claim including items or services resulting from a violation of the federal Anti-Kickback Statute constitutes a false or fraudulent claim for purposes of the federal False Claims Act. The majority of states also have anti-kickback laws, which establish similar prohibitions and in some cases may apply to items or services reimbursed by any third-party payor, including commercial insurers.

Additionally, the civil False Claims Act prohibits knowingly presenting or causing the presentation of a false, fictitious or fraudulent claim for payment to the U.S. government, knowingly making, using, or causing to be made or used a false record or statement material to a false or fraudulent claim to the U.S. government, or from knowingly making a false statement to avoid, decrease or conceal an obligation to pay money to the U.S. government. Actions under the False Claims Act may be brought by the Attorney General or as a qui tam action by a private individual in the name of the government. Violations of the False Claims Act can result in very significant monetary penalties and

treble damages. The federal government is using the False Claims Act, and the accompanying threat of significant liability, in its investigation and prosecution of pharmaceutical and biotechnology companies throughout the U.S., for example, in connection with the promotion of products for unapproved uses and other sales and marketing practices. The government has obtained multi-million and multi-billion dollar settlements under the False Claims Act in addition to individual criminal convictions under applicable criminal statutes. Given the significant size of actual and potential settlements, it is expected that the government will continue to devote substantial resources to investigating healthcare providers' and manufacturers' compliance with applicable fraud and abuse laws.

The U.S. federal Health Insurance Portability and Accountability Act of 1996 ("HIPAA"), also created new federal criminal statutes that prohibit among other actions, knowingly and willfully executing, or attempting to execute, a scheme to defraud any healthcare benefit program, including private third-party payors, knowingly and willfully embezzling or stealing from a healthcare benefit program, willfully obstructing a criminal investigation of a healthcare offense, and knowingly and willfully falsifying, concealing or covering up a material fact or making any materially false, fictitious or fraudulent statement in connection with the delivery of or payment for healthcare benefits, items or services. Similar to the federal Anti-Kickback Statute, a person or entity does not need to have actual knowledge of the statute or specific intent to violate it in order to have committed a violation.

There has also been a recent trend of increased federal and state regulation of payments made to physicians and other healthcare providers. The ACA, among other things, imposes new reporting requirements on drug manufacturers for payments made by them to physicians and teaching hospitals, as well as ownership and investment interests held by physicians and their immediate family members. Failure to submit required information may result in civil monetary penalties of up to an aggregate of $150,000 per year (or up to an aggregate of $1 million per year for "knowing failures"), for all payments, transfers of value or ownership or investment interests that are not timely, accurately and completely reported in an annual submission. Certain states also mandate implementation of compliance programs and compliance with the pharmaceutical industry's voluntary compliance guidelines and the relevant compliance guidance promulgated by the federal government, impose restrictions on drug manufacturer marketing practices and/or require the tracking and reporting of pricing and marketing information as well as gifts, compensation and other remuneration or items of value provided to physicians and other healthcare professionals and entities .

We may also be subject to data privacy and security regulation by both the federal government and the states in which we conduct our business. HIPAA, as amended by the Health Information Technology and Clinical Health Act ("HITECH") and their respective implementing regulations, including the final omnibus rule published on January 25, 2013, imposes specified requirements relating to the privacy, security and transmission of individually identifiable health information. Among other things, HITECH makes HIPAA's privacy and security standards directly applicable to "business associates," defined as independent contractors or agents of covered entities that create, receive, maintain or transmit protected health information in connection with providing a service for or on behalf of a covered entity. HITECH also increased the civil and criminal penalties that may be imposed against covered entities, business associates and possibly other persons, and gave state attorneys general new authority to file civil actions for damages or injunctions in federal courts to enforce the federal HIPAA laws and seek attorney's fees and costs associated with pursuing federal civil actions. In addition, state laws govern the privacy and security of health information in certain circumstances, many of which differ from each other in significant ways, thus complicating compliance efforts.

Environment

Our third-party manufacturers are subject to inspections by the FDA for compliance with cGMP and other U.S. regulatory requirements, including U.S. federal, state and local regulations regarding environmental protection and hazardous and controlled substance controls, among others. Environmental laws and regulations are complex, change frequently and have tended to become more stringent over time. We have incurred, and may continue to incur, significant expenditures to ensure we are in compliance with these laws and regulations. We would be subject to significant penalties for failure to comply with these laws and regulations.

Collaborations

AbbVie

In April 2016, we entered into two agreements, a CD71 Co-Development and Licensing Agreement ("CD 71 Agreement") and a Discovery Collaboration and Licensing Agreement ("Discovery Agreement"), with AbbVie. Under the CD71 Agreement, we will co-develop a PDC against CD71 with AbbVie where we will be responsible for pre-clinical and early clinical development. AbbVie will be responsible for later development and commercialization, with global late-stage development costs shared between the two companies. AbbVie and we will share 65% and 35%, respectively, of the net profits or net losses unless we opt-out of the co-development of the CD71 PDC. We received an upfront payment of $20 million, and are eligible to receive up to $470 million in development, regulatory and commercial milestone payments and royalties on ex-US sales in the high teens to low twenties if we participate in the co-development of the CD71 Licensed Product subject to a reduction in such royalties if the Company opts-out from the co-development of the CD71 PDC. The CD71 Agreement will continue in effect until the date of expiration of the last royalty term for the last licensed product and, if later, the date on which no co-development product is being

developed or commercialized in or for the U.S. AbbVie may terminate the agreement in its entirety or on a country-by-country basis after April 21, 2018 for no reason or at any time for certain development, regulatory or commercialization reasons. Either party may terminate the agreement upon the other party's uncured material breach or insolvency.

We received an upfront payment of $10 million under the Discovery Agreement and may receive an additional payment upon the selection by AbbVie of the second target. We are also eligible to receive up to $275 million in target nomination, development regulatory and commercial milestone payments and royalties in the high single to low teens from commercial sales of any resulting PDCs. The Discovery Agreement will continue in effect until the date of expiration of the last royalty term for the last licensed product. AbbVie may terminate the agreement in its entirety or on a country-by-country or target-by-target basis for no reason after April 21, 2017 or at any time for certain development, regulatory or commercialization reasons. Either party may terminate the agreement upon the other party's uncured material breach or insolvency.

BMS

In May 2014, we entered into a research collaboration and license agreement with BMS pursuant to which we agreed to collaborate to discover and conduct preclinical development of Probody therapeutics directed against four immune-oncology targets. BMS selected the first two targets upon the signing of the agreement, one of which is CTLA-4, and made a $50 million signing payment to us. In January 2016, BMS selected a third target and triggered a $10 million selection payment to us pursuant to the collaboration and license agreement. In December 2016, BMS selected a fourth target and triggered a $15 million selection payment pursuant to the collaboration and license agreement. BMS will provide a specified amount of research funding to us to perform the research by funding certain full-time employee expenses. BMS has the responsibility for and control of all development, manufacture and commercialization of any products resulting from the research collaboration. BMS agreed to use commercially reasonable efforts to develop and obtain regulatory approval for and commercialize at least one product for each target.

We granted BMS exclusive worldwide rights to develop and commercialize the Probody therapeutics we discover. The terms of the agreement provide that BMS will make a total of up to $2 million in preclinical milestone payments for each target, a total of up to $112 million in development and regulatory milestone payments for up to three indications for each target, a total of up to $124 million in milestone payments for the first commercial sale in various territories for up to three indications, and sales milestone payments of up to $60 million for each product. In December 2016, BMS selected a first clinical candidate probody and triggered a $2 million preclinical milestone payment to us pursuant to the collaboration and license agreement.

We will also be eligible to receive tiered mid-single digit royalties rising to low double-digit royalties on net sales of each product commercialized by BMS. BMS' royalty obligation continues on a licensed product-by-licensed product basis until the later of (i) the expiration of the last claim of the licensed patents covering the licensed products in the country, (ii) the twelfth anniversary of the first commercial sale of a licensed product in a country, or (iii) the expiration of any applicable regulatory, pediatric, orphan drug or data exclusivity with respect to such product. Pursuant to the agreement, BMS also purchased 833,333 shares of our common stock in our initial public offering of common stock closed on October 14, 2015 (the "IPO") at the IPO price and on the same terms as the other purchasers in the IPO.

Under the collaboration and license agreement, we also granted BMS certain exclusivity rights. We agreed that we will not, ourselves or with a third party, research, develop or commercialize any product developed from the research collaboration or on any of the four targets chosen by BMS.

The agreement with BMS will continue in effect on a licensed product-by-licensed product and country- by-country basis until neither party has any obligation to the other under the agreement in such country with respect to such product. BMS may terminate the agreement at will as a whole or on a country-by-country basis at any time after May 23, 2016 or at any time on a target-by-target basis by providing two months' advance written notice to us if no regulatory approval for any product has yet been obtained or otherwise upon four months' advance written notice to us. BMS may also terminate the agreement on a target-by-target basis in the event it determines that the medical benefit to risk ratio of a product is so unfavorable as to be incompatible with the welfare of patients. Either party may terminate the agreement upon the other party's uncured material breach that is not cured within 90 days after the breaching party receives notice of such breach and for the insolvency of the other party.

ImmunoGen

In January 2014, we entered into a research collaboration agreement with ImmunoGen pursuant to which we agreed to collaborate with ImmunoGen to use our Probody technology and ImmunoGen's ADC cell-killing agents and linkers to

produce PDCs for testing. We amended the agreement in April 2015. ImmunoGen was granted the right to select two targets and has selected two targets. We were granted the right to select one target and have selected our target. Each party provides its own antibodies for the collaboration. We use the antibodies to produce Probody therapeutics at our expense, then we provide them to ImmunoGen to conjugate them to ImmunoGen's linkers and cytotoxic compounds at ImmunoGen's expense. Each party does its own animal testing and IND-enabling studies for the Probody therapeutics directed at its chosen target(s). Each party has the option to obtain an exclusive development and commercialization license from the other for its selected target(s). The option can be exercised by a party at any time during the term of the research collaboration except that it generally must be exercised no later than six months after the first dosing of an animal with the party's PDC. No payment is required to exercise the option. Each company retains full development control of PDCs resulting from its target selection and is responsible for preclinical and clinical development, manufacturing and commercialization. The research collaboration will last until January 2018 unless it is terminated by one of the parties earlier due to the material breach or insolvency of the other party. The collaboration will end with respect to a particular target if the option to obtain a commercial license is exercised with respect to that target. We have agreed that, during the term of the collaboration, we will not research, develop or commercialize any PDC directed toward one of ImmunoGen's targets. ImmunoGen has agreed that, during the term of the collaboration, it will not research, develop or commercialize any ADC directed toward our target.

If a party exercises its right to obtain a commercial license, it will receive a worldwide, exclusive, sublicensable license for development and commercialization of products directed against the selected target under the terms of a separate license agreement, which have already been negotiated. Each party has development diligence obligations for its commercial license. We exercised our option in February 2016 to obtain the development and commercialization license with respect to the target selected by us under the research collaboration and entered into the license agreement in the pre-negotiated form attached to the research collaboration agreement. Under the license agreement, we will pay up to $60 million in development and regulatory milestones and up to $100 million in sales milestones to ImmunoGen, as well as tiered mid- to high-single-digit royalties. Our commercial license prohibits ImmunoGen from developing or commercializing or licensing any third party to develop or commercialize any PDC that is directed toward our licensed target. If ImmunoGen exercises its option(s) to obtain a commercial license, ImmunoGen will pay up to $30 million in development and regulatory milestones and up to $50 million in sales milestones for each target to us, as well as tiered mid-single digit royalties. ImmunoGen's commercial license prohibits us from developing or commercializing or licensing any third party to develop or commercialize any PDC that uses the cytotoxic compounds also used by ImmunoGen and is directed toward ImmunoGen's licensed target.

Each party's royalty obligations under its commercial license continue on a licensed product-by-licensed product basis until the later of (i) the expiration of the last claim of the licensed patents covering the licensed products in the country or (ii) the twelfth anniversary of the first commercial sale of a licensed product in a country, but, in the case of (ii), in no event later than the twentieth anniversary of the earlier of the date of the first commercial sale of the licensed product. Each license agreement continues in effect until the expiration of the royalty obligation on a licensed product-by-licensed product and country-by-country basis until the expiration of the royalty obligations. The licensee may terminate the agreement at any time prior to obtaining the first regulatory marketing approval in any country by providing not less than 90 days' prior written notice to the licensor. Either party may terminate a license agreement upon the other party's uncured material breach that is not cured within 90 days after the breaching party receives notice of such breach or in the event of the insolvency of the other party. A licensor may terminate a commercial license if the licensor has terminated the research collaboration due to the material breach of the research collaboration agreement by the licensee.

MD Anderson

In November 2015, we entered into a research collaboration agreement with MD Anderson to research Probody-enabled chimeric antigen receptor killer (CAR-NK) cell therapies, known as ProCAR-NK cell therapies. Under this collaboration, MD Anderson will use our Probody technology to conduct research of ProCAR-NK cell therapies against certain targets selected by us in cancer immunotherapy. MD Anderson and us will collaborate to develop ProCAR-NK cells, which are designed for more precise binding to tumors and reduced binding to healthy tissue, against the selected targets for which safety and toxicity are expected to be limiting factors for CAR cell therapies. Under the research collaboration agreement, we have the right to exercise an option, during the option period expiring on November 2, 2019 and upon payment of an option exercise fee, to negotiate and acquire a worldwide, exclusive, sublicensable license from MD Anderson for development and commercialization of products directed against any of the selected targets. The research collaboration agreement will continue in effect until the earlier of (i) the date that we exercise the option to acquire the license from MD Anderson and (ii) the expiration of the option period.

Pfizer

In May 2013, we entered into a research collaboration, option and license agreement with Pfizer to collaborate on the discovery and preclinical research activities related to Probody therapeutics, and PDCs for research project targets nominated by Pfizer. Pfizer nominated two research target in 2013 and, pursuant to the agreement, had the option of nominating two additional research targets. In December 2014, Pfizer selected an additional research target which

triggered an additional $1.5 million payment. The option to select a fourth target lapsed in May 2016 without a selection. Under the terms of the agreement, Pfizer will provide a specified amount of research funding to us to perform the research by funding certain full-time employee expenses. We continue to work with Pfizer on two of the three targets they selected under the collaboration. Pfizer can exercise the option to obtain a commercial license for each target within three to five years after the target is selected upon making a payment of $2 million to $2.5 million to us, depending on the target. Pfizer has the responsibility for and control of all development, manufacture and commercialization of any product candidates resulting from the research collaboration.

The commercial license will be a worldwide, exclusive, sublicensable license for development and commercialization of product candidates directed against the selected target. The terms of the license include approximately $19 million in regulatory milestone payments per collaboration target and $110 million in sales milestone payments as well as tiered mid-single digit royalties on potential future sales per collaboration target. Pfizer's royalty obligation continues on a licensed product-by-licensed product basis until the later of (i) the expiration of the last claim of the licensed patents covering the licensed products in the country or (ii) the tenth anniversary of the first commercial sale of a licensed product in a country, but, in the case of (ii), in no event later than the twentieth anniversary of the earlier of the date of the first commercial sale of the licensed product. If Pfizer obtains a commercial license for a target, it must use commercially reasonable efforts to develop a product in one major market country for that target, including seeking regulatory approval, and to commercialize one licensed product candidate in one major market country where Pfizer has obtained regulatory approval for that target. In addition to the other rights granted to Pfizer, we agreed not to engage in, license or collaborate on any Probody therapeutics or PDCs targeting a target for which Pfizer exercised its option for the term of the agreement, except that, for the first target, the exclusivity applies only to the PDC.

The agreement with Pfizer will continue in effect until the expiration of the royalty obligation on a licensed product-by-licensed product and country-by-country basis until the expiration of Pfizer's royalty obligations. Pfizer may terminate the agreement as a whole or on a target-by-target basis by providing 60 days' advance written notice to us for any reason or no reason at any time. Pfizer may also terminate the agreement in the event of our insolvency. Either party may terminate the agreement upon the other party's uncured material breach that is not cured within 90 days after the breaching party receives notice of such breach.

Our Company Origins and Team

Our Probody platform technology has its origins in work performed at the University of California, Santa Barbara ("UCSB"), by our scientific founder Professor Patrick Daugherty. Since our inception, we have continued developing and adding to this technology and aspire to design a pipeline of Probody therapeutics that will better the lives of cancer patients. We have assembled an experienced and talented group of individuals dedicated to the advancement of cancer care. Our chief executive officer, Dr. Sean McCarthy, leads a team that draws on robust experience in all phases of product discovery, clinical development and commercialization. Our research and preclinical development team is led by Dr. Michael Kavanaugh, chief scientific officer, and includes renowned and established researchers, and our clinical development team is led by Dr. Rachel Humphrey, chief medical officer. Our management team members have significant experience in oncology with previous experience at Amgen, Chiron, Five Prime, Genentech, Maxygen, Medarex, Millennium, Novartis, Onyx, SGX and other companies.

Employees

As of December 31, 2016, we had 78 full-time employees and 2 part-time employees. Of these employees, 56 of whom were primarily engaged in research and development activities.

Corporate Information

Our operations commenced in February 2008 when our predecessor entity was formed. We were incorporated in Delaware in September 2010. We maintain our executive offices at 151 Oyster Point Blvd., Suite 400, South San Francisco, California 94080, and our main telephone number is (650) 515-3185.

We are an "emerging growth company" as defined in the Jumpstart Our Business Startups Act of 2012. We will remain an emerging growth company until the earlier of: (1) the last day of the fiscal year (a) following the fifth anniversary of the completion of the IPO, (b) in which we have total annual gross revenue of at least $1.0 billion, or (c) in which we are deemed to be a large accelerated filer, which means the market value of our common stock that is held by

non-affiliates exceeds $700.0 million as of the prior June 30th, and (2) the date on which we have issued more than $1.0 billion in non-convertible debt during the prior three-year period. We refer to the Jumpstart Our Business Startups Act of 2012 herein as the "JOBS Act," and references herein to "emerging growth company" shall have the meaning associated with it in the JOBS Act.

We view our operations and measure our business as one reportable segment operating in the United States. See Note 3 to our audited financial statement included elsewhere in this Annual Report on Form 10-K for additional information. Additional information required by this item is incorporated herein by reference to PART II Item 6 of this Annual Report on Form 10-K.

Our research and development expenses were $54.8 million, $28.4 million and $28.3 million for the years ended December 31, 2016, 2015, and 2014, respectively. Please see "Management's Discussion and Analysis of Financial Condition and Results of Operations-Research and Development Expenses" for additional detail regarding our research and development activities.

We maintain a website at www.cytomx.com, which contains information about us. The information in, or that can be accessed through, our website is not part of this Annual Report on Form 10-K. Our annual reports on Form 10-K, quarterly reports on Form 10-Q and current reports on Form 8-K and amendments to those reports are available, free of charge, on or through our website as soon as reasonably practicable after we electronically file such material with, or furnish it to, the SEC. The public may read and copy any materials we file with the SEC at the SEC's Public Reference Room at 100 F Street, NE, Washington, D.C. 20549. Information on the operation of the Public Reference Room can be obtained by calling 1-800-SEC-0330. The SEC maintains an Internet site that contains reports, proxy and information statements and other information regarding our filings at www.sec.gov.

Item 1A. Risk Factors

You should consider carefully the risks and uncertainties described below, together with all of the other information in this Annual Report on Form 10-K. If any of the following risks are realized, our business, financial condition, results of operations and prospects could be materially and adversely affected. The risks described below are not the only risks facing the Company. Risks and uncertainties not currently known to us or that we currently deem to be immaterial also may materially adversely affect our business, financial condition, results of operations and/or prospects.

Risks Related to Our Business

We are a clinical-stage biopharmaceutical company with a history of losses, expect to continue to incur significant losses for the foreseeable future and may never achieve or maintain profitability, which could result in a decline in the market value of our common stock.

We are a clinical-stage biopharmaceutical company with a limited operating history, developing a novel class of therapeutic antibody product candidates, based on our proprietary biologic Probody technology platform. Since our inception, we have devoted our resources to the development of Probody therapeutics. We have had significant operating losses since our inception. As of December 31, 2016, we had an accumulated deficit of $176.4 million. For the year ended December 31, 2016, our net loss was $58.9 million. Substantially all of our losses have resulted from expenses incurred in connection with our research and development programs and from general and administrative costs associated with our operations. Though we have developed our Probody platform, our technologies and product candidates are in early stages of development, and we are subject to the risks of failure inherent in the development of product candidates based on novel technologies. We have never generated any revenue from product sales, and have not obtained regulatory approval for any of our product candidates.

Furthermore, we do not expect to generate any revenue from product sales for the foreseeable future, and we expect to continue to incur significant operating losses for the foreseeable future due to the cost of research and development, preclinical studies and clinical trials and the regulatory approval process for our product candidates. We expect our net losses to increase substantially as we enter into clinical development of our lead programs. However, the amount of our future losses is uncertain. Our ability to achieve profitability, if ever, will depend on, among other things, our, or our existing or future collaborators, successfully developing product candidates, obtaining regulatory approvals to market and commercialize product candidates, manufacturing any approved products on commercially reasonable terms, establishing a sales and marketing organization or suitable third-party alternatives for any approved product and raising sufficient funds to finance business activities. If we, or our existing or future collaborators, are unable to develop our technologies and commercialize one or more of our product candidates or if sales revenue from any product candidate that receives approval is insufficient, we will not achieve profitability, which could have a material and adverse effect on our business, financial condition, results of operations and prospects.

We expect that we will need to raise substantial additional funds to advance development of our product candidates and we cannot guarantee that this additional funding will be available on acceptable terms or at all. Failure to obtain this necessary capital when needed may force us to delay, limit or terminate our product development and commercialization of our current or future product candidates.

The development of biopharmaceutical product candidates is capital-intensive. If our product candidates enter and advance through preclinical studies and clinical trials, we will need substantial additional funds to expand our development, regulatory, manufacturing, marketing and sales capabilities. We have used substantial funds to develop our technology and product candidates and will require significant funds to conduct further research and development and preclinical testing and clinical trials of our product candidates, to seek regulatory approvals for our product candidates and to manufacture and market any products that are approved for commercial sale. In addition, we have

incurred and will continue to incur additional costs associated with operating as a public company.

As of December 31, 2016, we had $181.9 million in cash, cash equivalents and investments. Based on our current operating plan, we expect our existing capital resources will be sufficient to fund operations into 2019. Our future capital requirements and the period for which we expect our existing resources to support our operations may vary significantly from what we expect. Our monthly spending levels vary based on new and ongoing research and development and other corporate activities. Because the length of time and activities associated with successful research and development of our product candidates is highly uncertain, we are unable to estimate the actual funds we will require for development and any approved marketing and commercialization activities.

The timing and amount of our operating expenditures will depend largely on:

- the timing and progress of preclinical and clinical development activities;
- the number, size and type of preclinical studies and clinical trials that we may be required to complete for our product candidates, as well as the cost and time of such studies and trials;
- the number and scope of preclinical and clinical programs we decide to pursue;
- the time and cost necessary to produce clinical supplies of our product candidates;
- the progress of the development efforts of parties with whom we have entered or may in the future enter into collaborations and research and development agreements;
- the timing and amount of milestone payments we may receive under our collaborations agreements;
- our ability to maintain our current licenses and research and development programs and to establish new collaboration arrangements;
- the costs involved in prosecuting and enforcing patent and other intellectual property claims;
- the cost and timing of regulatory approvals; and
- our efforts to enhance operational systems and hire additional personnel, including personnel to support development of our product candidates and satisfy our obligations as a public company.

If we are unable to obtain funding on a timely basis or on acceptable terms, we may have to delay, reduce or terminate our research and development programs and preclinical studies or clinical trials, if any, limit strategic opportunities or undergo reductions in our workforce or other corporate restructuring activities. We also could be required to seek funds through arrangements with collaborators or others that may require us to relinquish rights to some of our technologies or product candidates that we would otherwise pursue on our own. We do not expect to realize revenue from sales of products or royalties from licensed products in the foreseeable future, if at all, and unless and until our product candidates are clinically tested, approved for commercialization and successfully marketed. To date, we have financed our operations primarily through sales of our common stock in conjunction with the IPO, sale of our convertible preferred securities and payments received under our collaboration agreements. We will be required to seek additional funding in the future and currently intend to do so through additional collaborations, public or private equity offerings or debt financings, credit or loan facilities or a combination of one or more of these funding sources. Our ability to raise additional funds will depend on financial, economic and other factors, many of which are beyond our control. Additional funds may not be available to us on acceptable terms or at all. If we raise additional funds by issuing equity securities, our stockholders will suffer dilution and the terms of any financing may adversely affect the rights of our stockholders. In addition, as a condition to providing additional funds to us, future investors may demand, and may be granted, rights superior to those of existing stockholders. Debt financing, if available, is likely to involve restrictive covenants limiting our flexibility in conducting future business activities, and, in the event of insolvency, debt holders would be repaid before holders of our equity securities received any distribution of our corporate assets.

Our product candidates are in early stages of development and only one of them has been tested in a human subject to date. Our product candidates may fail in development or suffer delays that materially and adversely affect their commercial viability.

We have no products on the market and all of our product candidates, including cancer immunotherapies, Probody Drug Conjugates (“PDCs”) and bispecific antibodies, are in preclinical stages of development, other than CX-072, our candidate directed against PD-L1, for cancer, for which we filed an IND with the FDA in September 2016 and treated the first patient in our Phase 1/2 clinical trial in January 2017. Our ability to achieve and sustain profitability depends on obtaining regulatory approvals for and successfully commercializing our product candidates, either alone or with third parties. Before obtaining regulatory approval for the commercial distribution of our product candidates, we or an existing or future collaborator must conduct extensive preclinical tests and clinical trials to demonstrate the safety and efficacy in humans of our product candidates.

We may not have the financial resources to continue development of, or to modify existing or enter into new collaborations for, a product candidate if we experience any issues that delay or prevent regulatory approval of, or our ability to commercialize, product candidates, including:

- negative or inconclusive results from our clinical trials or the clinical trials of others for product candidates similar to ours, leading to a decision or requirement to conduct additional preclinical testing or clinical trials or abandon a program;
- product-related side effects experienced by participants in our clinical trials or by individuals using drugs or therapeutic biologics similar to our product candidates;

- delays in submitting INDs or comparable foreign applications or delays or failure in obtaining the necessary approvals from regulators to commence a clinical trial, or a suspension or termination of a clinical trial once commenced;
- conditions imposed by the FDA or comparable foreign authorities regarding the scope or design of our clinical trials;
- delays in enrolling research subjects in clinical trials;
- high drop-out rates of research subjects;
- inadequate supply or quality of product candidate components or materials or other supplies necessary for the conduct of our clinical trials;
- greater than anticipated clinical trial costs;
- poor effectiveness of our product candidates during clinical trials;
- unfavorable FDA or other regulatory agency inspection and review of a clinical trial site;
- failure of our third-party contractors or investigators to comply with regulatory requirements or otherwise meet their contractual obligations in a timely manner, or at all;
- delays and changes in regulatory requirements, policy and guidelines, including the imposition of additional regulatory oversight around clinical testing generally or with respect to our technology in particular; or
- varying interpretations of data by the FDA and similar foreign regulatory agencies.

In addition, our current and future clinical trials will need to demonstrate sufficient safety and efficacy for approval by regulatory authorities in larger patient populations. Only recently, in our Phase 1/2 clinical trial, which we initiated in January 2017, has CX-072 been administered to cancer patients, and it is possible that patients enrolled in our Phase 1/2 clinical trial for CX-072 or any future clinical trials we commence for other product candidates could respond in unexpected ways. For instance, our Phase 1/2 clinical trial is conducted in patients with advanced cancers, including metastatic or locally advanced unresectable solid tumors or lymphomas, who have failed other approved therapies for their disease, and as such, it may be difficult to establish safety and efficacy in this type of patient population. Furthermore, a portion of our Phase 1/2 clinical trial includes the administration of CX-072 in combination with Yervoy® (ipilimumab) or Zelboraf®(vemurafenib), which could exacerbate immune system related adverse events, cause increased toxicity or otherwise lead to unexpected adverse events.

We may experience delays in completing our preclinical studies and initiating or completing clinical trials of our product candidates. We do not know whether planned preclinical studies and clinical trials will be completed on schedule or at all, or whether planned clinical trials will begin on time, need to be redesigned, enroll patients on time or be completed on schedule, if at all. Our development programs may be delayed for a variety of reasons, including delays related to:

- the FDA or other regulatory authorities requiring us to submit additional data or imposing other requirements before permitting us to initiate a clinical trial;
- obtaining regulatory approval to commence a clinical trial;
- reaching agreement on acceptable terms with prospective CROs and clinical trial sites, the terms of which can be subject to extensive negotiation and may vary significantly among different CROs and clinical trial sites;
- obtaining institutional review board (“IRB”) approval at each clinical trial site;
- recruiting suitable patients to participate in a clinical trial;
- developing and validating the companion diagnostic to be used in a clinical trial;
- having patients complete a clinical trial or return for post-treatment follow-up;
- clinical trial sites deviating from trial protocol or dropping out of a trial;
- adding new clinical trial sites; or
- manufacturing sufficient quantities of our product candidates for use in clinical trials.

Patient enrollment, a significant factor in the timing of clinical trials, is affected by many factors including the size and nature of the patient population, the proximity of patients to clinical sites, the eligibility criteria for the trial, the design of the clinical trial, competing clinical trials and clinicians' and patients' perceptions as to the potential advantages of the product candidate being studied in relation to other available therapies, including any new drugs or therapeutic biologics that may be approved for the indications we are investigating. For example, CX-072 is directed against PD-L1. There are currently many clinical studies exploring the use of PD-1 and PD-L1 agents and patients may not choose to enroll in our study. Furthermore, we expect to rely on our collaborators, CROs and clinical trial sites to ensure the proper and timely conduct of our clinical trials and while we expect to enter into agreements governing their committed activities, we have limited influence over their actual performance.

We could encounter delays if prescribing physicians encounter unresolved ethical issues associated with enrolling patients in clinical trials of our product candidates in lieu of prescribing existing treatments that have established safety and efficacy profiles. Further, a clinical trial may be suspended or terminated by us, our collaborators, the IRBs of the institutions in which such trials are being conducted, the Data Safety Monitoring Board for such trial or by the FDA or other regulatory authorities due to a number of factors, including failure to conduct the clinical trial in accordance with regulatory requirements or our clinical protocols, inspection of the clinical trial operations or trial site by the FDA or other regulatory authorities resulting in the imposition of a clinical hold, unforeseen safety issues or adverse side effects, failure to demonstrate a benefit from using a drug or therapeutic biologic, changes in governmental regulations or administrative actions or lack of adequate funding to continue the clinical trial. If we experience delays in the completion of, or termination of, any clinical trial of our product candidates, the commercial prospects of our product candidates will be harmed, and our ability to generate product revenues from any of these product candidates will be delayed. In addition, any delays in completing our clinical trials will increase our costs, slow down our product development and approval process and jeopardize our ability to commence product sales and generate revenues. Any of these occurrences may materially and adversely affect our business, financial condition, results of operations and prospects. In addition, many of the factors that cause, or lead to, a delay in the commencement or completion of clinical trials may also ultimately lead to the denial of regulatory approval of our product candidates.

Our approach to the discovery and development of our therapeutic treatments is based on novel technologies that are unproven and may not result in marketable products.

We plan to develop a pipeline of product candidates using our proprietary Probody platform. We believe that product candidates (including cancer immunotherapies, PDCs and bispecific antibodies) identified with our product discovery platform may offer an improved therapeutic approach by taking advantage of unique conditions in the tumor microenvironment, thereby reducing the dose-limiting toxic effects associated with existing products, which also attack healthy tissue. However, the scientific research that forms the basis of our efforts to develop product candidates based on our Probody platform is ongoing. Further, the scientific evidence to support the feasibility of developing therapeutic treatments based on our Probody platform is both preliminary and limited.

We may ultimately discover that our Probody platform and any product candidates resulting therefrom do not possess certain properties required for therapeutic effectiveness. For example, when administered in a human, the peptide mask may not be cleaved, which would limit the potential efficacy of the antibody and reduce the potential to limit the toxicity of the anti-cancer agent. In addition, if the peptide mask is released, it may result in unforeseen events when administered in humans. Furthermore, Probody product candidates may also be unable to remain stable in the human body for the period of time required for the drug to reach the target tissue or they may trigger immune responses that inhibit the ability of the product candidate to reach the target tissue or that cause adverse side effects in humans. We currently have only limited data, and no conclusive evidence, to suggest that we can introduce these necessary properties into our Probody platform and any product candidates. We may spend substantial funds attempting to introduce these properties and may never succeed in doing so. In addition, product candidates based on our Probody

platform may demonstrate different chemical and pharmacological properties in patients than they do in laboratory studies. Although our Probody platform and certain product candidates have successful results in animal studies, they may not demonstrate the same chemical and pharmacological properties in humans and may interact with human biological systems in unforeseen, ineffective or harmful ways. As a result, we may never succeed in developing a marketable product and we may never become profitable, which would cause the value of our common stock to decline.

Further, we are not aware of any company currently in clinical development with a therapeutic using a prodrug approach to antibody drug development and no regulatory authority has granted approval for a therapeutic of this kind. As such, we believe the FDA has limited early experience with Probody-based therapeutics in oncology or other disease areas, which may increase the complexity, uncertainty and length of the regulatory approval process for our product candidates. For example, while we intend to commence our Phase 1 clinical trial of CX-2009, our PDC candidate directed against CD-166 for cancer in the first half of 2017, the commencement of this clinical trial is subject to finalization of the trial design and the filing of an IND with the FDA or similar filing with a similar foreign regulatory authority. However, we successfully filed an IND for CX-072 in September 2016, received clearance of the IND from FDA in December 2016 and treated the first patient in our Phase 1/2 clinical trial in January 2017. As there is limited historical precedent for the approval of Probody-based therapeutics in oncology, there is a higher degree of risk that the FDA or other regulatory authorities could disagree that we have satisfied their requirements to commence our clinical trials for products other than CX-072 or disagree with our study designs, which may require us to complete additional preclinical studies or amend our protocols or impose stricter conditions on the commencement of clinical trials. As a result, we and our existing or future collaborators may never receive approval to market and commercialize any product candidate. Even if we or an existing or future collaborator obtains regulatory approval, the approval may be for targets, disease indications or patient populations that are not as broad as we intended or desired or may require labeling that includes significant use or distribution restrictions or safety warnings. We or an existing or future collaborator may be required to perform additional or unanticipated clinical trials to obtain approval or be subject to post-marketing testing requirements to maintain regulatory approval. If our Probody technologies prove to be ineffective, unsafe or commercially unviable, our entire platform and pipeline would have little, if any, value, which would have a material and adverse effect on our business, financial condition, results of operations and prospects.

The market may not be receptive to our product candidates based on a novel therapeutic modality, and we may not generate any future revenue from the sale or licensing of product candidates.

Even if regulatory approval is obtained for a product candidate, we may not generate or sustain revenue from sales of the product due to factors such as whether the product can be sold at a competitive cost and whether it will otherwise be accepted in the market. The product candidates that we are developing are based on our Probody platform, which is a new technology and therapeutic approach. Market participants with significant influence over acceptance of new treatments, such as physicians and third-party payors, may not adopt a product or treatment based on our Probody platform and technologies, and we may not be able to convince the medical community and third-party payors to accept and use, or to provide favorable reimbursement for, any product candidates developed by us or our existing or future collaborators. Market acceptance of our product candidates will depend on, among other factors:

- the timing of our receipt of any marketing and commercialization approvals;
- the terms of any approvals and the countries in which approvals are obtained;
- the safety and efficacy of our product candidates;
- the prevalence and severity of any adverse side effects associated with our product candidates;
- limitations or warnings contained in any labeling approved by the FDA or other regulatory authority;
- relative convenience and ease of administration of our product candidates;
- the willingness of patients to accept any new methods of administration;
- the success of our physician education programs;
- the availability of adequate government and third-party payor reimbursement;
- the pricing of our products, particularly as compared to alternative treatments; and
- the availability of alternative effective treatments for the disease indications our product candidates are intended to treat and the relative risks, benefits and costs of those treatments.

If any product candidate we commercialize fails to achieve market acceptance, it could have a material and adverse effect on our business, financial condition, results of operations and prospects.

35

We have entered, and may in the future seek to enter, into collaborations with third parties for the development and commercialization of our product candidates using our Probody platform. If we fail to enter into such collaborations, or such collaborations are not successful, we may not be able to capitalize on the market potential of our Probody platform and resulting product candidates.

Since 2013, we have entered into collaborations with Pfizer, BMS, ImmunoGen and AbbVie to develop certain Probody therapeutics. We may in the future seek third-party collaborators for development and commercialization of other therapeutic technologies or product candidates. Biopharmaceutical companies are our prior and likely future collaborators for any marketing, distribution, development, licensing or broader collaboration arrangements. With respect to our existing collaboration agreements, and what we expect will be the case with any future collaboration agreements, we have and would expect to have limited control over whether such collaborations pursue the development of our product candidates or the amount and timing of resources that such collaborators dedicate to the development or commercialization of our product candidates. For instance, Pfizer allowed its option to select a fourth target pursuant to our collaboration agreement lapsed in May 2016 without a selection. Further, our ability to generate revenues from these arrangements will depend on our collaborators' abilities to successfully perform the functions assigned to them in these arrangements.

Collaborations involving our product candidates currently pose, and will continue to pose, the following risks to us:

- collaborators have significant discretion in determining the efforts and resources that they will apply to these collaborations;
    - collaborators may not pursue development and commercialization of our product candidates or may elect not to continue or renew development or commercialization programs based on preclinical or clinical trial results, changes in the collaborators' strategic focus or available funding, or external factors such as an acquisition that diverts resources or creates competing priorities;
- collaborators may delay clinical trials, provide insufficient funding for a clinical trial program, stop a clinical trial or abandon a product candidate, repeat or conduct new clinical trials or require a new formulation of a product candidate for clinical testing;
- collaborators may independently develop, or develop with third parties, products that compete directly or indirectly with our product candidate if the collaborators believe that competitive products are more likely to be successfully developed or can be commercialized under terms that are more economically attractive than ours;
- collaborators with marketing and distribution rights to one or more products may not commit sufficient resources to the marketing and distribution of such product or products;
- collaborators may not properly maintain or defend our intellectual property rights or may use our proprietary information in such a way as to invite litigation that could jeopardize or invalidate our intellectual property or proprietary information or expose us to litigation or potential liability;
- collaborators may infringe the intellectual property rights of third parties, which may expose us to litigation and potential liability;
- disputes may arise between the collaborators and us that result in the delay or termination of the research, development or commercialization of our product candidate or that result in costly litigation or arbitration that diverts management attention and resources; and
    - collaborations may be terminated and, if terminated, may result in a need for additional capital to pursue further development or commercialization of the applicable product candidates.

As a result of the foregoing, our current and any future collaboration agreements may not lead to development or commercialization of our product candidates in the most efficient manner or at all. Any failure to successfully develop or commercialize our product candidates pursuant to our current or any future collaboration agreements could have a material and adverse effect on our business, financial condition, results of operations and prospects.

If our collaborators cease development efforts under our existing or future collaboration agreements, or if any of those agreements are terminated, these collaborations may fail to lead to commercial products and we may never receive milestone payments or future royalties under these agreements.

Substantially all of our revenue to date has been derived from our existing collaboration agreements, and a significant portion of our future revenue and cash resources is expected to be derived from these agreements or other similar agreements we may enter into in the future. Revenue from research and development collaborations depend upon continuation of the collaborations, reimbursement of development costs, the achievement of milestones and royalties, if any, derived from future products developed from our research. If we are unable to successfully advance the development of our product candidates or achieve milestones, revenue and cash resources from milestone payments under our collaboration agreements will be substantially less than expected.

In addition, to the extent that any of our existing or future collaborators were to terminate a collaboration agreement or to forego the selection of target product candidates, we may be forced , in some cases, to independently develop these product candidates, including funding preclinical or clinical trials, assuming marketing and distribution costs and defending intellectual property rights, or, in certain instances, abandoning product candidates altogether, any of which could result in a change to our business plan and have a material adverse effect on our business, financial condition, results of operations and prospects.

We may not successfully engage in strategic transactions, including any additional collaborations we seek, which could adversely affect our ability to develop and commercialize product candidates, impact our cash position, increase our expense and present significant distractions to our management.

From time to time, we may consider strategic transactions, such as additional collaborations, acquisitions of companies, asset purchases and out- or in-licensing of product candidates or technologies. In particular, we will evaluate and, if strategically attractive, seek to enter into additional collaborations, including with major biotechnology or biopharmaceutical companies. The competition for collaborators is intense, and the negotiation process is time-consuming and complex. Any new collaboration may be on terms that are not optimal for us, and we may not be able to maintain any new collaboration if, for example, development or approval of a product candidate is delayed, sales of an approved product candidate do not meet expectations or the collaborator terminates the collaboration. Any such collaboration, or other strategic transaction, may require us to incur non-recurring or other charges, increase our near- and long-term expenditures and pose significant integration or implementation challenges or disrupt our management or business. These transactions would entail numerous operational and financial risks, including exposure to unknown liabilities, disruption of our business and diversion of our management’s time and attention in order to manage a collaboration or develop acquired products, product candidates or technologies, incurrence of substantial debt or dilutive issuances of equity securities to pay transaction consideration or costs, higher than expected collaboration, acquisition or integration costs, write-downs of assets or goodwill or impairment charges, increased amortization expenses, difficulty and cost in facilitating the collaboration or combining the operations and personnel of any acquired business, impairment of relationships with key suppliers, manufacturers or customers of any acquired business due to changes in management and ownership and the inability to retain key employees of any acquired business. Accordingly, although there can be no assurance that we will undertake or successfully complete any transactions of the nature described above, any transactions that we do complete may be subject to the foregoing or other risks and have a material and adverse effect on our business, financial condition, results of operations and prospects. Conversely, any failure to enter any additional collaboration or other strategic transaction that would be beneficial to us could delay the development and potential commercialization of our product candidates and have a negative impact on the competitiveness of any product candidate that reaches market.

If third parties on which we intend to rely to conduct our preclinical studies or clinical trials do not perform as contractually required, fail to satisfy regulatory or legal requirements or miss expected deadlines, our development

program could be delayed with material and adverse effects on our business, financial condition, results of operations and prospects.

We intend to rely on third-party clinical investigators, contract research organizations ("CROs"), clinical data management organizations and consultants to design, conduct, supervise and monitor preclinical studies and clinical trials of our product candidates. Because we intend to rely on these third parties, we will have less control over the timing, quality and other aspects of preclinical studies and clinical trials than we would have had we conducted them on our own. These investigators, CROs and consultants will not be our employees and we will have limited control over the amount of time and resources that they dedicate to our programs. These third parties may have contractual relationships with other entities, some of which may be our competitors, which may draw time and resources from our programs. The third parties with which we may contract might not be diligent, careful or timely in conducting our preclinical studies or clinical trials, resulting in the preclinical studies or clinical trials being delayed or unsuccessful.

If we cannot contract with acceptable third parties on commercially reasonable terms, or at all, or if these third parties do not carry out their contractual duties, satisfy legal and regulatory requirements for the conduct of preclinical studies or clinical trials or meet expected deadlines, our clinical development programs could be delayed and otherwise adversely affected. In all events, we will be responsible for ensuring that each of our preclinical studies and clinical trials are conducted in accordance with the general investigational plan and protocols for the trial. The FDA requires preclinical studies to be conducted in accordance with good laboratory practices ("GLPs") and clinical trials to be conducted in accordance with good clinical practices ("GCPs"), including for designing, conducting, recording and reporting the results of preclinical studies and 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 will not relieve us of these responsibilities and requirements. Any adverse development or delay in our clinical trials could have a material and adverse effect on our business, financial condition, results of operations and prospects.

Because we rely on third-party manufacturing and supply partners, our supply of research and development, preclinical and clinical development materials may become limited or interrupted or may not be of satisfactory quantity or quality.

We rely on third-party contract manufacturers to manufacture our preclinical and clinical trial product supplies. We do not own manufacturing facilities for producing such supplies. There can be no assurance that our preclinical and clinical development product supplies will not be limited, interrupted, or of satisfactory quality or continue to be available at acceptable prices. In particular, any replacement of our manufacturer could require significant effort and expertise because there may be a limited number of qualified replacements.

The manufacturing process for a product candidate is subject to FDA and foreign regulatory authority review. Suppliers and manufacturers must meet applicable manufacturing requirements and undergo rigorous facility and process validation tests required by regulatory authorities in order to comply with regulatory standards, such as current Good Manufacturing Practices ("cGMPs"). In the event that any of our manufacturers fails to comply with such requirements or to perform its obligations to us in relation to quality, timing or otherwise, or if our supply of components or other materials becomes limited or interrupted for other reasons, we may be forced to manufacture the materials ourselves, for which we currently do not have the capabilities or resources, or enter into an agreement with another third party, which we may not be able to do on reasonable terms, if at all. In some cases, the technical skills or technology required to manufacture our product candidates may be unique or proprietary to the original manufacturer and we may have difficulty transferring such skills or technology to another third party and a feasible alternative may not exist. These factors would increase our reliance on such manufacturer or require us to obtain a license from such manufacturer in order to have another third party manufacture our product candidates. If we are required to change manufacturers for any reason, we will be required to verify that the new manufacturer maintains facilities and procedures that comply with quality standards and with all applicable regulations and guidelines. The delays associated with the verification of a new manufacturer could negatively affect our ability to develop product candidates in a timely manner or within budget.

We expect to continue to rely on third-party manufacturers if we receive regulatory approval for any product candidate. To the extent that we have existing, or enter into future, manufacturing arrangements with third parties, we will depend on these third parties to perform their obligations in a timely manner consistent with contractual and regulatory requirements, including those related to quality control and assurance. If we are unable to obtain or maintain third-party manufacturing for product candidates, or to do so on commercially reasonable terms, we may not be able to develop and commercialize our product candidates successfully. Our or a third party's failure to execute on our manufacturing requirements and comply with cGMPs could adversely affect our business in a number of ways, including:

- an inability to initiate or continue clinical trials of product candidates under development;
- delay in submitting regulatory applications, or receiving regulatory approvals, for product candidates;
- loss of the cooperation of an existing or future collaborator;
- subjecting third-party manufacturing facilities or our manufacturing facilities to additional inspections by regulatory authorities;
- requirements to cease distribution or to recall batches of our product candidates; and
- in the event of approval to market and commercialize a product candidate, an inability to meet commercial demands for our products.

We, or third-party manufacturers, may be unable to successfully scale-up manufacturing of our product candidates in sufficient quality and quantity, which would delay or prevent us from developing our product candidates and commercializing approved products, if any.

It may prove more challenging to manufacture products that incorporate our technology. In order to conduct clinical trials of our product candidates, including our Phase 1/2 clinical trial for CX-072, which we treated our first patient in January 2017, we will need to manufacture them in large quantities. We, or any manufacturing partners, may be unable to successfully increase the manufacturing capacity for any of our product candidates in a timely or cost-effective manner, or at all, although we have been able to manufacture clinical quantities for CX-072. In addition, quality issues may arise during scale-up activities. If we, or any manufacturing partners, are unable to successfully scale up the manufacture of our product candidates in sufficient quality and quantity, the development, testing, and clinical trials of that product candidate may be delayed or infeasible, and regulatory approval or commercial launch of any resulting product may be delayed or not obtained, which could significantly harm our business.

We may acquire assets or form strategic alliances in the future, and we may not realize the benefits of such acquisitions.

We may acquire additional technologies and assets, form strategic alliances or create joint ventures with third parties that we believe will complement or augment our existing business. If we acquire assets with promising markets or technologies, we may not be able to realize the benefit of acquiring such assets if we are unable to successfully integrate them with our existing technologies.

We may encounter numerous difficulties in developing, manufacturing and marketing any new products resulting from a strategic alliance or acquisition that delay or prevent us from realizing their expected benefits or enhancing our business. We cannot assure you that, following any such acquisition, we will achieve the expected synergies to justify the transaction.

We may expend our limited resources to pursue a particular product candidate and fail to capitalize on product candidates that may be more profitable or for which there is a greater likelihood of success.

Because we have limited financial and managerial resources, we focus on specific product candidates, including CX-072 and CX-2009. As a result, we may forgo or delay pursuit of opportunities with other product candidates that later prove to have greater commercial potential. Our resource allocation decisions may cause us to fail to capitalize on viable commercial products or profitable market opportunities. Our spending on current and future research and development programs and product candidates for specific indications may not yield any commercially viable product candidates. If we do not accurately evaluate the commercial potential or target market for a particular product candidate, we may relinquish valuable rights to that product candidate through collaboration, licensing or other royalty arrangements in cases in which it would have been more advantageous for us to retain sole development and commercialization rights to such product candidate.

We face competition from entities that have developed or may develop product candidates for cancer, including companies developing novel treatments and technology platforms. If these companies develop technologies or product candidates more rapidly than we do or their technologies are more effective, our ability to develop and successfully commercialize product candidates may be adversely affected.

The development and commercialization of drugs and therapeutic biologics is highly competitive. We compete with a variety of multinational biopharmaceutical companies and specialized biotechnology companies, as well as technology being developed at universities and other research institutions. Our competitors have developed, are developing or will develop product candidates and processes competitive with our product candidates. Competitive

therapeutic treatments include those that have already been approved and accepted by the medical community and any new treatments that enter the market. We believe that a significant number of products are currently under development, and may become commercially available in the future, for the treatment of conditions for which we may try to develop product candidates. There is intense and rapidly evolving competition in the biotechnology, biopharmaceutical and antibody and immunoregulatory therapeutics fields. We believe that while our Probody platform, its associated intellectual property and our scientific and technical know-how give us a competitive advantage in this space, competition from many sources remains. Our competitors include larger and better funded biopharmaceutical, biotechnological and therapeutics companies. Moreover, we also compete with current and future therapeutics developed at universities and other research institutions.

We are aware of several companies that are developing cancer immunotherapies and ADCs. Many of these companies are well-capitalized and, in contrast to us, have significant clinical experience, and may include our existing or future collaborators. In addition, these companies compete with us in recruiting scientific and managerial talent.

Our success will partially depend on our ability to develop and protect therapeutics that are safer and more effective than competing products. Our commercial opportunity and success will be reduced or eliminated if competing products that are safer, more effective, or less expensive than the therapeutics we develop.

If our lead product candidates, CX-072 and CX-2009, are approved, they will compete with a range of therapeutic treatments that are either in development or currently marketed. Indeed, a variety of oncology drugs and therapeutic biologics are on the market or in clinical development. Such marketed therapies range from ADCs such as Genentech, Inc.'s Kadcyla, immune checkpoint inhibitors such as BMS's Opdivo and T-cell engager immunotherapies such as Amgen, Inc.'s BLINCYTO. In addition, numerous compounds are in clinical development for cancer treatment. With respect to immunogenic cancers such as melanoma, the most common treatments are chemotherapeutic compounds, radiation therapy and now immunotherapeutic antibodies such as Opdivo, Yervoy and Merck & Co., Inc.'s Keytruda. The clinical development pipeline for cancer includes small molecules, antibodies and immunotherapies from a variety of groups.

Many of our competitors have significantly greater financial, technical, manufacturing, marketing, sales and supply resources or experience than we do. If we successfully obtain approval for any product candidate, we will face competition based on many different factors, including the safety and effectiveness of our products, the ease with which our products can be administered and the extent to which patients accept relatively new routes of administration, the timing and scope of regulatory approvals for these products, the availability and cost of manufacturing, marketing and sales capabilities, price, reimbursement coverage and patent position. Competing products could present superior treatment alternatives, including by being more effective, safer, less expensive or marketed and sold more effectively than any products we may develop. Competitive products may make any products we develop obsolete or noncompetitive before we recover the expense of developing and commercializing our product candidates. Such competitors could also recruit our employees, which could negatively impact our level of expertise and our ability to execute our business plan.

Any inability to attract and retain qualified key management and technical personnel would impair our ability to implement our business plan.

Our success largely depends on the continued service of key management, advisors and other specialized personnel, including Sean A. McCarthy, D.Phil., our president and chief executive officer, W. Michael Kavanaugh, M.D., our chief scientific officer and Rachel W. Humphrey, M.D., our chief medical officer. The loss of one or more members of our management team or other key employees or advisors could delay our research and development programs and have a material and adverse effect on our business, financial condition, results of operations and prospects. The relationships that our key managers have cultivated within our industry make us particularly dependent upon their continued employment with us. We are dependent on the continued service of our technical personnel because of the highly technical nature of our product candidates and technologies and the specialized nature of the regulatory approval process. Because our management team and key employees are not obligated to provide us with continued service, they could terminate their employment with us at any time without penalty. Our future success will depend in large part on our continued ability to attract and retain other highly qualified scientific, technical and management personnel, as well as personnel with expertise in clinical testing, manufacturing, governmental regulation and commercialization. We face competition for personnel from other companies, universities, public and private research institutions, government entities and other organizations.

We may experience difficulties in managing our growth and expanding our operations successfully.

We will need to grow our organization substantially to continue development and pursue the potential commercialization for CX-072 and our other product candidates, as well as function as a public company. We have conducted limited product development to date and have not begun clinical trials for any of our product candidates, other than CX-072, for which we treated our first patient in our Phase 1/2 clinical trial in January 2017. As our product candidates enter and advance through preclinical studies and any clinical trials, we will need to expand our development, regulatory and manufacturing capabilities or contract with other organizations to provide these capabilities for us. In the future, we expect to have to manage additional relationships with collaborators or partners,

suppliers and other organizations. Our ability to manage our operations and future growth will require us to continue to improve our operational, financial and management controls, reporting systems and procedures. We may not be able to implement improvements to our management information and control systems in an efficient or timely manner and may discover deficiencies in existing systems and controls.

If any of our product candidates are approved for marketing and commercialization and we are unable to develop sales, marketing and distribution capabilities on our own or enter into agreements with third parties to perform these functions on acceptable terms, we will be unable to commercialize successfully any such future products.

We currently have no sales, marketing or distribution capabilities or experience. If any of our product candidates is approved, we will need to develop internal sales, marketing and distribution capabilities to commercialize such products, which would be expensive and time-consuming, or enter into collaborations with third parties to perform these services. If we decide to market our products directly, we will need to commit significant financial and managerial resources to develop a marketing and sales force with technical expertise and supporting distribution, administration and compliance capabilities. If we rely on third parties with such capabilities to market our products or decide to co-promote products with collaborators, we will need to establish and maintain marketing and distribution arrangements with third parties, and there can be no assurance that we will be able to enter into such arrangements on acceptable terms or at all. In entering into third-party marketing or distribution arrangements, any revenue we receive will depend upon the efforts of the third parties and there can be no assurance that such third parties will establish adequate sales and distribution capabilities or be successful in gaining market acceptance of any approved product. If we are not successful in commercializing any product approved in the future, either on our own or through third parties, our business, financial condition, results of operations and prospects could be materially and adversely affected.

Our future growth may depend, in part, on our ability to operate in foreign markets, where we would be subject to additional regulatory burdens and other risks and uncertainties.

Our future growth may depend, in part, on our ability to develop and commercialize our product candidates in foreign markets for which we may rely on collaboration with third parties. We are not permitted to market or promote any of our product candidates before we receive regulatory approval from the applicable regulatory authority in that foreign market, and we may never receive such regulatory approval for any of our product candidates. To obtain separate regulatory approval in many other countries we must comply with numerous and varying regulatory requirements of such countries regarding safety and efficacy and governing, among other things, clinical trials and commercial sales, pricing and distribution of our product candidates, and we cannot predict success in these jurisdictions. If we obtain approval of our product candidates and ultimately commercialize our product candidates in foreign markets, we would be subject to the risks and uncertainties, including the burden of complying with complex and changing foreign regulatory, tax, accounting and legal requirements and the reduced protection of intellectual property rights in some foreign countries.

Price controls imposed in foreign markets may adversely affect our future profitability.

In some countries, particularly member states of the European Union, the pricing of prescription drugs is subject to governmental control. In these countries, pricing negotiations with governmental authorities can take considerable time after receipt of marketing approval for a product. In addition, there can be considerable pressure by governments and other stakeholders on prices and reimbursement levels, including as part of cost containment measures. Political, economic and regulatory developments may further complicate pricing negotiations, and pricing negotiations may continue after reimbursement has been obtained. Reference pricing used by various European Union member states and parallel distribution, or arbitrage between low-priced and high-priced member states, can further reduce prices. In some countries, we or future collaborators may be required to conduct a clinical trial or other studies that compare the cost-effectiveness of our Probody therapeutic candidates to other available therapies in order to obtain or maintain reimbursement or pricing approval. Publication of discounts by third-party payors or authorities may lead to further pressure on the prices or reimbursement levels within the country of publication and other countries. If reimbursement of any product candidate approved for marketing is unavailable or limited in scope or amount, or if pricing is set at unsatisfactory levels, our business, financial condition, results of operations or prospects could be materially and

adversely affected. We currently do not know how the exit of the United Kingdom from the European Union will affect the pricing of prescription drugs, either in the United Kingdom or in the remaining European Union member states.

Our business entails a significant risk of product liability and our ability to obtain sufficient insurance coverage could have a material and adverse effect on our business, financial condition, results of operations and prospects.

We are exposed to significant product liability risks inherent in the development, testing, manufacturing and marketing of therapeutic treatments, including as a result of the clinical testing of CX-072 and any other product candidates we may conduct clinical trials for in the future. Product liability claims could delay or prevent completion of our development programs. If we succeed in marketing products, such claims could result in an FDA investigation of the safety and effectiveness of our products, our manufacturing processes and facilities or our marketing programs and potentially a recall of our products or more serious enforcement action, limitations on the approved indications for which they may be used or suspension or withdrawal of approvals. Regardless of the merits or eventual outcome, liability claims may also result in decreased demand for our products, injury to our reputation, costs to defend the related litigation, a diversion of management's time and our resources, substantial monetary awards to trial participants or patients and a decline in our stock price. We currently have insurance that we believe is appropriate for our stage of development and may need to obtain higher levels of insurance prior to marketing any of our product candidates. Any insurance we have or may obtain may not provide sufficient coverage against potential liabilities. Furthermore, clinical trial and product liability insurance is becoming increasingly expensive. As a result, we may be unable to obtain sufficient insurance at a reasonable cost to protect us against losses caused by product liability claims that could have a material and adverse effect on our business, financial condition, results of operations and prospects.

Our employees and independent contractors may engage in misconduct or other improper activities, including noncompliance with regulatory standards and requirements.

We are exposed to the risk of fraud or other misconduct by our employees or independent contractors. Misconduct by these parties could include intentional failures to comply with FDA regulations, provide accurate information to the FDA, comply with manufacturing standards we may establish, comply with federal and state data privacy, security, fraud and abuse, and other healthcare laws and regulations, report financial information or data accurately or disclose unauthorized activities to us. In particular, sales, marketing and business arrangements in the healthcare industry are subject to extensive laws and regulations intended to prevent fraud, kickbacks, self-dealing and other abusive practices. These laws and regulations may restrict or prohibit a wide range of pricing, discounting, marketing and promotion, sales commission, customer incentive programs and other business arrangements. Activities subject to these laws could also involve the improper use or misrepresentation of information obtained in the course of clinical trials, which could result in regulatory sanctions and cause serious harm to our reputation. It is not always possible to identify and deter misconduct by employees and other third parties, 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 or regulations. Additionally, we are subject to the risk that a person or government could allege such fraud or other misconduct, even if none occurred. 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 material and adverse effect on our business, financial condition, results of operations and prospects, including the imposition of significant fines or other sanctions.

Our internal computer systems, or those of our CROs or other contractors or consultants we may utilize, may fail or suffer security breaches, which could result in a material disruption of our product development programs.

Despite the implementation of security measures, our internal computer systems and those of our CROs and other contractors and consultants we may utilize, may be vulnerable to damage from computer viruses, unauthorized access, natural disasters, terrorism, war and telecommunication and electrical failures. Such events could cause interruptions of our operations. For instance, the loss of preclinical data or data from any current or future clinical trial involving our product candidates could result in delays in our development and regulatory filing efforts and significantly increase our costs. To the extent that any disruption or security breach were to result in a loss of, or damage to, our

data, or inappropriate disclosure of confidential or proprietary information, we could incur liability and the development of our product candidates could be delayed.

If we do not comply with laws regulating the protection of the environment and health and human safety, our business could be adversely affected.

Our research, development and manufacturing involve the use of hazardous materials and various chemicals. We maintain quantities of various flammable and toxic chemicals in our facilities in South San Francisco, California that are required for our research, development and manufacturing activities. We are subject to federal, state and local laws and regulations governing the use, manufacture, storage, handling and disposal of these hazardous materials. We believe our procedures for storing, handling and disposing these materials in our South San Francisco facilities comply with the relevant guidelines of South San Francisco, the state of California and the Occupational Safety and Health Administration of the U.S. Department of Labor. Although we believe that our safety procedures for handling and disposing of these materials comply with the standards mandated by applicable regulations, the risk of accidental contamination or injury from these materials cannot be eliminated. If an accident occurs, we could be held liable for resulting damages, which could be substantial. We are also subject to numerous environmental, health and workplace safety laws and regulations, including those governing laboratory procedures, exposure to blood-borne pathogens and the handling of animals and biohazardous materials. 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 these 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 or hazardous materials. Additional federal, state and local laws and regulations affecting our operations may be adopted in the future. We may incur substantial costs to comply with, and substantial fines or penalties if we violate, any of these laws or regulations.

Our information technology systems could face serious disruptions that could adversely affect our business.

Our information technology and other internal infrastructure systems, including corporate firewalls, servers, leased lines and connection to the Internet, face the risk of systemic failure that could disrupt our operations. A significant disruption in the availability of our information technology and other internal infrastructure systems could cause interruptions and delays in our research and development work.

Our current operations are concentrated in one location, and we or the third parties upon whom we depend may be adversely affected by earthquakes or other natural disasters and our business continuity and disaster recovery plans may not adequately protect us from a serious disaster.

Our current operations are located in our facilities in South San Francisco, California. Any unplanned event, such as flood, fire, explosion, earthquake, extreme weather condition, medical epidemics, power shortage, telecommunication failure or other natural or manmade accidents or incidents that result in us being unable to fully utilize our facilities, or the manufacturing facilities of our third-party contract manufacturers, may have a material and adverse effect on our ability to operate our business, particularly on a daily basis, and have significant negative consequences on our financial and operating conditions. Loss of access to these facilities may result in increased costs, delays in the development of our product candidates or interruption of our business operations. Earthquakes or other natural disasters could further disrupt our operations, and have a material and adverse effect on our business, financial condition, results of operations and prospects. If a natural disaster, power outage or other event occurred that prevented us from using all or a significant portion of our headquarters, that damaged critical infrastructure, such as our research facilities or the manufacturing facilities of our third-party contract manufacturers, or that otherwise disrupted operations, it may be difficult or, in certain cases, impossible, for us to continue our business for a substantial period of time. The disaster recovery and business continuity plans we have in place may prove inadequate in the event of a serious disaster or similar event. We may incur substantial expenses as a result of the limited nature of our disaster recovery and business continuity plans, which, could have a material and adverse effect on our business. As part of our risk management policy, we maintain insurance coverage at levels that we believe are

appropriate for our business. However, in the event of an accident or incident at these facilities, we cannot assure you that the amounts of insurance will be sufficient to satisfy any damages and losses. If our facilities, or the manufacturing facilities of our third-party contract manufacturers, are unable to operate because of an accident or incident or for any other reason, even for a short period of time, any or all of our research and development programs may be harmed. Any business interruption may have a material and adverse effect on our business, financial condition, results of operations and prospects.

Our Reported Financial Results May be Adversely Affected by Changes in Accounting Principles Generally Accepted in the U.S.

We prepare our financial statements in conformity with accounting principles generally accepted in the U.S. These accounting principles are subject to interpretation by the Financial Accounting Standards Board ("FASB") and the Securities and Exchange Commission. A change in these policies or interpretations could have a significant effect on our reported financial results, may retroactively affect previously reported results, could cause unexpected financial reporting fluctuations, and may require us to make costly changes to our operational processes and accounting systems. In May 2014, the FASB issued Accounting Standards Update ("ASU") 2014-09, Revenue from Contracts with Customers, which requires an entity to recognize the amount of revenue to which it expects to be entitled for the transfer of promised goods or services to customers. The ASU will replace most existing revenue recognition guidance in the U.S. GAAP when it becomes effective. The new standard will be effective for our fiscal year 2018 with early adoption permitted for our fiscal year 2017. Although we are currently in the process of evaluating the impact of ASU 2014-09 on our financial statements, it could change the way we account for certain of our sales transactions. Thus, adoption of the standard could have a significant impact on our financial statements and may retroactively affect the accounting treatment of transactions completed before adoption. See "Note 3 – Summary of Significant Accounting Policies" for additional discussion of the accounting changes.

Our ability to utilize our net operating loss carryforwards and certain other tax attributes may be limited.

Under Sections 382 and 383 of the Internal Revenue Code of 1986, as amended (the "IRC"), if a corporation undergoes an "ownership change" (generally defined as a greater than 50 percentage points change (by value) in the ownership of its equity over a rolling three-year period), the corporation's ability to use its pre-change net operating loss carryforwards and certain other pre-change tax attributes to offset its post-change income and taxes may be limited. California has similar rules. We have performed an IRC Section 382 analysis and determined there was an ownership change in 2015. As a result, the federal and state carryforwards associated with the net operating loss and credit deferred tax assets were reduced by the amount of tax attributes estimated to expire during their respective carryforward periods. We may experience ownership changes in the future as a result of shifts in our stock ownership, some of which are outside our control. As of December 31, 2016, we had federal and state net operating loss carryforwards of approximately $71.5 million and $14.3 million, respectively, and our ability to utilize those net operating loss carryforwards could be limited by an "ownership change" as described above, which could result in increased tax liability to our company.

Risks Related to Intellectual Property

If we are not able to obtain and enforce patent protection for our technologies or product candidates, development and commercialization of our product candidates may be adversely affected.

Our success depends in part on our ability to obtain and maintain patents and other forms of intellectual property rights, including in-licenses of intellectual property rights of others, for our product candidates, methods used to manufacture our product candidates and methods for treating patients using our product candidates, as well as our ability to preserve our trade secrets, to prevent third parties from infringing upon our proprietary rights and to operate without infringing upon the proprietary rights of others. As of February 15, 2017, we solely own 17 patents and 144 pending patent applications; we co-own six patents and seven pending patent applications with UC, acting through its Santa Barbara Campus and one patent and one pending patent application with UC, acting through its San Francisco Campus; and, under an exclusive, worldwide license agreement with UC, acting through its Santa Barbara Campus (the "UC Agreement"), we have licensed fifteen patents and eight pending patent applications that cover compositions and methods related to the screening and identification of the masks and protease-cleavable linkers that we incorporate into our Probody candidates. We also exclusively licensed UCSB's rights in the co-owned patent family. We may not

be able to apply for patents on certain aspects of our product candidates in a timely fashion or at all. Our existing issued and granted patents and any future patents we obtain may not be sufficiently broad to prevent others from using our technology or from developing competing products and technology. There is no guarantee that any of our pending patent applications will result in issued or granted patents, that any of our issued or granted patents will not later be found to be invalid or unenforceable or that any issued or granted patents will include claims that are sufficiently broad to cover our product candidates or to provide meaningful protection from our competitors. Moreover, the patent position of biotechnology and biopharmaceutical companies can be highly uncertain because it involves complex legal and factual questions. We will be able to protect our proprietary rights from unauthorized use by third parties only to the extent that our current and future proprietary technology and product candidates are covered by valid and enforceable patents or are effectively maintained as trade secrets. If third parties disclose or misappropriate our proprietary rights, it may materially and adversely affect our position in the market.

The U.S. Patent and Trademark Office ("USPTO") and various foreign governmental patent agencies require compliance with a number of procedural, documentary, fee payment and other provisions during the patent process. There are situations in which noncompliance can result in abandonment or lapse of a patent or patent application, resulting in partial or complete loss of patent rights in the relevant jurisdiction. In such an event, competitors might be able to enter the market earlier than would otherwise have been the case. The standards applied by the USPTO and foreign patent offices in granting patents are not always applied uniformly or predictably. For example, there is no uniform worldwide policy regarding patentable subject matter or the scope of claims allowable in biotechnology and biopharmaceutical patents. As such, we do not know the degree of future protection that we will have on our proprietary products and technology. While we will endeavor to try to protect our product candidates with intellectual property rights such as patents, as appropriate, the process of obtaining patents is time-consuming, expensive and sometimes unpredictable.

In addition, there are numerous recent changes to the patent laws and proposed changes to the rules of the USPTO that may have a significant impact on our ability to protect our technology and enforce our intellectual property rights. For example, the America Invents Act ("AIA") enacted within the last several years involves significant changes in patent legislation. The Supreme Court has ruled on several patent cases in recent years, some of which cases either narrow the scope of patent protection available in certain circumstances or weaken the rights of patent owners in certain situations. The recent decision by the Supreme Court in Association for Molecular Pathology v. Myriad Genetics, Inc. precludes a claim to a nucleic acid having a stated nucleotide sequence that is identical to a sequence found in nature and unmodified. We currently are not aware of an immediate impact of this decision on our patents or patent applications because we are developing product candidates that contain modifications, such as our Probody substrates and masks, that we believe are not found in nature. However, this decision has yet to be clearly interpreted by courts and by the USPTO. We cannot assure you that the interpretations of this decision or subsequent rulings will not adversely impact our patents or patent applications. In addition to increasing uncertainty with regard to our ability to obtain patents in the future, this combination of events has created uncertainty with respect to the value of patents, once obtained. Depending on decisions by the U.S. Congress, the federal courts and the USPTO, the laws and regulations governing patents could change in unpredictable ways that would weaken our ability to obtain new patents or to enforce our existing patents and patents that we might obtain in the future.

Once granted, patents may remain open to opposition, interference, re-examination, post-grant review, inter partes review, nullification or derivation action in court or before patent offices or similar proceedings for a given period after allowance or grant, during which time third parties can raise objections against such initial grant. In the course of such proceedings, which may continue for a protracted period of time, the patent owner may be compelled to limit the scope of the allowed or granted claims thus attacked, or may lose the allowed or granted claims altogether. In addition, there can be no assurance that:

- Others will not or may not be able to make, use or sell compounds that are the same as or similar to our product candidates but that are not covered by the claims of the patents that we own or license.
- We or our licensors, or our existing or future collaborators are the first to make the inventions covered by each of our issued patents and pending patent applications that we own or license.
- We or our licensors, or our existing or future collaborators are the first to file patent applications covering certain aspects of our inventions.
- Others will not independently develop similar or alternative technologies or duplicate any of our technologies without infringing our intellectual property rights.
- A third party may not challenge our patents and, if challenged, a court would hold that our patents are valid, enforceable and infringed.
- Any issued patents that we own or have licensed will provide us with any competitive advantages, or will not be challenged by third parties.
- We may develop additional proprietary technologies that are patentable.

- The patents of others will not have a material or adverse effect on our business, financial condition, results of operations and prospects.
- Our competitors do not conduct research and development activities in countries where we do not have enforceable patent rights and then use the information learned from such activities to develop competitive products for sale in our major commercial markets.

Other companies or organizations may challenge our or our licensors' patent rights or may assert patent rights that prevent us from developing and commercializing our products.

Probody therapeutics are a relatively new scientific field. We have obtained grants and issuances of Probody therapeutic patents and have licensed several of these patents from a third party on an exclusive basis for therapeutics applications. The issued patents and pending patent applications in the U.S. and in key markets around the world that we own or license claim many different methods, compositions and processes relating to the discovery, development, manufacture and commercialization of antibody and immunoregulatory therapeutics. Specifically, we own and have licensed a portfolio of patents, patent applications and other intellectual property covering Probody compositions of matter as well as their methods of manufacturing and use.

As the field of antibody and immunoregulatory therapeutics matures, patent applications are being processed by national patent offices around the world. There is uncertainty about which patents will issue, and, if they do, as to when, to whom, and with what claims. In addition, third parties may attempt to invalidate our intellectual property rights. Even if our rights are not directly challenged, disputes could lead to the weakening of our intellectual property rights. Our defense against any attempt by third parties to circumvent or invalidate our intellectual property rights could be costly to us, could require significant time and attention of our management and could have a material and adverse effect on our business, financial condition, results of operations and prospects or our ability to successfully compete.

There are many issued and pending patents that claim aspects of our product candidates and modifications that we may need to apply to our product candidates. There are also many issued patents that claim antibodies or portions of antibodies that may be relevant for Probody products we wish to develop. Thus, it is possible that one or more organizations will hold patent rights to which we will need a license. If those organizations refuse to grant us a license to such patent rights on reasonable terms, we may not be able to market products or perform research and development or other activities covered by these patents.

We may not be able to protect our intellectual property rights throughout the world.

Obtaining a valid and enforceable issued or granted patent covering our technology in the U.S. and worldwide can be extremely costly. In jurisdictions where we have not obtained patent protection, competitors may use our technology to develop their own products and further, may export otherwise infringing products to territories where we have patent protection, but where it is more difficult to enforce a patent as compared to the U.S. Competitor products may compete with our future products in jurisdictions where we do not have issued or granted patents or where our issued or granted patent claims or other intellectual property rights are not sufficient to prevent competitor activities in these jurisdictions. The legal systems of certain countries, particularly certain developing countries, make it difficult to enforce patents and such countries may not recognize other types of intellectual property protection, particularly that relating to biopharmaceuticals. This could make it difficult for us to prevent the infringement of our patents or marketing of competing products in violation of our proprietary rights generally in certain jurisdictions. Proceedings to enforce our patent rights in foreign jurisdictions could result in substantial cost and divert our efforts and attention from other aspects of our business.

We generally file a provisional patent application first (a priority filing) at the USPTO. An international application under the Patent Cooperation Treaty ("PCT") is usually filed within twelve months after the priority filing. Based on the PCT filing, national and regional patent applications may be filed in the United States, European Union, Japan, Australia and Canada and, depending on the individual case, also in any or all of, inter alia, Brazil, China, Hong Kong, India, Israel, Mexico, New Zealand, Russia, South Africa, South Korea and other jurisdictions. We have so far not filed for patent protection in all national and regional jurisdictions where such protection may be available. In addition, we may decide to abandon national and regional patent applications before grant. Finally, the grant

proceeding of each national or regional patent is an independent proceeding which may lead to situations in which applications might in some jurisdictions be refused by the relevant registration authorities, while granted by others. It is also quite common that depending on the country, various scopes of patent protection may be granted on the same product candidate or technology.

The laws of some jurisdictions do not protect intellectual property rights to the same extent as the laws in the U.S., and many companies have encountered significant difficulties in protecting and defending such rights in such jurisdictions. If we or our licensors encounter difficulties in protecting, or are otherwise precluded from effectively protecting, the intellectual property rights important for our business in such jurisdictions, the value of these rights may be diminished and we may face additional competition from others in those jurisdictions. Many countries have compulsory licensing laws under which a patent owner may be compelled to grant licenses to third parties. In addition, many countries limit the enforceability of patents against government agencies or government contractors. In these countries, the patent owner may have limited remedies, which could materially diminish the value of such patent. If we or any of our licensors are forced to grant a license to third parties with respect to any patents relevant to our business, our competitive position in the relevant jurisdiction may be impaired and our business and results of operations may be adversely affected.

We or our licensors, or any future strategic partners may become subject to third party claims or litigation alleging infringement of patents or other proprietary rights or seeking to invalidate patents or other proprietary rights, and we may need to resort to litigation to protect or enforce our patents or other proprietary rights, all of which could be costly, time consuming, delay or prevent the development and commercialization of our product candidates, or put our patents and other proprietary rights at risk.

We or our licensors, or any future strategic partners may be subject to third-party claims for infringement or misappropriation of patent or other proprietary rights. We are generally obligated under our license or collaboration agreements to indemnify and hold harmless our licensors or collaborators for damages arising from intellectual property infringement by us. If we or our licensors, or any future strategic partners are found to infringe a third-party patent or other intellectual property rights, we could be required to pay damages, potentially including treble damages, if we are found to have willfully infringed. In addition, we or our licensors, or any future strategic partners may choose to seek, or be required to seek, a license from a third party, which may not be available on acceptable terms, if at all. Even if a license can be obtained on acceptable terms, the rights may be non-exclusive, which could give our competitors access to the same technology or intellectual property rights licensed to us. If we fail to obtain a required license, we or our existing or future collaborators may be unable to effectively market product candidates based on our technology, which could limit our ability to generate revenue or achieve profitability and possibly prevent us from generating revenue sufficient to sustain our operations. In addition, we may find it necessary to pursue claims or initiate lawsuits to protect or enforce our patent or other intellectual property rights. The cost to us in defending or initiating any litigation or other proceeding relating to patent or other proprietary rights, even if resolved in our favor, could be substantial, and litigation would divert our management's attention. Some of our competitors may be able to sustain the costs of complex patent litigation more effectively than we can because they have substantially greater resources. Uncertainties resulting from the initiation and continuation of patent litigation or other proceedings could delay our research and development efforts and limit our ability to continue our operations.

If we were to initiate legal proceedings against a third party to enforce a patent covering one of our products or our technology, the defendant could counterclaim that our patent is invalid or unenforceable. In patent litigation in the U.S., defendant counterclaims alleging invalidity or unenforceability are commonplace. Grounds for a validity challenge could be an alleged failure to meet any of several statutory requirements, for example, lack of novelty, obviousness or non-enablement. Grounds for an unenforceability assertion could be an allegation that someone connected with prosecution of the patent withheld relevant information from the USPTO, or made a misleading statement, during prosecution. The outcome following legal assertions of invalidity and unenforceability during patent litigation is unpredictable. With respect to the validity question, for example, we cannot be certain that there is no invalidating prior art, of which we and the patent examiner were unaware during prosecution. If a defendant were to prevail on a legal assertion of invalidity or unenforceability, we would lose at least part, and perhaps all, of the patent protection on one or more of our products or certain aspects of our platform technology. Such a loss of patent protection could have a material and adverse effect on our business, financial condition, results of operations and prospects. Patents and other intellectual property rights also will not protect our technology if competitors design around our protected technology without legally infringing our patents or other intellectual property rights.

Intellectual property rights of third parties could adversely affect our ability to commercialize our product candidates, and we might be required to litigate or obtain licenses from third parties in order to develop or market our product candidates. Such litigation or licenses could be costly or not available on commercially reasonable terms.

Because the antibody landscape is still evolving, including the masked antibody landscape, it is difficult to conclusively assess our freedom to operate without infringing on third-party rights. There are numerous companies that have pending patent applications and issued patents broadly covering antibodies generally or covering antibodies directed against the same targets as, or targets similar to, those we are pursuing. An increasing number of third parties are filing masked antibody patent applications, several of which contain claims that are patterned after our own patent

claims. Our competitive position may suffer if patents issued to third parties or other third-party intellectual property rights cover our products or product candidates or elements thereof, or our manufacture or uses relevant to our development plans. In such cases, we may not be in a position to develop or commercialize products or product candidates unless we successfully pursue litigation to nullify or invalidate the third-party intellectual property right concerned, or enter into a license agreement with the intellectual property right holder, if available on commercially reasonable terms. There may be issued patents of which we are not aware, held by third parties that, if found to be valid and enforceable, could be alleged to be infringed by our Probody technologies. There also may be pending patent applications of which we are not aware that may result in issued patents, which could be alleged to be infringed by our Probody technologies. If such an infringement claim should be brought and be successful, we may be required to pay substantial damages, be forced to abandon our product candidates or seek a license from any patent holders. No assurances can be given that a license will be available on commercially reasonable terms, if at all.

It is also possible that we have failed to identify relevant third-party patents or applications. For example, U.S. applications filed before November 29, 2000 and certain U.S. applications filed after that date that will not be filed outside the U.S. remain confidential until patents issue. Patent applications in the U.S. and elsewhere are published approximately 18 months after the earliest filing for which priority is claimed, with such earliest filing date being commonly referred to as the priority date. Therefore, patent applications covering our products or platform technology could have been filed by others without our knowledge. Additionally, pending patent applications that have been published can, subject to certain limitations, be later amended in a manner that could cover our platform technologies, our products or the use of our products. Third-party intellectual property right holders may also actively bring infringement claims against us. We cannot guarantee that we will be able to successfully settle or otherwise resolve such infringement claims. If we are unable to successfully settle future claims on terms acceptable to us, we may be required to engage in or continue costly, unpredictable and time-consuming litigation and may be prevented from or experience substantial delays in marketing our products. If we fail in any such dispute, in addition to being forced to pay damages, we may be temporarily or permanently prohibited from commercializing any of our product candidates that are held to be infringing. We might, if possible, also be forced to redesign product candidates so that we no longer infringe the third-party intellectual property rights. Any of these events, even if we were ultimately to prevail, could require us to divert substantial financial and management resources that we would otherwise be able to devote to our business.

Intellectual property litigation could cause us to spend substantial resources and distract our personnel from their normal responsibilities.

Litigation or other legal proceedings relating to intellectual property claims, with or without merit, is unpredictable and generally expensive and time consuming and is likely to divert significant resources from our core business, including distracting our technical and management personnel from their normal responsibilities. Furthermore, because of the substantial amount of discovery required in connection with intellectual property litigation, there is a risk that some of our confidential information could be compromised by disclosure during this type of litigation. In addition, there could be public announcements of the results of hearings, motions or other interim proceedings or developments and if securities analysts or investors perceive these results to be negative, it could have a substantial adverse effect on the price of our common stock. Such litigation or proceedings could substantially increase our operating losses and reduce the resources available for development activities or any future sales, marketing or distribution activities.

We may not have sufficient financial or other resources to adequately conduct such litigation or proceedings. Some of our competitors may be able to sustain the costs of such litigation or proceedings more effectively than we can because of their greater financial resources and more mature and developed intellectual property portfolios. Accordingly, despite our efforts, we may not be able to prevent third parties from infringing upon or misappropriating or from successfully challenging our intellectual property rights. Uncertainties resulting from the initiation and continuation of patent litigation or other proceedings could have a material and adverse effect on our ability to compete in the marketplace.

If we fail to comply with our obligations under any license, collaboration or other agreements, we may be required to pay damages and could lose intellectual property rights that are necessary for developing and protecting our product candidates or we could lose certain rights to grant sublicenses.

Our current license imposes, and any future licenses we enter into are likely to impose, various development, commercialization, funding, milestone, royalty, diligence, sublicensing, insurance, patent prosecution and enforcement and/or other obligations on us. If we breach any of these obligations, or use the intellectual property licensed to us in an unauthorized manner, we may be required to pay damages and the licensor may have the right to terminate the license, which could result in us being unable to develop, manufacture and sell products that are covered

by the licensed technology or enable a competitor to gain access to the licensed technology. Moreover, our licensors may own or control intellectual property that has not been licensed to us and, as a result, we may be subject to claims, regardless of their merit, that we are infringing or otherwise violating the licensor's rights. In addition, while we cannot currently determine the amount of the royalty obligations we would be required to pay on sales of future products, if any, the amounts may be significant. The amount of our future royalty obligations will depend on the technology and intellectual property we use in products that we successfully develop and commercialize, if any. Therefore, even if we successfully develop and commercialize products, we may be unable to achieve or maintain profitability.

If we are unable to protect the confidentiality of our trade secrets, our business and competitive position would be harmed.

In addition to seeking patent protection for certain aspects of our product candidates, we also consider trade secrets, including confidential and unpatented know-how important to the maintenance of our competitive position. We protect trade secrets and confidential and unpatented know-how, in part, by entering into non-disclosure and confidentiality agreements with parties who have access to such knowledge, such as our employees, corporate collaborators, outside scientific collaborators, CROs, contract manufacturers, consultants, advisors and other third parties. We also enter into confidentiality and invention or patent assignment agreements with our employees and consultants that obligate them to maintain confidentiality and assign their inventions to us.

Despite these efforts, any of these parties may breach the agreements and disclose our proprietary information, including our trade secrets, and we may not be able to obtain adequate remedies for such breaches. Enforcing a claim that a party illegally disclosed or misappropriated a trade secret is difficult, expensive and time-consuming, and the outcome is unpredictable. In addition, some courts in the U.S. and certain foreign jurisdictions are less willing or unwilling to protect trade secrets. If any of our trade secrets were to be lawfully obtained or independently developed by a competitor, we would have no right to prevent them from using that technology or information to compete with us. If any of our trade secrets were to be disclosed to or independently developed by a competitor, our competitive position would be harmed.

We may be subject to claims that we or our employees or consultants have wrongfully used or disclosed alleged trade secrets of our employees' or consultants' former employers or their clients. These claims may be costly to defend and if we do not successfully do so, we may be required to pay monetary damages and may lose valuable intellectual property rights or personnel.

Many of our employees were previously employed at universities or biotechnology or biopharmaceutical companies, including our competitors or potential competitors. Although no claims against us are currently pending, we may be subject to claims that these employees or we have inadvertently or otherwise used or disclosed trade secrets or other proprietary information of their former employers. Litigation may be necessary to defend against these claims. If we fail in defending such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights or personnel. A loss of key research personnel or their work product could hamper our ability to commercialize, or prevent us from commercializing, our product candidates, which could severely harm our business. Even if we are successful in defending against these claims, litigation could result in substantial costs and be a distraction to management.

If our trademarks and trade names are not adequately protected, then we may not be able to build name recognition in our markets of interest and our business may be adversely affected.

Our trademarks or trade names may be challenged, infringed, circumvented or declared generic or determined to be infringing on other marks. We may not be able to protect our rights to these trademarks and trade names or may be forced to stop using these names, which we need for name recognition by potential partners or customers in our markets of interest. If we are unable to establish name recognition based on our trademarks and trade names, we may not be able to compete effectively and our business may be adversely affected.

Risks Related to Government Regulation

Clinical development involves a lengthy and expensive process with an uncertain outcome, and results of earlier studies and trials may not be predictive of future trial results.

All of our product candidates are in preclinical development or at the beginning of clinical development and their risk of failure is high. It is impossible to predict when or if any of our product candidates will prove effective and safe in humans or will receive regulatory approval. Before obtaining marketing approval from regulatory authorities for the sale of any product candidate, we must complete preclinical studies and then conduct extensive clinical trials to demonstrate the safety and efficacy of our product candidates in humans. Clinical testing is expensive and can take many years to complete, and its outcome is inherently uncertain. Failure can occur at any time during the development process. The results of preclinical studies and early clinical trials of our product candidates may not be predictive of the results of later-stage clinical trials. Product candidates in later stages of clinical trials may fail to show the desired safety and efficacy traits despite having progressed through preclinical studies and initial clinical trials. A number of companies in the biopharmaceutical industry have suffered significant setbacks in advanced clinical trials due to lack of efficacy or safety profiles, notwithstanding promising results in earlier trials.

We have commenced enrollment of our Phase 1/2 clinical trial of CX-072, our candidate directed against PD-L1, for cancer and treated our first patient in January 2017. We intend to commence a Phase 1 clinical trial of CX-2009, our PDC candidate directed against CD-166, for cancer in 2017. Commencement of the clinical trials is subject to finalizing the trial design and filing an IND or similar filing with the FDA or similar foreign regulatory authority. We expect to file an IND for CX-2009 in the first half of 2017. However, even after we file our IND or comparable submissions in other jurisdictions, the FDA or other regulatory authorities could disagree that we have satisfied their requirements to commence our clinical trials or disagree with our study design, which may require us to complete additional preclinical studies or amend our protocols or impose stricter conditions on the commencement of clinical trials and may delay our ability to begin Phase 1 clinical trials, causing an increase in the amount of time and expense required to develop our product candidates.

We may be unable to obtain U.S. or foreign regulatory approval and, as a result, unable to commercialize our product candidates.

Our product candidates are subject to extensive governmental regulations relating to, among other things, research, testing, development, manufacturing, safety, efficacy, approval, recordkeeping, reporting, labeling, storage, packaging, advertising and promotion, pricing, marketing and distribution of drugs and therapeutic biologics. Rigorous preclinical testing and clinical trials and an extensive regulatory approval process are required to be successfully completed in the U.S. and in many foreign jurisdictions before a new drug or therapeutic biologic can be marketed. Satisfaction of these and other regulatory requirements is costly, time consuming, uncertain and subject to unanticipated delays. It is possible that none of the product candidates we may develop will obtain the regulatory approvals necessary for us or our existing or future collaborators to begin selling them.

As a company, we have very limited experience in conducting and managing the clinical trials necessary to obtain regulatory approvals, including approval by the FDA. The time required to obtain FDA and other approvals is unpredictable but typically takes many years following the commencement of clinical trials, depending upon the type, complexity and novelty of the product candidate. The standards that the FDA and its foreign counterparts use when regulating us require judgment and can change, which makes it difficult to predict with certainty how they will be applied. Any analysis we perform of data from preclinical and clinical activities is subject to confirmation and interpretation by regulatory authorities, which could delay, limit or prevent regulatory approval. We may also encounter unexpected delays or increased costs due to new government regulations, for example, from future legislation or administrative action, or from changes in FDA policy during the period of product development, clinical trials and FDA regulatory review. It is impossible to predict whether legislative changes will be enacted, or whether FDA or foreign regulations, guidance or interpretations will be changed, or what the impact of such changes, if any, may be.

Because the product candidates we are developing may represent a new class of therapeutic biologics, the FDA and its foreign counterparts have not yet established any definitive policies, practices or guidelines in relation to these product candidates. While we believe the product candidates that we are currently developing are regulated as therapeutic biologics that are subject to requirements for review and approval of a BLA by the FDA's Center for Drug Evaluation and Research ("CDER"), the FDA could decide to regulate them as drugs that are subject to requirements for review and approval of an NDA by CDER or as biological products that are subject to requirements for review and approval of a BLA by the FDA's Center for Biologics Evaluation and Research ("CBER"). The lack of policies, practices or guidelines may hinder or slow review by the FDA of any regulatory filings that we may submit. Moreover, the FDA may respond to these submissions by defining requirements we may not have anticipated. Such responses could lead to significant delays in the clinical development of our product candidates. In addition, because there may be approved treatments for some of the diseases for which we may seek approval, in order to receive regulatory approval, we may need to demonstrate through clinical trials that the product candidates we develop to treat these diseases, if any, are not only safe and effective, but safer or more effective than existing products. Furthermore, in recent years, there has been increased public and political pressure on the FDA with respect to the approval process for new drugs and therapeutic biologics, and the FDA's standards, especially regarding product safety, appear to have become more stringent.

Any delay or failure in obtaining required approvals could have a material and adverse effect on our ability to generate revenues from the particular product candidate for which we are seeking approval. Furthermore, any regulatory approval to market a product may be subject to limitations on the approved uses for which we may market the product or the labeling or other restrictions. In addition, the FDA has the authority to require a risk evaluation and mitigation strategies ("REMS") plan as part of an NDA or BLA or after approval, which may impose further requirements or restrictions on the distribution or use of an approved drug or biologic, such as limiting prescribing to certain physicians or medical centers that have undergone specialized training, limiting treatment to patients who meet certain

safe-use criteria and requiring treated patients to enroll in a registry. These limitations and restrictions may limit the size of the market for the product and affect reimbursement by third-party payors.

We are also subject to numerous foreign regulatory requirements governing, among other things, the conduct of clinical trials, manufacturing and marketing authorization, pricing and third-party reimbursement. The foreign regulatory approval process varies among countries and may include all of the risks associated with FDA approval described above as well as risks attributable to the satisfaction of local regulations in foreign jurisdictions. Moreover, the time required to obtain approval may differ from that required to obtain FDA approval. Approval by the FDA does not ensure approval by regulatory authorities outside the U.S. and vice versa.

Even if we receive regulatory approval for any of our product candidates, we will be subject to ongoing regulatory obligations and continued regulatory review, which may result in significant additional expense. Additionally, our product candidates, if approved, could be subject to labeling and other restrictions and market withdrawal and we may be subject to penalties if we fail to comply with regulatory requirements or experience unanticipated problems with our products.

Any regulatory approvals that we or our existing or future collaborators obtain for our product candidates may also be subject to limitations on the approved indicated uses for which a product may be marketed or to the conditions of approval, or contain requirements for potentially costly post-marketing testing, including "Phase 4" clinical trials, and surveillance to monitor the safety and efficacy of the product candidate. In addition, if the FDA or a comparable foreign regulatory authority approves any of our product candidates, the manufacturing processes, labeling, packaging, distribution, adverse event reporting, storage, import, export, advertising, promotion and recordkeeping for the product will be subject to extensive and ongoing regulatory requirements. These requirements include submissions of safety and other post-marketing information and reports, registration, as well as continued compliance with cGMPs and good clinical practices for any clinical trials that we conduct post-approval. Later discovery of previously unknown problems with a product, including adverse events of unanticipated severity or frequency, or with our third-party manufacturers or manufacturing processes, or failure to comply with regulatory requirements, may result in, among other things:

- restrictions on the marketing or manufacturing of the product, withdrawal of the product from the market or voluntary or mandatory product recalls;
- fines, warning letters or holds on clinical trials;
- refusal by the FDA to approve pending applications or supplements to approved applications filed by us or our strategic partners;
- suspension or revocation of product license approvals;
- product seizure or detention or refusal to permit the import or export of products; and
- injunctions or the imposition of civil or criminal penalties.

The FDA's policies may change and additional government regulations may be enacted that could prevent, limit or delay regulatory approval of our product candidates. For example, in December 2016, the 21st Century Cures Act, or "Cures Act", was signed into law. The Cures Act, among other things, is intended to modernize the regulation of drugs and biologics and to spur innovation, but its ultimate implementation is unclear. If we are slow or unable to adapt to changes in existing requirements or the adoption of new requirements or policies, or if we are not able to maintain regulatory compliance, we may lose any marketing approval that we may have obtained and we may not achieve or sustain profitability, which would adversely affect our business.

We also cannot predict the likelihood, nature or extent of government regulation that may arise from future legislation or administrative or executive action, either in the United States or abroad. For example, certain policies of the Trump administration may impact our business and industry. Namely, the Trump administration has taken several executive actions, including the issuance of a number of Executive Orders, that could impose significant burdens on, or otherwise materially delay, FDA's ability to engage in routine regulatory and oversight activities such as implementing statutes through rulemaking, issuance of guidance, and review and approval of marketing applications. Notably, on January 23, 2017, President Trump ordered a hiring freeze for all executive departments and agencies, including the FDA, which prohibits the FDA from filling employee vacancies or creating new positions. Under the terms of the order, the freeze will remain in effect until implementation of a plan to be recommended by the Director for the Office of Management and Budget, or OMB, in consultation with the Director of the Office of Personnel Management, to reduce the size of the federal workforce through attrition. While it is possible that certain positions at the FDA may be subject to an exemption from the hiring freeze, an under-staffed FDA could result in delays in FDA's responsiveness or in its ability to review submissions or applications, issue regulations or guidance, or implement or enforce

regulatory requirements in a timely fashion or at all. Moreover, on January 30, 2017, President Trump issued an Executive Order, applicable to all executive agencies, including the FDA, that requires that for each notice of proposed rulemaking or final regulation to be issued in fiscal year 2017, the agency shall identify at least two existing regulations to be repealed, unless prohibited by law. These requirements are referred to as the "two-for-one" provisions. This Executive Order includes a budget neutrality provision that requires the total incremental cost of all new regulations in the 2017 fiscal year, including repealed regulations, to be no greater than zero, except in limited circumstances. For fiscal years 2018 and beyond, the Executive Order requires agencies to identify regulations to offset any incremental cost of a new regulation and approximate the total costs or savings associated with each new regulation or repealed regulation. In interim guidance issued by the Office of Information and Regulatory Affairs within OMB on February 2, 2017, the administration indicates that the "two-for-one" provisions may apply not only to agency regulations, but also to significant agency guidance documents. It is difficult to predict how these requirements will be implemented, and the extent to which they will impact the FDA's ability to exercise its regulatory authority. If these executive actions impose constraints on FDA's ability to engage in oversight and implementation activities in the normal course, our business may be negatively impacted.

Healthcare legislative reform measures may have a material and adverse effect on our business and results of operations.

In the United States, there have been and continue to be a number of legislative initiatives to contain healthcare costs. For example, in March 2010, the Patient Protection and Affordable Care Act, as amended by the Healthcare and Education Reconciliation Act (together, the "ACA"), was passed, which substantially changes the way healthcare is financed by both governmental and private insurers, and significantly impacts the U.S. pharmaceutical industry. The ACA, among other things, subjects therapeutic biologics to potential competition by lower-cost biosimilars, addresses a new methodology by which rebates owed by manufacturers under the Medicaid Drug Rebate Program are calculated for drugs and therapeutic biologics that are inhaled, infused, instilled, implanted or injected, increases the minimum Medicaid rebates owed by manufacturers under the Medicaid Drug Rebate Program and extends the rebate program to individuals enrolled in Medicaid managed care organizations, establishes annual fees and taxes on manufacturers of certain branded prescription drugs and therapeutic biologics, and 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 drugs and therapeutic biologics to eligible beneficiaries during their coverage gap period, as a condition for the manufacturer's outpatient drugs and therapeutic biologics to be covered under Medicare Part D.

We expect that the new presidential administration and U.S. Congress will seek to modify, repeal, or otherwise invalidate all, or certain provisions of, the ACA. Since taking office, President Trump has continued to support the repeal of all or portions of the ACA. In January 2017, the House and Senate passed a budget resolution that authorizes congressional committees to draft legislation to repeal all or portions of the ACA and permits such legislation to pass with a majority vote in the Senate. President Trump has also recently issued an executive order in which he stated that it is his administration's policy to seek the prompt repeal of the ACA and directed executive departments and federal agencies to waive, defer, grant exemptions from, or delay the implementation of the provisions of the ACA to the maximum extent permitted by law. There is still uncertainty with respect to the impact President Trump's administration and the U.S. Congress may have, if any, and any changes will likely take time to unfold, and could have an impact on coverage and reimbursement for healthcare items and services covered by plans that were authorized by the ACA. However, we cannot predict the ultimate content, timing or effect of any healthcare reform legislation or the impact of potential legislation on us.

In addition, other legislative changes have been proposed and adopted in the United States since the ACA was enacted to reduce healthcare expenditures. Additionally, U.S. federal government agencies currently face potentially significant spending reductions, which may further impact healthcare expenditures. On August 2, 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 2013 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 2% per fiscal year. These reductions went into effect on April 1, 2013 and, due to subsequent legislative amendments to the statute, will remain in effect through 2024 unless additional Congressional action is taken. On January 2, 2013, the American Taxpayer Relief Act of 2012 was signed into law, which, among other things, further reduced Medicare payments to several types of 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. If federal spending is further reduced, anticipated budgetary shortfalls may also impact the ability of relevant agencies, such as the FDA or the National Institutes of Health to continue to function at current levels. Amounts allocated to federal grants and contracts may be reduced or eliminated. These reductions may also impact the ability of relevant agencies to timely review and approve research and development, manufacturing, and marketing activities, which may delay our ability to develop, market and sell any products we may develop.

Moreover, payment methodologies, including payment for companion diagnostics, may be subject to changes in healthcare legislation and regulatory initiatives. For example, the Centers for Medicare & Medicaid Services ("CMS") has begun bundling the Medicare payments for certain laboratory tests ordered while a patient received services in a hospital outpatient setting and, beginning in 2018, CMS will pay for clinical laboratory services based on a weighted average of reported prices that private payors, Medicare Advantage plans, and Medicaid Managed Care plans pay for laboratory services. In addition, recently there has been heightened governmental scrutiny over the manner in which manufacturers set prices for their marketed products, which has resulted in several Congressional inquiries and proposed bills designed to, among other things, bring more transparency to product pricing, review the relationship between pricing and manufacturer patient programs, and reform government program reimbursement methodologies for drug products. For example, the 21st Century Cures Act changed the reimbursement methodology for infusion drugs and biologics furnished through durable medical equipment in an attempt to remedy over- and underpayment of certain products. We expect that additional state and federal healthcare reform measures will be adopted in the future, any of which could limit the amounts that federal and state governments will pay for healthcare products and services, which could result in reduced demand for our product candidates or companion diagnostics or additional pricing pressures.

If we or existing or future collaborators, manufacturers or service providers fail to comply with healthcare laws and regulations, we or they could be subject to enforcement actions, which could affect our ability to develop, market and sell our products and may harm our reputation.

Although we do not currently have any products on the market, once we begin commercializing our product candidates, we will be subject to additional healthcare statutory and regulatory requirements and enforcement by the federal government and the states and foreign governments in which we conduct our business. Healthcare providers, physicians and third-party payors play a primary role in the recommendation and prescription of any product candidates for which we obtain marketing approval. Our future arrangements with third-party payors and customers 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 our product candidates for which we obtain marketing approval. In addition, we may be subject to patient data privacy and security regulation by both the U.S. federal government and the states in which we conduct our business. Restrictions under applicable federal and state healthcare laws and regulations, include the following:

- the U.S. federal Anti-Kickback Statute, which 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, or order or recommendation of, any good or service, for which payment may be made under federal and state healthcare programs such as Medicare and Medicaid. A person or entity does not need to have actual knowledge of the statute or specific intent to violate it in order to have committed a violation;
- the U.S. federal False Claims Act, which imposes criminal and civil penalties, including through 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, knowingly making, using or causing to be made or used, a false record or statement material to a false or fraudulent claim, or from knowingly making a false statement to avoid, decrease or conceal an obligation to pay money to the federal government. In addition, the government may assert that a claim including items and services resulting from a violation of the federal Anti-Kickback Statute constitutes a false or fraudulent claim for purposes of the False Claims Act;
- the U.S. federal Health Insurance Portability and Accountability Act of 1996 (“HIPAA”), which imposes criminal and civil liability for, among other things, knowingly and willfully executing, or attempting to execute a scheme to defraud any healthcare benefit program, or 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; similar to the federal Anti-Kickback Statute, a person or entity does not need to have actual knowledge of the statute or specific intent to violate it in order to have committed a violation;
- HIPAA, as amended by the Health Information Technology for Economics and Clinical Health Act (“HITECH”), which impose obligations on certain covered entity healthcare providers, health plans, and healthcare clearinghouse as well as their business associates that perform certain services involving the use or disclosure of individually identifiable health information, including mandatory contractual terms, with respect to safeguarding the privacy, security, and transmission of individually identifiable health information, and require notification to affected individuals and regulatory authorities of certain breaches of security of individually identifiable health information;
- the U.S. federal legislation commonly referred to as Physician Payments Sunshine Act, enacted as part of the ACA, and its implementing regulations, which requires certain manufacturers of drugs, devices, biologics and medical supplies that are reimbursable under Medicare, Medicaid, or the Children’s Health Insurance Program to report annually to the CMS information related to certain payments and other transfers of value to physicians (defined to include doctors, dentists, optometrists, podiatrists and chiropractors) and teaching hospitals, as well as ownership and investment interests held by the physicians described above and their immediate family members; and
- analogous state laws and regulations, such as state anti-kickback and false claims laws that may apply to sales or marketing arrangements and claims involving healthcare items or services reimbursed by non-governmental third-party payors, including private insurers; and 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 and therapeutic biologics manufacturers to report information related to payments to physicians and other healthcare providers or marketing expenditures and pricing information, and state laws governing the privacy and security of health information in certain circumstances, many of which differ from each other in significant ways and often are not preempted by HIPAA, thus complicating compliance efforts.

Ensuring that our future business arrangements with third-parties comply with applicable healthcare laws and regulations could involve substantial costs. It is possible that governmental authorities will conclude that our business practices do not comply with current or future statutes, regulations, agency guidance 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 such requirements, we may be subject to penalties, including civil or criminal penalties, monetary damages, the curtailment or restructuring of our operations, loss of eligibility to obtain approvals from the FDA, or exclusion from participation in government contracting, healthcare reimbursement or other government programs, including Medicare and Medicaid, any of which could adversely our financial results. Although effective compliance programs can mitigate the risk of investigation and prosecution for violations of these laws, these risks cannot be entirely eliminated. Any action against us for an alleged or suspected violation could cause us to incur significant legal expenses and could divert our management's attention from the operation of our business, even if our defense is successful. In addition, achieving and sustaining compliance with applicable laws and regulations may be costly to us in terms of money, time and resources.

If we or future collaborators, manufacturers or service providers fail to comply with applicable federal, state or foreign laws or regulations, we could be subject to enforcement actions, which could affect our ability to develop, market and sell our products successfully and could harm our reputation and lead to reduced acceptance of our products by the market. These enforcement actions include, among others:

- adverse regulatory inspection findings;
- warning letters;
- voluntary or mandatory product recalls or public notification or medical product safety alerts to healthcare professionals;
- restrictions on, or prohibitions against, marketing our products;
- restrictions on, or prohibitions against, importation or exportation of our products;
- suspension of review or refusal to approve pending applications or supplements to approved applications;
- exclusion from participation in government-funded healthcare programs;
- exclusion from eligibility for the award of government contracts for our products;
- suspension or withdrawal of product approvals;
- seizures or administrative detention of products;
- injunctions; and
- civil and criminal penalties and fines.

If we fail to comply with U.S. and foreign regulatory requirements, regulatory authorities could limit or withdraw any marketing or commercialization approvals we may receive and subject us to other penalties that could materially harm our business.

Even if we receive marketing and commercialization approval of a product candidate, we will be subject to continuing regulatory requirements, including in relation to adverse patient experiences with the product and clinical results that are reported after a product is made commercially available, both in the U.S. and any foreign jurisdiction in which we seek regulatory approval. The FDA has significant post-market authority, including the authority to require labeling changes based on new safety information and to require post-market studies or clinical trials to evaluate safety risks related to the use of a product or to require withdrawal of the product from the market. The FDA also has the authority to require a REMS plan after approval, which may impose further requirements or restrictions on the distribution or use of an approved drug or therapeutic biologic. The manufacturer and manufacturing facilities we use to make a future product, if any, will also be subject to periodic review and inspection by the FDA and other regulatory agencies, including for continued compliance with cGMP requirements. The discovery of any new or previously unknown problems with our third-party manufacturers, manufacturing processes or facilities may result in restrictions on the product, manufacturer or facility, including withdrawal of the product from the market. If we rely on third-party manufacturers, we will not have control over compliance with applicable rules and regulations by such manufacturers.

Any product promotion and advertising will also be subject to regulatory requirements and continuing regulatory review. If we or our existing or future collaborators, manufacturers or service providers fail to comply with applicable continuing regulatory requirements in the U.S. or foreign jurisdictions in which we seek to market our products, we or they may be subject to, among other things, fines, warning letters, holds on clinical trials, delay of approval or refusal by the FDA to approve pending applications or supplements to approved applications, suspension or withdrawal of regulatory approval, product recalls and seizures, administrative detention of products, refusal to permit the import or export of products, operating restrictions, injunction, civil penalties and criminal prosecution.

Even if we are able to commercialize any product candidate, such product candidate may become subject to unfavorable pricing regulations or third-party coverage and reimbursement policies, which would harm our business.

The regulations that govern regulatory approvals, pricing and reimbursement for new drugs and therapeutic biologics vary widely from country to country. Some countries require approval of the sale price of a drug or therapeutic biologic before it can be marketed. In many countries, the pricing review period begins after marketing approval is granted. In some foreign markets, prescription biopharmaceutical pricing remains subject to continuing governmental control even after initial approval is granted. As a result, we might obtain regulatory approval for a product in a particular country, but then be subject to price regulations that delay our commercial launch of the product, possibly for lengthy time periods and negatively impact the revenues we are able to generate from the sale of the product in that country. Adverse pricing limitations may hinder our ability to recoup our investment in one or more product candidates, even if our product candidates obtain regulatory approval.

Our ability to commercialize any products successfully also will depend in part on the extent to which coverage and reimbursement for these products and related treatments will be available from government authorities, private health insurers and other organizations. Even if we succeed in bringing one or more products to the market, these products may not be considered cost-effective, and the amount reimbursed for any products may be insufficient to allow us to sell our products on a competitive basis. Because our programs are in the early stages of development, we are unable at this time to determine their cost effectiveness or the likely level or method of reimbursement. Increasingly, the third-party payors who reimburse patients or healthcare providers, such as government and private insurance plans, are requiring that drug companies provide them with predetermined discounts from list prices, and are seeking to reduce the prices charged or the amounts reimbursed for biopharmaceutical products. If the price we are able to charge for any products we develop, or the reimbursement provided for such products, is inadequate in light of our development and other costs, our return on investment could be adversely affected. There may be significant delays in obtaining reimbursement for newly-approved drugs or therapeutic biologics, and coverage may be more limited than the purposes for which the drug or therapeutic biologic is approved by the FDA or similar regulatory authorities outside of the United States. Moreover, eligibility for reimbursement does not imply that any drug or therapeutic biologic will be reimbursed in all cases or at a rate that covers our costs, including research, development, manufacture, sale and distribution. Interim reimbursement levels for new drugs or therapeutic biologics, if applicable, may also not be sufficient to cover our costs and may not be made permanent. Reimbursement rates may be based on payments allowed for lower-cost drugs or therapeutic biologics that are already reimbursed, may be incorporated into existing payments for other services and may reflect budgetary constraints or imperfections in Medicare data. Net prices for drugs or therapeutic biologics may be reduced by mandatory discounts or rebates required by government healthcare programs or private payors and by any future relaxation of laws that presently restrict imports of drugs or therapeutic biologics from countries where they may be sold at lower prices than in the U.S. Third-party payors often rely upon Medicare coverage policy and payment limitations in setting their own reimbursement rates. Our inability to promptly obtain coverage and adequate reimbursement rates from both government-funded and private payors for new drugs or therapeutic biologics that we develop and for which we obtain regulatory approval could have a material and adverse effect on our operating results, our ability to raise capital needed to commercialize products and our financial condition.

If any of our product candidates receives marketing approval and we or others later identify undesirable side effects caused by the product candidate, our ability to market and derive revenue from the product candidates could be compromised.

Undesirable side effects caused by our product candidates could cause regulatory authorities to interrupt, delay or halt clinical trials and could result in a more restrictive label or the delay or denial of regulatory approval by the FDA or other regulatory authorities. While we have not yet initiated clinical trials for any of our product candidates, it is likely that there may be side effects associated with their use. Results of our trials could reveal a high and unacceptable

severity and prevalence of these or other side effects. In such an event, our trials could be suspended or terminated and the FDA or comparable foreign regulatory authorities could order us to cease further development of or deny approval of our product candidates for any or all targeted indications. Such side effects could also affect patient recruitment or the ability of enrolled patients to complete the trial or result in potential product liability claims. Any of these occurrences may materially and adversely affect our business, financial condition, results of operations and prospects. Further, clinical trials by their nature utilize a sample of the potential patient population. With a limited number of patients and limited duration of exposure, rare and severe side effects of our product candidates may only be uncovered with a significantly larger number of patients exposed to the product candidate.

In the event that any of our product candidates receives regulatory approval and we or others identify undesirable side effects caused by one of our products, any of the following adverse events could occur, which could result in the loss of significant revenue to us and materially and adversely affect our results of operations and business:

- regulatory authorities may withdraw their approval of the product or seize the product;
- we may be required to recall the product or change the way the product is administered to patients;

- additional restrictions may be imposed on the marketing of the particular product or the manufacturing processes for the product or any component thereof;
- we may be subject to fines, injunctions or the imposition of civil or criminal penalties;
- regulatory authorities may require the addition of labeling statements, such as a “black box” warning or a contraindication;
- we may be required to create a Medication Guide outlining the risks of such side effects for distribution to patients;
- we could be sued and held liable for harm caused to patients;
- the product may become less competitive; and
- our reputation may suffer.

A Breakthrough Therapy Designation by the FDA for our product candidates may not lead to a faster development or regulatory review or approval process, and it does not increase the likelihood that our product candidates will receive marketing approval.

We may seek a Breakthrough Therapy Designation for some of our product candidates. A breakthrough therapy is defined as a product that is intended, alone or in combination with one or more other products, 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. For products 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. Products designated as breakthrough therapies by the FDA can also be eligible for accelerated approval.

Designation as a breakthrough therapy is within the discretion of the FDA. Accordingly, even if we believe one of our product 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 product candidate may not result in a faster development process, review or approval compared to products 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 product candidates qualify as breakthrough therapies, the FDA may later decide that the products no longer meet the conditions for qualification and rescind the breakthrough designation.

A Fast Track Designation by the FDA may not actually lead to a faster development or regulatory review or approval process.

We may seek Fast Track Designation for some of our product candidates. If a product is intended for the treatment of a serious or life-threatening condition and the product demonstrates the potential to address unmet medical needs for this condition, the product sponsor may apply for Fast Track Designation. The FDA has broad discretion whether or not to grant this designation, so even if we believe a particular product 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.

We may seek Orphan Drug Designation for some of our product candidates, and we may be unsuccessful or may be unable to maintain the benefits associated with Orphan Drug Designation, including the potential for market exclusivity.

As part of our business strategy, we may seek Orphan Drug Designation for our product candidates, and we may be unsuccessful. Regulatory authorities in some jurisdictions, including the United States and Europe, may designate drugs and therapeutic biologics for relatively small patient populations as orphan drugs. Under the Orphan Drug Act,

the FDA may designate a drug or therapeutic biologic as an orphan drug if it is a drug or therapeutic biologic intended to treat a rare disease or condition, which is generally defined as a patient population of fewer than 200,000 individuals annually in the United States, or a patient population greater than 200,000 in the United States where there is no reasonable expectation that the cost of developing the drug or therapeutic biologic will be recovered from sales in the United States. In the United States, Orphan Drug Designation entitles a party to financial incentives such as opportunities for grant funding toward clinical trial costs, tax advantages and user-fee waivers. In addition, if a product that has Orphan Drug Designation subsequently receives the first FDA approval for the disease for which it has such designation, the product is entitled to orphan drug exclusivity, which means that the FDA may not approve any other applications, including a full NDA or BLA, to market the same product for the same indication for seven years, except in limited circumstances, such as a showing of clinical superiority to the product with orphan drug exclusivity or where the manufacturer is unable to assure sufficient product quantity.

Even if we obtain Orphan Drug Designation for our product candidates in specific indications, we may not be the first to obtain marketing approval of these product candidates for the orphan-designated indication due to the uncertainties associated with developing pharmaceutical products. In addition, exclusive marketing rights in the United States may be limited if we seek approval for an indication broader than the orphan-designated indication or may be lost if the FDA later determines that the request for designation was materially defective or if the manufacturer is unable to assure sufficient quantities of the product to meet the needs of patients with the rare disease or condition. Further, even if we obtain orphan drug exclusivity for a product, that exclusivity may not effectively protect the product from competition because different drugs or therapeutic biologics with different active moieties can be approved for the same condition. Even after an orphan product is approved, the FDA can subsequently approve the same drug or therapeutic biologic with the same active moiety for the same condition if the FDA concludes that the later drug or therapeutic biologic is safer, more effective or makes a major contribution to patient care. Orphan Drug Designation neither shortens the development time or regulatory review time of a drug or therapeutic biologic nor gives the drug or therapeutic biologic any advantage in the regulatory review or approval process. In addition, while we may seek Orphan Drug Designation for our product candidates, we may never receive such designations.

Risks Related to Ownership of Our Common Stock

Our quarterly operating results may fluctuate significantly or may fall below the expectations of investors or securities analysts, each of which may cause our stock price to fluctuate or decline.

We expect our operating results to be subject to quarterly fluctuations. Our net loss and other operating results will be affected by numerous factors, including:

- variations in the level of expense related to the ongoing development of our Probody platform, our product candidates or future development programs;
- results of clinical trials, or the addition or termination of clinical trials or funding support by us, or existing or future collaborators or licensing partners;
- our execution of any additional collaboration, licensing or similar arrangements, and the timing of payments we may make or receive under existing or future arrangements or the termination or modification of any such existing or future arrangements;
- any intellectual property infringement lawsuit or opposition, interference or cancellation proceeding in which we may become involved;
- additions and departures of key personnel;
- strategic decisions by us or our competitors, such as acquisitions, divestitures, spin-offs, joint ventures, strategic investments or changes in business strategy;
- if any of our product candidates receives regulatory approval, the terms of such approval and market acceptance and demand for such product candidates;
- regulatory developments affecting our product candidates or those of our competitors; and
- changes in general market and economic conditions.

If our quarterly operating results fall below the expectations of investors or securities analysts, the price of our common stock could decline substantially. Furthermore, any quarterly fluctuations in our operating results may, in turn, cause the price of our stock to fluctuate substantially. We believe that quarterly comparisons of our financial results are not necessarily meaningful and should not be relied upon as an indication of our future performance.

Our stock price may be volatile and purchasers of our common stock could incur substantial losses.

Our stock price is volatile. From October 8, 2015, the first day of trading our common stock, through March 1, 2017, our stock had high and low sales prices in the range of $24.68 and $9.01 per share. The market price for our common stock may be influenced by many factors, including the other risks described in this section titled “Risk Factors” and the

following:

- results of preclinical and clinical studies of our product candidates, or those of our competitors or our existing or future collaborators;
- regulatory or legal developments in the U.S. and other countries, especially changes in laws or regulations applicable to our products;

- the success of competitive products or technologies;
- introductions and announcements of new products by us, our future commercialization partners, or our competitors, and the timing of these introductions or announcements;
- actions taken by regulatory agencies with respect to our products, clinical studies, manufacturing process or sales and marketing terms;
- actual or anticipated variations in our financial results or those of companies that are perceived to be similar to us;
- the success of our efforts to acquire or in-license additional technologies, products or product candidates;
- developments concerning any future collaborations, including but not limited to those with our sources of manufacturing supply and our commercialization partners;
- market conditions in the pharmaceutical and biotechnology sectors;
- announcements by us or our competitors of significant acquisitions, strategic collaborations, joint ventures or capital commitments;
- developments or disputes concerning patents or other proprietary rights, including patents, litigation matters and our ability to obtain patent protection for our products;
- our ability or inability to raise additional capital and the terms on which we raise it;
- the recruitment or departure of key personnel;
- changes in the structure of healthcare payment systems;
- actual or anticipated changes in earnings estimates or changes in stock market analyst recommendations regarding our common stock, other comparable companies or our industry generally;
- our failure or the failure of our competitors to meet analysts' projections or guidance that we or our competitors may give to the market;
- fluctuations in the valuation of companies perceived by investors to be comparable to us;
- announcement and expectation of additional financing efforts;
- speculation in the press or investment community;
- trading volume of our common stock;
- sales of our common stock by us or our stockholders;
- the concentrated ownership of our common stock;
- changes in accounting principles;
- terrorist acts, acts of war or periods of widespread civil unrest;
- natural disasters and other calamities; and
- general economic, industry and market conditions.

In addition, the stock markets in general, and the markets for pharmaceutical, biopharmaceutical and biotechnology stocks in particular, have experienced extreme volatility that has been often unrelated to the operating performance of the issuer. These broad market and industry factors may seriously harm the market price of our common stock, regardless of our operating performance.

The future issuance of equity or of debt securities that are convertible into equity will dilute our share capital.

We may choose to raise additional capital in the future, depending on market conditions, strategic considerations and operational requirements. To the extent that additional capital is raised through the issuance of shares or other securities convertible into shares, our stockholders will be diluted. Future issuances of our common stock or other equity securities, or the perception that such sales may occur, could adversely affect the trading price of our common stock and impair our ability to raise capital through future offerings of shares or equity securities. No prediction can be made as to the effect, if any, that future sales of common stock or the availability of common stock for future sales will have on the trading price of our common stock.

The employment agreements with our executive officers may require us to pay severance benefits to officers in connection with termination of employment or upon a change of control of us, which could harm our financial condition.

Each of our executive officers is entitled to receive a lump sum payment equal to nine months or one year of his or her base salary as well as continued medical and dental coverage for a period of nine months or one year following his or her termination of employment due to good reason or without cause. In the event of a change in control and a termination of employment without cause or due to good reason, each of our executive officers would similarly receive nine months or one year of his or her base salary as well as continued medical and dental coverage for a period of nine months or one year, as well as an additional lump sum payment equal to three-fourths or 100% of his or her target annual bonus for the calendar year in which his or her employment is terminated and full vesting of his or her outstanding option awards. The accelerated vesting of options could result in dilution to our existing stockholders and harm the market price of our common stock. Furthermore, the payment of these severance benefits could harm our financial condition. In addition, these potential severance payments may discourage or prevent third parties from seeking a business combination with us.

An active market for our common stock may not be maintained.

Prior to our IPO in October 2015, there had been no public market for shares of our common stock. Our stock only recently began trading on The NASDAQ Global Select Market, and we can provide no assurance that we will be able to maintain an active trading market on The NASDAQ Global Select Market or any other exchange in the future. If an active market for our common stock does not develop or is not maintained, it may be difficult for our stockholders to sell shares without depressing the market price for the shares or at all. An inactive market may also impair our ability to raise capital by selling shares and may impair our ability to acquire other businesses, applications or technologies using our shares as consideration

If securities or industry analysts do not publish research or reports about our business, or if they issue adverse or misleading opinions regarding our stock, our stock price and trading volume could decline.

The trading market for our common stock will be influenced by the research and reports that industry or securities analysts publish about us or our business. If any of the analysts who cover us issue an adverse or misleading opinion regarding us, our business model, our intellectual property or our stock performance, or if our target studies and operating results fail to meet the expectations of analysts, our stock price would likely decline. If one or more of these analysts cease coverage of us or fail to publish reports on us regularly, we could lose visibility in the financial markets, which in turn could cause our stock price or trading volume to decline.

Our principal stockholders and management own a significant percentage of our stock and will be able to exert significant control over matters subject to stockholder approval.

As of December 31, 2016, our executive officers, directors, holders of 5% or more of our capital stock based on publicly available filings made with the SEC and their respective affiliates beneficially owned approximately 52% of our outstanding common stock. Therefore, these stockholders have the ability to influence us through this ownership position. These stockholders may be able to determine all matters requiring stockholder approval. For example, these stockholders may be able to control elections of directors, amendments of our organizational documents, or approval of any merger, sale of assets, or other major corporate transaction. This may prevent or discourage unsolicited acquisition proposals or offers for our common stock that our stockholders may feel are in their best interest.

59

We are an “emerging growth company” and we cannot be certain if the reduced reporting requirements applicable to emerging growth companies will make our common stock less attractive to investors.

We are an “emerging growth company” as defined in the JOBS Act. For as long as we continue to be an emerging growth company, we may take advantage of exemptions from various reporting requirements that are applicable to other public companies that are not emerging growth companies, including (1) not being required to comply with the auditor attestation requirements of Section 404 of the Sarbanes-Oxley Act of 2002 (“Sarbanes-Oxley Act”), (2) reduced disclosure obligations regarding executive compensation in our periodic reports and proxy statements and (3) exemptions from the requirements of holding a nonbinding advisory vote on executive compensation and stockholder approval of any golden parachute payments not previously approved. We could be an emerging growth company for up to five years following the consummation of the IPO, although circumstances could cause us to lose that status earlier, including if we are deemed to be a “large accelerated filer,” which occurs when the market value of our common stock that is held by non-affiliates exceeds $700 million as of the prior June 30, or if we have total annual gross revenue of $1.0 billion or more during any fiscal year before that time, in which cases we would no longer be an emerging growth company as of the following December 31, or if we issue more than $1.0 billion in non-convertible debt during any three-year period before that time, in which case we would no longer be an emerging growth company immediately. Even after we no longer qualify as an emerging growth company, we may still qualify as a “smaller reporting company” which would allow us to take advantage of many of the same exemptions from disclosure requirements including not being required to comply with the auditor attestation requirements of Section 404 of the Sarbanes-Oxley Act and reduced disclosure obligations regarding executive compensation in our periodic reports and proxy statements. We cannot predict if investors will find our common stock less attractive because we may rely on these exemptions. If some investors find our common stock less attractive as a result, there may be a less active trading market for our common stock and our share price may be more volatile.

Under the JOBS Act, emerging growth companies can also delay adopting new or revised accounting standards until such time as those standards apply to private companies. We have irrevocably elected not to avail ourselves of this exemption from new or revised accounting standards and, therefore, will be subject to the same new or revised accounting standards as other public companies that are not emerging growth companies.

Anti-takeover provisions in our charter documents and under Delaware law could make an acquisition of us, which may be beneficial to our stockholders, more difficult and may prevent attempts by our stockholders to replace or remove our current management.

Provisions in our amended and restated certificate of incorporation and our amended and restated bylaws may delay or prevent an acquisition of us or a change in our management. In addition, these provisions may frustrate or prevent any attempts by our stockholders to replace or remove our current management by making it more difficult for stockholders to replace members of our board of directors. Because our board of directors is responsible for appointing the members of our management team, these provisions could in turn affect any attempt by our stockholders to replace current members of our management team. These provisions include:

- a prohibition on actions by our stockholders by written consent;
- a requirement that special meetings of stockholders, which our company is not obligated to call more than once per calendar year, be called only by the chairman of our board of directors, our chief executive officer, our board of directors pursuant to a resolution adopted by a majority of the total number of authorized directors, or, subject to certain conditions, by our secretary at the request of the stockholders holding of record, in the aggregate, shares entitled to cast not less than ten percent of the votes at a meeting of the stockholders (assuming all shares entitled to vote at such meeting were present and voted);
- advance notice requirements for election to our board of directors and for proposing matters that can be acted upon at stockholder meetings;

- division of our board of directors into three classes, serving staggered terms of three years each; and
- the authority of the board of directors to issue preferred stock with such terms as the board of directors may determine.

Moreover, because we are incorporated in Delaware, we are governed by the provisions of Section 203 of the Delaware General Corporation Law, as amended, which prohibits a person who owns in excess of 15 percent of our outstanding voting stock from merging or combining with us for a period of three years after the date of the transaction in which the person acquired in excess of 15 percent of our outstanding voting stock, unless the merger or combination is approved in a prescribed manner. These provisions would apply even if the proposed merger or acquisition could be considered beneficial by some stockholders.

We incur increased costs as a result of operating as a public company, and our management is required to devote substantial time to new compliance initiatives and corporate governance practices.

As a public company, and particularly after we are no longer an emerging growth company, we incur significant legal, accounting and other expenses that we did not incur as a private company. The Sarbanes-Oxley Act, the Dodd-Frank Wall Street Reform and Consumer Protection Act, the listing requirements of The NASDAQ Global Select Market and other applicable securities rules and regulations impose various requirements on public companies, including establishment and maintenance of effective disclosure and financial controls and corporate governance practices. Our management and other personnel need to devote a substantial amount of time to these compliance initiatives. Moreover, these rules and regulations increase our legal and financial compliance costs and make some activities more time-consuming and costly. For example, we expect that these rules and regulations may make it more difficult and more expensive for us to obtain director and officer liability insurance, which in turn could make it more difficult for us to attract and retain qualified members of our board of directors. However, these rules and regulations are often subject to varying interpretations, in many cases due to their lack of specificity, and, as a result, their application in practice may evolve over time as new guidance is provided by regulatory and governing bodies. This could result in continuing uncertainty regarding compliance matters and higher costs necessitated by ongoing revisions to disclosure and governance practices.

We are not currently required to comply with the rules of the SEC that implement Section 404, and are therefore not required to make a formal assessment of the effectiveness of our internal control over financial reporting for that purpose. Pursuant to Section 404, we will be required to furnish a report by our management on our internal control over financial reporting. However, while we remain an emerging growth company, we will not be required to include an attestation report on internal control over financial reporting issued by our independent registered public accounting firm. To achieve compliance with Section 404 within the prescribed period, we will be engaged in a process to document and evaluate our internal control over financial reporting, which is both costly and challenging. In this regard, we will need to continue to dedicate internal resources, potentially engage outside consultants and adopt a detailed work plan to assess and document the adequacy of internal control over financial reporting, continue steps to improve control processes as appropriate, validate -through testing that controls are functioning as documented and implement a continuous reporting and improvement process for internal control over financial reporting. Despite our efforts, there is a risk that we will not be able to conclude, within the prescribed timeframe or at all, that our internal control over financial reporting is effective as required by Section 404. If we identify one or more material weaknesses, it could result in an adverse reaction in the financial markets due to a loss of confidence in the reliability of our financial statements. In addition, if we are not able to continue to meet these requirements, we may not be able to remain listed on The NASDAQ Global Select Market.

Because we do not anticipate paying any cash dividends on our capital stock in the foreseeable future, capital appreciation, if any, will be your sole source of gain.

We have never declared or paid cash dividends on our capital stock. We currently intend to retain all of our future earnings, if any, to finance the growth and development of our business. As a result, capital appreciation, if any, of our common stock will be your sole source of gain for the foreseeable future.

We may incur significant costs from class action litigation due to our expected stock volatility.

Our stock price may fluctuate for many reasons, including as a result of public announcements regarding the progress of our development efforts or the development efforts of future collaborators or competitors, the addition or departure of our key personnel, variations in our quarterly operating results and changes in market valuations of biopharmaceutical and biotechnology companies.

This risk is especially relevant to us because biopharmaceutical and biotechnology companies have experienced significant stock price volatility in recent years. When the market price of a stock has been volatile as our stock price may be, holders of that stock have occasionally brought securities class action litigation against the company that issued the stock. If any of our stockholders were to bring a lawsuit of this type against us, even if the lawsuit is without merit, we could incur substantial costs defending the lawsuit. The lawsuit could also divert the time and attention of our management.

Our amended and restated bylaws designate the Court of Chancery of the State of Delaware as the sole and exclusive forum for certain types of actions and proceedings that may be initiated by our stockholders, which could limit our stockholders' ability to obtain a favorable judicial forum for disputes with us or our directors, officers or employees.

Our amended and restated bylaws provide that, subject to limited exceptions, the Court of Chancery of the State of Delaware will be the sole and exclusive forum for any derivative action or proceeding brought on our behalf, any action asserting a claim of breach of a fiduciary duty owed by any of our directors, officers or other employees to us or our stockholders, any action asserting a claim against us arising pursuant to any provision of the Delaware General Corporation Law, as amended, our amended and restated certificate of incorporation or our amended and restated bylaws, any action to interpret, apply, enforce or determine the validity of our amended and restated certificate of incorporation or our amended and restated bylaws or any other action asserting a claim against us that is governed by the internal affairs doctrine. Any person or entity purchasing or otherwise acquiring any interest in shares of our capital stock shall be deemed to have notice of and to have consented to the provisions of our amended and restated certificate of incorporation described above. This choice of forum provision may limit a stockholder's ability to bring a claim in a judicial forum that it finds favorable for disputes with us or our directors, officers or other employees, which may discourage such lawsuits against us and our directors, officers and employees. Alternatively, if a court were to find these provisions of our amended and restated certificate of incorporation inapplicable to, or unenforceable in respect of, one or more of the specified types of actions or proceedings, we may incur additional costs associated with resolving such matters in other jurisdictions, which could adversely affect our business and financial condition.

Item 1B. Unresolved Staff Comments
None

Item 2. Properties
Our principle executive office is currently located in South San Francisco, California, and consists of approximately 76,000 square feet of office and research and development space, all of which is located in a single building, under a lease that expires in October 2026. We believe that our existing facilities are sufficient for our current needs.

Item 3. Legal Proceedings
We are not currently a party to any material litigation or legal proceedings.

| | | | | | |
|---|---|---|---|---|---|
| Net loss per share—basic and diluted | $ (0.56) | $ (1.00) | $ (1.39) | $ (2.35) | $ (0.68) |
| Weighted average number of common shares used in net loss per share—basic and diluted: | 144,928 | 142,155 | 136,811 | 115,852 | 106,403 |

(1) Collaborative arrangements revenue for the year ended December 31, 2016 included approximately $217.7 million related to our share of net profits from sales of LINZESS in the U.S. and $30.0 million related to the receipt of milestone payments under our license agreement with Astellas for the filing and approval of a new drug application for LINZESS with the Japanese Ministry of Health, Labor and Welfare. Additionally, we recognized an insignificant amount of product revenue for the year ended December 31, 2016 related to the sales of ZURAMPIC in the U.S. after the launch of the product in October 2016 was included within total collaborative arrangements revenue.

Collaborative arrangements revenue for the year ended December 31, 2014 includes approximately $10.2 million related to the receipt of a milestone payment under our license agreement with Astellas for the enrollment of the first study subject in a Phase III study for linaclotide in Japan, which was achieved in November 2014, and also includes approximately $1.9 million in payments from Almirall related to the achievement of two commercial milestones under the license agreement with Almirall.

Collaborative arrangements revenue for the year ended December 31, 2013 includes approximately $1.9 million in payments from Almirall related to the achievement of two milestones under the license agreement with Almirall.

Table of Contents

Collaborative arrangements revenue for the year ended December 31, 2012 includes an $85.0 million milestone payment received from Allergan under the collaboration agreement for North America for the achievement of two development milestones upon the FDA's approval of the linaclotide NDA for both IBS C and CIC.

(2) During the year ended December 31, 2015, we recorded expenses of approximately $17.6 million for the write down of inventory and an accrual for excess non cancelable inventory purchase commitments related to linaclotide API. These charges primarily related to a reduction in the near term demand forecast for CONSTELLA in the European territory by Almirall, our former European partner; regulatory changes made by the China Food and Drug Administration to the marketing approval process in China; and the amendment to the license agreement with Allergan pertaining to the development and commercialization of linaclotide for Europe executed in October 2015. Pursuant to the terms of the amendment, Allergan assumed responsibility for the manufacturing of linaclotide API for Europe, as well as the associated costs, which resulted in accruing for a loss on non cancelable inventory purchase commitments under one of our API supply agreements covering the commercial supply of linaclotide API for the European market.

During the year ended December 31, 2014, we recorded approximately $20.3 million as a write down of inventory to an estimated net realizable value of approximately $5.0 million. This write down was primarily attributable to Almirall's reduced inventory demand forecasts for the European territory, mainly due to the suspension of commercialization of CONSTELLA in Germany and a challenging commercial environment throughout Europe.

These charges are more fully described in Note 8, Inventory, to our consolidated financial statements appearing elsewhere in this Annual Report on Form 10 K.

(3) During the year ended December 31, 2014, we recorded approximately $4.2 million of costs related to a reduction in workforce in the three months ended March 31, 2014, including employee severance, benefits and related costs and adjustments. These costs are reflected in our Consolidated Statement of Operations for the year ended December 31, 2014 as approximately $3.0 million in research and development expenses and approximately $1.2 million in selling, general and administrative expenses.

(4) Amortization of acquired intangible asset is based on the economic consumption of intangible assets. Our amortization is related to the ZURAMPIC intangible asset, which is amortized on a straight-line basis over the estimated useful life.

(5) Loss on fair value remeasurement of contingent consideration is related to our contingent consideration pursuant to our exclusive license to develop, manufacture, and commercialize products containing lesinurad as an active ingredient, including ZURAMPIC, in the U.S. The contingent consideration obligation is revalued at each reporting period and changes in the fair value, other than changes due to payments, are recognized as a (gain)/loss on fair value remeasurement of contingent consideration in our statement of operations.

(6) Gain (loss) on derivatives consists of the change in fair value of our Convertible Note Hedges and Note Hedge Warrants, which are recorded as derivative assets and liabilities. The Convertible Note Hedges and the Note Hedge Warrants are recorded at fair value at each reporting period and changes in fair value are recorded in our consolidated statements of operations. The Convertible Note Hedges and Note Hedge Warrants are more fully

Table of Contents

described in Note 6, Fair Value of Financial Instruments, and Note 11, Notes Payable, to our consolidated financial statements appearing elsewhere in this Annual Report on Form 10 K.

| | Year Ended December 31, | | | | |
|---|---|---|---|---|---|
| | 2016 | 2015 | 2014 | 2013 | 2012 |
| | (in thousands) | | | | |
| Consolidated Balance Sheet Data: | | | | | |
| Cash, cash equivalents and available-for-sale securities | $ 305,216 | $ 439,394 | $ 248,334 | $ 197,602 | $ 168,228 |
| Working capital (excluding deferred revenue) | 289,050 | 430,931 | 234,957 | 191,636 | 132,883 |
| Total assets | 709,821 | 619,121 | 329,322 | 273,292 | 229,907 |
| Deferred revenue, including current portion | — | 8,989 | 16,180 | 16,490 | 21,405 |
| Debt financing and convertible notes, including current portion (1) | 366,492 | 378,548 | 169,405 | 169,002 | — |
| Capital lease obligations, including current portion | 6,309 | 2,937 | 3,723 | 4,273 | 569 |
| Total liabilities | 643,105 | 523,996 | 240,770 | 235,067 | 85,855 |
| Total stockholders' equity | 66,716 | 95,125 | 88,552 | 38,225 | 144,052 |

(1) Debt financing and convertible notes, including current portion, as of December 31, 2016 includes approximately $132.2 relating to the PhaRMA Notes, which were redeemed, in full, in connection with the funding and issuance in January 2017 of the 8.375% notes due 2026, or the 2026 Notes, and approximately $234.2 relating to the convertible notes.

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

The following discussion of our financial condition and results of operations should be read in conjunction with our consolidated financial statements and the notes to those financial statements appearing elsewhere in this Annual Report on Form 10 K. This discussion contains forward looking statements that involve significant risks and uncertainties. As a result of many factors, such as those set forth under "Risk Factors" in Item 1A of this Annual Report on Form 10 K, our actual results may differ materially from those anticipated in these forward looking statements.

### Overview

We are a commercial biotechnology company leveraging our proven development and commercial capabilities as we seek to bring multiple medicines to patients. We are advancing innovative product opportunities in areas of large unmet need, including irritable bowel syndrome with constipation, or IBS C, and chronic idiopathic constipation, or CIC, hyperuricemia associated with uncontrolled gout, uncontrolled gastroesophageal reflux disease, or uncontrolled GERD, and vascular and fibrotic diseases.

Our first commercial product, linaclotide, is available to adult men and women suffering from IBS-C or CIC in the United States, or the U.S., under the trademarked name LINZESS®, and is available to adult men and women suffering from IBS-C in certain European countries under the trademarked name CONSTELLA®. We and our U.S. partner Allergan plc (together with its affiliates), or Allergan, began commercializing LINZESS in the U.S. in December 2012. Under our collaboration with Allergan for North America, total net sales of LINZESS in the U.S., as

recorded by Allergan, are reduced by commercial costs incurred by each party, and the resulting amount is shared equally between us and Allergan. Our former European partner, Almirall, S.A., or Almirall, began commercializing CONSTELLA in Europe for the symptomatic treatment of moderate to severe IBS-C in adults in the second quarter of 2013. In October 2015, Almirall transferred its exclusive license to develop and commercialize linaclotide in Europe to Allergan, and we and Allergan entered into an amendment to the European license agreement. Currently, CONSTELLA is commercially available in a number of European countries, including the United Kingdom, Italy and Spain. In January 2017, we and Allergan entered into an amendment to the European license agreement, pursuant to which the license granted to Allergan was extended to a territory consisting of all countries worldwide not previously covered by the European license agreement, other than China, Hong Kong, Macau, Japan, and the countries and territories of North America. On a country-by-country and product-by-product basis in such additional territory, Allergan will pay us an annual royalty as a percentage of net sales of products containing linaclotide as an active ingredient. This agreement is more fully described in Note 20, Subsequent Events, to our consolidated financial statements appearing elsewhere in this Annual Report on Form 10-K.

Table of Contents

In December 2013 and February 2014, linaclotide was approved in Canada and Mexico, respectively, as a treatment for adult men and women suffering from IBS-C or CIC. Allergan has exclusive rights to commercialize linaclotide in Canada as CONSTELLA and in Mexico as LINZESS. In May 2014, CONSTELLA became commercially available in Canada and in June 2014, LINZESS became commercially available in Mexico.

Astellas Pharma Inc., or Astellas, our partner in Japan, is developing linaclotide for the treatment of patients with IBS-C, chronic constipation, and other gastrointestinal, or GI, conditions in its territory. In December 2016, the Japanese Ministry of Health, Labor and Welfare approved LINZESS for the treatment of adults with IBS-C in Japan. In October 2012, we entered into a collaboration agreement with AstraZeneca AB (together with its affiliates), or AstraZeneca, to co-develop and co-commercialize linaclotide in China, Hong Kong and Macau, with AstraZeneca having primary responsibility for the local operational execution. In December 2015, we and AstraZeneca filed for approval with the China Food and Drug Administration, or CFDA, to market linaclotide in China.

We and Allergan are also advancing two linaclotide colonic release formulations. Linaclotide colonic release-1, or CR1, is a second generation product candidate with the potential to improve abdominal pain relief in adult IBS C patients. Linaclotide colonic release-2, or CR2, is a product candidate with the potential to improve abdominal pain in patients with additional GI disorders where lower abdominal pain is a predominant symptom such as non-constipation subtypes of IBS. Further, we and Allergan are exploring ways to enhance the clinical profile of LINZESS by studying linaclotide in additional indications and populations to assess its potential to treat various GI conditions. Linaclotide is being developed and commercialized in other parts of the world by certain of our partners. In December 2016, we and Allergan reported positive top-line data from a Phase IIb clinical trial evaluating linaclotide CR1 in adult IBS-C patients. The data from this study demonstrate numerically greater abdominal pain improvement with linaclotide CR1 300 mcg compared to placebo and to the 290 mcg immediate release formulation of linaclotide. We believe the data support advancement into a Phase III clinical trial in adult IBS-C patients. Also in December 2016, we and Allergan reported positive top-line data from a Phase IIb clinical trial evaluating linaclotide CR2 in IBS-C patients. The data from this study demonstrate numerically improved abdominal pain and other abdominal symptoms relative to placebo, as intended, with no apparent effect on bowel movement function. We believe the data support further investigation of linaclotide CR2 in additional GI indications associated with abdominal pain, including non-constipation subtypes of IBS.

We are also advancing IW-3718, a gastric retentive formulation of a bile acid sequestrant with the potential to provide symptomatic relief in patients with uncontrolled GERD.

In April 2016, we discontinued development of IW-9179 for gastroparesis, as top-line data from our exploratory Phase IIa clinical study indicated that IW-9179 did not meaningfully reduce the severity of symptoms in patients with diabetic gastroparesis. In July 2016, we also discontinued advancing IW-9179 for the treatment of functional dyspepsia and are no longer advancing the program.

In June 2016, we closed a transaction with AstraZeneca, or the Lesinurad Transaction, pursuant to which we received an exclusive license to develop, manufacture, and commercialize in the U.S. products containing lesinurad as an active ingredient, or the Lesinurad License, including ZURAMPIC® and DUZALLOTM. Lesinurad 200mg tablets were approved as ZURAMPIC by the U.S. Food and Drug Organization, or FDA, in December 2015 for use in combination with a xanthine oxidase inhibitor, or XOI, for the treatment of hyperuricemia associated with uncontrolled gout. In October 2016, ZURAMPIC became commercially available in the U.S. We are developing DUZALLO, a fixed-dose combination product of lesinurad and allopurinol, an XOI, which is included under the Lesinurad License. In January 2017, the FDA accepted for review a new drug application, or NDA, for DUZALLO for the treatment of hyperuricemia in patients with uncontrolled gout. We have accounted for the Lesinurad Transaction in accordance with Accounting Standards Codification, or ASC, Topic 805, Business Combinations, or ASC 805, as the Lesinurad Transaction meets the requirements of a business combination. The transaction is more fully described in Note 4, Business Combinations, to our consolidated financial statements appearing elsewhere in this Annual Report on Form 10-K.

We are also leveraging our pharmacological expertise in guanylate cyclase, or GC, pathways gained through the discovery and development of linaclotide to advance development programs, including IW-1973 and IW-1701, targeting soluble guanylate cyclase, or sGC. sGC is a validated mechanism with the potential for broad therapeutic utility and multiple opportunities for product development in vascular and fibrotic diseases, as well as other therapeutic areas.

As part of our strategy, we have also established development and commercial capabilities that we plan to leverage as we seek to bring multiple medicines to patients. We intend to play an active role in the development and

Table of Contents

commercialization of our products in the U.S., and to establish a strong global brand by out-licensing commercialization rights in other territories to high-performing partners.

We and Exact Sciences Corp., or Exact Sciences, entered into an agreement, or the Cologuard Co-Promotion Agreement, to co-promote Cologuard®, the first and only FDA-approved noninvasive stool DNA screening test for colorectal cancer in March 2015. We and Exact Sciences co-promoted Cologuard through July 2016 and the Cologuard Co-Promotion Agreement was terminated in August 2016. Under the terms of the Cologuard Co-Promotion Agreement, our sales team promoted and educated health care practitioners regarding Cologuard. Exact Sciences maintained responsibility for all other aspects of the commercialization of Cologuard outside of the co-promotion. We are compensated primarily via royalties earned on the net sales of Cologuard generated from the healthcare practitioners on whom we called. Under the terms of the Cologuard Co-Promotion Agreement, we will continue to receive royalty payments through July 2017.

In August 2015, we and Allergan entered into an agreement for the co-promotion of VIBERZI™ (eluxadoline) in the U.S., Allergan's treatment for adults suffering from IBS with diarrhea, or IBS-D. Under the terms of the agreement, our clinical sales specialists are detailing VIBERZI to the approximately 25,000 health care practitioners to whom they detail LINZESS. Allergan is responsible for all costs and activities relating to the commercialization of VIBERZI outside the co-promotion. Our promotional efforts are compensated based on the volume of calls delivered by our sales force, with the terms of the agreement reducing or eliminating certain of the unfavorable adjustments to the share of net profits stipulated by the linaclotide collaboration agreement with Allergan for North America, provided that we deliver a minimum number of VIBERZI calls on physicians. We are also compensated via reimbursement for medical education initiatives.

In January 2017, we and Allergan entered into a commercial agreement under which the adjustments to our or Allergan's share of the net profits under the share adjustment provision of the collaboration agreement for linaclotide in North America are eliminated, in full, in 2018 and all subsequent years. This agreement is more fully described in Note 20, Subsequent Events, to our consolidated financial statements appearing elsewhere in this Annual Report on Form 10-K.

In June 2015, we issued approximately $335.7 million in aggregate principal amount of 2.25% Convertible Senior Notes due 2022, or the 2022 Notes. We received net proceeds of approximately $324.0 million from the sale of the 2022 Notes, after deducting fees and expenses of approximately $11.7 million. The net proceeds from these financings are being used to support the commercialization of LINZESS and ZURAMPIC in the U.S. and to fund linaclotide, lesinurad and other development opportunities to advance our strategy to grow a leading commercial biotechnology company, in addition to other general corporate purposes. In September 2016, we closed a direct private placement, pursuant to which we subsequently issued $150.0 million in aggregate principal amount of 8.375% notes due 2026, or the 2026 Notes, on January 5, 2017, or the Funding Date. The proceeds from the issuance of the 2026 Notes were used to redeem the outstanding principal balance of the 11% PhaRMA Notes due 2024, or the PhaRMA Notes, on the Funding Date. These transactions are more fully described in Note 11, Notes Payable, and Note 20, Subsequent Events, to our consolidated financial statements appearing elsewhere in this Annual Report on Form 10 K.

We were incorporated in Delaware on January 5, 1998 as Microbia, Inc. On April 7, 2008, we changed our name to Ironwood Pharmaceuticals, Inc. We operate in one reportable business segment—human therapeutics.

To date, we have dedicated a majority of our activities to the research, development and commercialization of linaclotide, as well as to the research and development of our other product candidates. We have incurred significant operating losses since our inception in 1998. As of December 31, 2016, we had an accumulated deficit of approximately $1.2 billion. We are unable to predict the extent of any future losses or guarantee when, or if, our company will become cash flow positive.

Financial Overview

Revenue. Revenue to date has been generated primarily through our collaboration agreements for the development and commercialization of linaclotide with Allergan for North America and AstraZeneca for China, Hong Kong and Macau, our license agreements for the development and commercialization of linaclotide in Japan with Astellas and the development and commercialization of linaclotide in Europe with Allergan (formerly with Almirall), and our co promotion agreements with Allergan for VIBERZI and Exact Sciences for Cologuard in the U.S. The terms

Table of Contents

of these agreements contain multiple deliverables which may include (i) licenses, (ii) research and development activities, (iii) the manufacture of finished drug product, active pharmaceutical ingredient, or API, or development materials for a partner which are reimbursed at a contractually determined rate, and (iv) co promotion activities by our clinical sales specialists. Payments to us may include (i) up front license fees, (ii) payments for research and development activities, (iii) payments for the manufacture of finished drug product, API or development materials, (iv) payments based upon the achievement of certain milestones, (v) payments for sales detailing, promotional support services and medical education initiatives and (vi) royalties on product sales. Additionally, we receive our share of the net profits or bear our share of the net losses from the sale of linaclotide in the U.S. and China. LINZESS launched in the U.S. in December 2012 and CONSTELLA became commercially available in certain European countries beginning in the second quarter of 2013. Linaclotide is also approved in a number of other countries.

We record our share of the net profits and losses from the sales of LINZESS in the U.S. on a net basis and present the settlement payments to and from Allergan as collaboration expense or collaborative arrangements revenue, as applicable. Net profits or losses consist of net sales to third party customers and sublicense income in the U.S. less the cost of goods sold as well as selling, general and administrative expenses. Although we expect net sales to increase over time, the settlement payments between Allergan and us, resulting in collaborative arrangements revenue or collaboration expense, are subject to fluctuation based on the ratio of selling, general and administrative expenses incurred by each party. In addition, our collaborative arrangements revenue may fluctuate as a result of the timing and amount of license fees and clinical and commercial milestones received and recognized under our current and future strategic partnerships as well as timing and amount of royalties from the sales of linaclotide in the European, Canadian or Mexican markets or any other markets where linaclotide receives approval.

In June 2016, we closed the Lesinurad Transaction with AstraZeneca pursuant to which we received an exclusive license to develop, manufacture, and commercialize products containing lesinurad as an active ingredient, including ZURAMPIC, in the U.S. Beginning in October 2016, ZURAMPIC became commercially available in the U.S. We record product revenue related to the sales of ZURAMPIC in the U.S. in accordance with ASC 605, Revenue Recognition, or ASC 605, when persuasive evidence of an arrangement exists, delivery has occurred and title of the product and associated risk of loss has passed to the customer, the price is fixed or determinable and collection from the customer has been reasonably assured. ZURAMPIC product revenue is more fully described in Note 2, Summary of Significant Accounting Policies.

Cost of Revenues. Cost of revenues includes cost of collaborative arrangements revenue related to the sales of linaclotide API, as well as the cost of product revenue related to sales of ZURAMPIC in the U.S. Cost of collaborative arrangements revenue related to the sales of linaclotide API is recognized upon shipment of linaclotide API to certain of our partners outside of the U.S. Our cost of collaborative arrangements revenue for linaclotide consists of the internal and external costs of producing such API. Cost of product revenue related to the sales of ZURAMPIC in the U.S. includes the cost of producing finished goods that correspond with product revenue for the reporting period, as well as certain period costs related to freight, packaging, stability and quality testing, and customer acquisition.

Write down of Inventory to Net Realizable Value and Loss on Non cancelable Inventory Purchase Commitments. During the year ended December 31, 2016, we wrote-down approximately $0.4 million of prepaid ZURAMPIC commercial supply as result of revised demand forecasts.

During the year ended December 31, 2015, we recorded expenses of approximately $17.6 million for the write down of inventory and an accrual for excess non cancelable inventory purchase commitments related to linaclotide API. These

charges primarily related to a reduction in the near term demand forecast for CONSTELLA in the European territory by Almirall; regulatory changes made by the CFDA to the marketing approval process in China; and the amendment to the license agreement with Allergan pertaining to the development and commercialization of linaclotide for Europe executed in October 2015. Pursuant to the terms of the amendment, Allergan assumed responsibility for the manufacturing of linaclotide API for Europe, as well as the associated costs, which resulted in accruing for a loss on non cancelable inventory purchase commitments during the three months ended September 30, 2015, under one of our API supply agreements covering the commercial supply of linaclotide API for the European market. We have evaluated all remaining minimum purchase commitments under our linaclotide API supply agreements through 2023 and concluded that the approximately $20.1 million of purchase commitments from the second API supply agreement covering the Japan, China, Hong Kong and Macau markets are realizable based on the current forecasts received from our partners in these territories and our internal forecasts, as well as purchase orders received from our partners for the coming year.

Table of Contents

During the year ended December 31, 2014, we wrote down approximately $20.3 million in inventory to an estimated net realizable value of approximately $5.0 million. This write down was primarily attributable to Almirall's reduced inventory demand forecasts, mainly due to the suspension of commercialization of CONSTELLA in Germany and a challenging commercial environment throughout Europe.

These charges are more fully described in Note 8, Inventory, and Note 12, Commitments and Contingencies to our consolidated financial statements appearing elsewhere in this Annual Report on Form 10 K.

Research and Development Expense. Research and development expense consists of expenses incurred in connection with the discovery and development of our product candidates. These expenses consist primarily of compensation, benefits and other employee related expenses, research and development related facility costs, third party contract costs relating to nonclinical study and clinical trial activities, development of manufacturing processes, regulatory registration of third party manufacturing facilities, as well as licensing fees for our product candidates. We charge all research and development expenses to operations as incurred. Under our linaclotide collaboration agreements with Allergan for the U.S. and AstraZeneca for China, Hong Kong and Macau, we are reimbursed for certain research and development expenses, and we net these reimbursements against our research and development expenses as incurred. Amounts owed to Allergan or AstraZeneca for such linaclotide territories are recorded as incremental research and development expense.

The core of our research and development strategy is to leverage our development capabilities, as well as our pharmacologic expertise, to bring multiple medicines to patients. We are advancing innovative product opportunities in areas of large unmet need, including IBS-C and CIC, hyperuricemia associated with uncontrolled gout, uncontrolled GERD, and vascular and fibrotic diseases.

Linaclotide. Linaclotide is the first FDA approved guanylate cyclase type C, or GC C, agonist. Linaclotide is approved in the U.S., Japan and in a number of E.U. and other countries.

We and Allergan are exploring development opportunities in the U.S. to enhance the clinical profile of LINZESS by studying linaclotide in additional indications, populations and formulations to assess its potential to treat various GI conditions. In January 2017, the FDA approved a 72 mcg dose of linaclotide for adults with CIC. The 72 mcg dose would provide a broader range of treatment options to physicians and adult CIC patients in the U.S.

Our linaclotide development opportunities also include linaclotide colonic release, a targeted oral delivery formulation of linaclotide designed to potentially improve abdominal pain relief in adult IBS C patients, as well as in patients with additional GI disorders where lower abdominal pain is a predominant symptom, such as IBS M, ulcerative colitis and diverticulitis, among others. Additionally, we and Allergan are evaluating linaclotide as a potential treatment of the GI dysfunction associated with opioid induced constipation, or OIC, in adult patients and have established a plan with the FDA for clinical pediatric studies with linaclotide, as described below.

Lesinurad. The FDA has required a post-marketing clinical study to further evaluate the renal and cardiovascular safety of lesinurad, and has required that enrollment include patients with moderate renal impairment. Pursuant to the terms of the Lesinurad License, AstraZeneca is obligated to undertake certain activities related to this post-marketing clinical study and we are obligated to reimburse AstraZeneca up to $100.0 million over up to ten years for completion

of such activities. In January 2017, the FDA accepted for review the NDA for DUZALLO. We and AstraZeneca, on our behalf, are undertaking additional development activities related to lesinurad.

Development Candidates. We are advancing our uncontrolled GERD program through the development of IW-3718, a gastric retentive formulation of a bile acid sequestrant.

Within our vascular/fibrotic program, we are leveraging our pharmacological expertise in GC pathways gained through the discovery and development of linaclotide to advance development programs targeting sGC. We are currently progressing two sGC development candidates in clinical development, IW-1973 and IW-1701, which have distinct pharmacologic profiles that we believe may be differentiating and enable opportunities in multiple indications.

We have additional assets in early development that we continue to advance, and we are exploring strategic options for further development of these assets.

Table of Contents

Discovery Research. Our discovery efforts are primarily focused on identifying novel clinical candidates that draw on our proprietary and expanding expertise in GI disorders and GC.

The following table sets forth our research and development expenses related to our product pipeline for the years ended December 31, 2016, 2015 and 2014. These expenses relate primarily to external costs associated with nonclinical studies and clinical trial costs, costs incurred to develop manufacturing processes and register manufacturing facilities with the FDA and licensing fees for our product candidates. We allocate costs related to facilities, depreciation, share based compensation, research and development support services, laboratory supplies and certain other costs directly to programs.

| | Year Ended December 31, | | |
|---|---|---|---|
| | 2016 | 2015 | 2014 |
| | (in thousands) | | |
| Linaclotide(1) | $ 40,130 | $ 48,981 | $ 48,340 |
| Lesinurad(2) | 18,413 | — | — |
| Development candidates: | | | |
| GI disorders (three compounds)(3) | 27,795 | 19,152 | 15,992 |
| Vascular and fibrotic disorders (two compounds)(3) | 29,809 | 20,465 | 11,775 |
| Central nervous system disorders (one compound)(3) | 853 | 1,653 | 2,190 |
| Total development candidates | 58,457 | 41,270 | 29,957 |
| Discovery research | 22,492 | 18,495 | 23,593 |
| | $ 139,492 | $ 108,746 | $ 101,890 |

(1) Includes linaclotide in all indications, populations and formulations.
(2) Includes lesinurad in all indications, populations and formulations.
(3) Number of compounds is for the year ended December 31, 2016.

Since 2004, the date we began tracking costs by program, we have incurred approximately $395.8 million of research and development expenses related to linaclotide. The expenses for linaclotide include both our portion of the research and development costs incurred by Allergan for the U.S. and AstraZeneca for China, Hong Kong and Macau and invoiced to us under the cost sharing provisions of our collaboration agreements, as well as the unreimbursed portion of research and development costs incurred by us under such cost sharing provisions.

The lengthy process of securing regulatory approvals for new drugs requires the expenditure of substantial resources. Any failure by us to obtain, or any delay in obtaining, regulatory approvals would materially adversely affect our product development efforts and our business overall.

In connection with the FDA approval of LINZESS, we are required to conduct certain nonclinical and clinical studies, including those aimed at understanding: (a) whether orally administered linaclotide can be detected in breast milk, (b) the potential for antibodies to be developed to linaclotide, and if so, (c) whether antibodies specific for linaclotide could have any therapeutic or safety implications. In addition, we and Allergan established a nonclinical and clinical post-marketing plan with the FDA to understand the efficacy and safety of LINZESS in pediatric patients. We and Allergan have initiated two Phase II clinical pediatric studies in IBS-C patients age seven to 17 and functional constipation patients age six to 17. We and Allergan are also exploring development opportunities to enhance the clinical profile of LINZESS by studying linaclotide in additional indications, populations and formulations to assess its potential to treat various GI conditions. In October 2012, we entered into a collaboration agreement with AstraZeneca to co-develop and co-commercialize linaclotide in China, Hong Kong and Macau, with AstraZeneca having primary responsibility for the local operational execution. We cannot currently estimate with any degree of certainty the amount of time or money that we will be required to expend in the future on linaclotide for other

geographic markets within IBS-C and CIC, or in additional indications, populations or formulations.

In December 2015, the FDA approved ZURAMPIC for use in conjunction with an XOI for the treatment of hyperuricemia associated with uncontrolled gout. In connection with the FDA approval, the FDA has required a post-marketing clinical study to further evaluate the renal and cardiovascular safety of ZURAMPIC, and has required that enrollment include patients with moderate renal impairment. Pursuant to the terms of the Lesinurad License, AstraZeneca is obligated to undertake certain activities related to this post-marketing clinical study and we are obligated

Table of Contents

to reimburse AstraZeneca up to $100.0 million over up to ten years for completion of such activities. Furthermore, we and AstraZeneca, on our behalf, are undertaking additional development activities related to lesinurad.

We are also advancing other development programs such as IW-3718, a development program targeting uncontrolled GERD, DUZALLO, the fixed dose combination product containing lesinurad and allopurinol targeting uncontrolled gout, and sGC development programs targeting vascular and fibrotic diseases.

Given the inherent uncertainties that come with the development of pharmaceutical products, we cannot estimate with any degree of certainty how our programs will evolve, and therefore the amount of time or money that would be required to obtain regulatory approval to market them.

As a result of these uncertainties surrounding the timing and outcome of any approvals, we are currently unable to estimate precisely when, if ever, linaclotide or lesinurad's utility will be expanded within their currently approved indications, if or when linaclotide or lesinurad will be developed outside of their current markets, indications, populations or formulations, or when, if ever, any of our other product candidates will generate revenues and cash flows.

We invest carefully in our pipeline, and the commitment of funding for each subsequent stage of our development programs is dependent upon the receipt of clear, supportive data. In addition, we intend to access externally discovered drug candidates that fit within our core strategy. In evaluating these potential assets, we apply the same investment criteria as those used for investments in internally discovered assets.

The successful development of our product candidates is highly uncertain and subject to a number of risks including, but not limited to:

- The duration of clinical trials may vary substantially according to the type, complexity and novelty of the product candidate.

- The FDA and comparable agencies in foreign countries impose substantial and varying requirements on the introduction of therapeutic pharmaceutical products, typically requiring lengthy and detailed laboratory and clinical testing procedures, sampling activities and other costly and time-consuming procedures.

- Data obtained from nonclinical and clinical activities at any step in the testing process may be adverse and lead to discontinuation or redirection of development activity. Data obtained from these activities also are susceptible to varying interpretations, which could delay, limit or prevent regulatory approval.

- The duration and cost of discovery, nonclinical studies and clinical trials may vary significantly over the life of a product candidate and are difficult to predict.

- The costs, timing and outcome of regulatory review of a product candidate may not be favorable, and, even if approved, a product may face post-approval development and regulatory requirements.

- There may be substantial costs, delays and difficulties in successfully integrating externally developed product candidates into our business operations.

- The emergence of competing technologies and products and other adverse market developments may negatively impact us.

As a result of the factors discussed above, including the factors discussed under “Risk Factors” in Item 1A of this Annual Report on Form 10 K, we are unable to determine the duration and costs to complete current or future nonclinical and clinical stages of our product candidates or when, or to what extent, we will generate revenues from the commercialization and sale of our product candidates. Development timelines, probability of success and development costs vary widely. We anticipate that we will make determinations as to which additional programs to pursue and how much funding to direct to each program on an ongoing basis in response to the data of each product candidate, the competitive landscape and ongoing assessments of such product candidate’s commercial potential.

We expect our research and development costs will be substantial for the foreseeable future. We will continue to invest in linaclotide and lesinurad, including the investigation of ways to enhance the clinical profile within their currently approved indications, and the exploration of their potential utility in other indications, populations and

Table of Contents

formulations. We will also invest in our other product candidates as we advance them through nonclinical studies and clinical trials, in addition to funding full-time equivalents for research and development activities under our external collaboration and license agreements.

Selling, General and Administrative Expense. Selling, general and administrative expense consists primarily of compensation, benefits and other employee related expenses for personnel in our administrative, finance, legal, information technology, business development, commercial, sales, marketing, communications and human resource functions. Other costs include the legal costs of pursuing patent protection of our intellectual property, general and administrative related facility costs, insurance costs and professional fees for accounting and legal services. As we continue to invest in the commercialization of LINZESS and ZURAMPIC, we expect our selling, general and administrative expenses will be substantial for the foreseeable future. We record all selling, general and administrative expenses as incurred.

Under our AstraZeneca collaboration agreement for linaclotide, we are reimbursed for certain selling, general and administrative expenses and we net these reimbursements against our selling, general and administrative expenses as incurred. We include Allergan's selling, general and administrative cost sharing payments in the calculation of the net profits and net losses from the sale of LINZESS in the U.S. and present the net payment to or from Allergan as collaboration expense or collaborative arrangements revenue, respectively.

Amortization of Acquired Intangible Asset. Amortization expense is based on the economic consumption of intangible assets. Our amortization is related to the ZURAMPIC intangible asset, which is amortized on a straight-line basis over the estimated useful life. We believe that the straight-line method of amortization represents the pattern in which the economic benefits of the ZURAMPIC intangible asset are consumed.

(Gain)/Loss on Fair Value Remeasurement of Contingent Consideration. Our contingent consideration obligation related to the Lesinurad Transaction consists of the fair value of estimated future milestone and royalty payments. This liability is revalued at each reporting period. Changes in the fair value of our contingent consideration, other than changes due to payments, are recognized as a (gain)/loss on fair value remeasurement of contingent consideration in our consolidated statement of operations. Adjustments are recorded when there are changes in significant assumptions, including net sales projections, probability weighted net cash outflow projections, the discount rate, passage of time, and the yield curve equivalent to our credit risk, which is based on the estimated cost of debt for market participants.

Other (Expense) Income. Interest expense consists primarily of cash and non cash interest costs related to the 2022 Notes and our outstanding PhaRMA Notes, which were redeemed, in full, in connection with the funding and issuance in January 2017 of the 2026 Notes. Non cash interest expense consists of amortization of the debt discount and associated debt issuance costs associated with the 2022 Notes and PhaRMA Notes. We amortize these costs using the effective interest rate method over the life of the respective note agreements as interest expense in our consolidated statements of operations.

Interest income consists of interest earned on our cash, cash equivalents and marketable securities.

In June 2015, in connection with the issuance of the 2022 Notes, we entered into convertible note hedge transactions, or the Convertible Note Hedges. Concurrently with entering into the Convertible Note Hedges, we also entered into certain warrant transactions in which we sold note hedge warrants, or the Note Hedge Warrants, to the Convertible

Note Hedge counterparties to acquire 20,249,665 shares of our Class A common stock, subject to customary anti dilution adjustments. Loss on derivatives consists of the change in fair value of the Convertible Note Hedges and Note Hedge Warrants, which are recorded as derivative assets and liabilities. The Convertible Note Hedges and the Note Hedge Warrants are recorded at fair value at each reporting period and changes in fair value are recorded in our consolidated statements of operations.

In September 2016, we closed a direct private placement, pursuant to which we issued $150.0 million in aggregate principal amount of 8.375% notes due 2026 on January 5, 2017, or the Funding Date. The proceeds from the issuance of the 2026 Notes were used to redeem the outstanding principal balance of the PhaRMA Notes on the Funding Date. This transaction is more fully described in Note 11, Notes Payable, and Note 20, Subsequent Events, to our consolidated financial statements appearing elsewhere in this Annual Report on Form 10 K.

Table of Contents

Critical Accounting Policies and Estimates

Our discussion and analysis of our financial condition and results of operations is based upon our consolidated financial statements prepared in accordance with U.S. generally accepted accounting principles. The preparation of these financial statements requires us to make certain estimates and assumptions that may affect the reported amounts of assets and liabilities and disclosure of contingent assets and liabilities at the date of the consolidated financial statements, and the amounts of revenues and expenses during the reported periods. Significant estimates and assumptions in our consolidated financial statements include those related to revenue recognition, including returns, rebates, and other pricing adjustments; available-for-sale securities; inventory valuation, and related reserves; impairment of long-lived assets; initial valuation procedures for the issuance of convertible notes; fair value of derivatives; balance sheet classification of notes payable and convertible notes; income taxes, including the valuation allowance for deferred tax assets; research and development expenses; goodwill; contingent consideration; acquired intangible assets; contingencies and share-based compensation. We base our estimates on our historical experience and on various other assumptions that are believed to be reasonable, the results of which form the basis for making judgments about the carrying values of assets and liabilities. Actual results may differ materially from our estimates under different assumptions or conditions. Changes in estimates are reflected in reported results in the period in which they become known.

We believe that our application of the following accounting policies, each of which require significant judgments and estimates on the part of management, are the most critical to aid in fully understanding and evaluating our reported financial results. Our significant accounting policies are more fully described in Note 2, Summary of Significant Accounting Policies, to our consolidated financial statements appearing elsewhere in this Annual Report on Form 10 K.

Fair Value Measurements

We have certain assets and liabilities that are measured at fair value on a recurring basis, and which have been classified as Level 1, 2 or 3 within the fair value hierarchy as described in the accounting standards for fair value measurements. In general, fair values determined by Level 1 inputs utilize observable inputs such as quoted prices in active markets for identical assets or liabilities. Fair values determined by Level 2 inputs utilize data points that are either directly or indirectly observable, such as quoted prices for similar instruments in active markets, interest rates and yield curves. Fair values determined by Level 3 inputs utilize unobservable data points in which there is little or no market data, which require us to develop our own assumptions for the asset or liability.

Our investment portfolio includes mainly fixed income securities that do not always trade on a daily basis. As a result, the pricing services we use apply other available information as applicable through processes such as benchmark yields, benchmarking of like securities, sector groupings and matrix pricing to prepare valuations. In addition, model processes are used to assess interest rate impact and develop prepayment scenarios. These models take into consideration relevant credit information, perceived market movements, sector news and economic events. The inputs into these models may include benchmark yields, reported trades, broker dealer quotes, issuer spreads and other relevant data. We validate the prices provided by our third party pricing services by obtaining market values from other pricing sources and analyzing pricing data in certain instances.

We classify our derivative financial instruments and contingent consideration as Level 3 under the fair value hierarchy. The derivatives are not actively traded and are valued using the Black-Scholes option pricing model which requires the use of subjective assumptions, primarily the expected stock price volatility assumption. The contingent consideration is not actively traded and is valued using the Monte-Carlo simulation which requires the use of

subjective assumptions, including probability weighted net cash outflow projections, discounted using a yield curve equivalent to the Company's credit risk, which was the estimated cost of debt financing for market participants.

Inventory Valuation

Inventory is stated at the lower of cost or net realizable value with cost determined under the first in, first out basis in accordance with Accounting Standards Update, or ASU, No. 2015-11, Inventory (Topic 330): Simplifying the Measurement of Inventory.

We evaluate inventory levels quarterly and any inventory that has a cost basis in excess of its expected net realizable value, inventory that becomes obsolete, inventory in excess of expected sales requirements, inventory that fails to meet commercial sale specifications or is otherwise impaired is written down with a corresponding charge to the

Table of Contents

statement of operations in the period that the impairment is first identified. We also assess, on a quarterly basis, whether we have any excess non cancelable purchase commitments resulting from minimum supply agreements with our suppliers. We rely on data from several sources to estimate the net realizable value of inventory and non cancelable purchase commitments, including partner forecasts of projected inventory purchases that are received quarterly, our internal forecasts and related process, historical sales by geographic region, and the status of and progress toward commercialization of linaclotide in partnered territories.

We capitalize inventories manufactured in preparation for initiating sales of a product candidate when the related product candidate is considered to have a high likelihood of regulatory approval and the related costs are expected to be recoverable through sales of the inventories. In determining whether or not to capitalize such inventories, we evaluate, among other factors, information regarding the product candidate's safety and efficacy, the status of regulatory submissions and communications with regulatory authorities and the outlook for commercial sales, including the existence of current or anticipated competitive drugs and the availability of reimbursement. In addition, we evaluate risks associated with manufacturing the product candidate, including the ability of our third party suppliers to complete the validation batches, and the remaining shelf life of the inventories.

Costs associated with developmental products prior to satisfying the inventory capitalization criteria are charged to research and development expense as incurred.

There is a risk inherent in these judgments and any changes in these judgments may have a material impact on our financial results in future periods.

Finite-Lived and Indefinite-Lived Intangible Assets

We record the fair value of purchased intangible assets with finite useful lives as of the transaction date of a business combination. Purchased intangible assets with finite useful lives are amortized to their estimated residual values over their estimated useful lives. We evaluate the finite-lived intangible assets for impairment whenever events or changes in circumstances indicate the reduction in the fair value below their respective carrying amounts. If we determine that an impairment has occurred, a write-down of the carrying value and an impairment charge to operating expenses in the period the determination is made is recorded. In addition, the remaining estimated useful life of the finite-lived intangible asset would be reassessed.

In accordance with Accounting Standards Codification, or ASC, Topic 350, Intangibles — Goodwill and Other, or ASC 350, during the period that an asset is considered indefinite-lived, such as in-process research and development, or IPR&D, it will not be amortized. Acquired IPR&D represents the fair value assigned to research and development assets that have not reached technological feasibility. The value assigned to acquired IPR&D is determined by estimating the costs to develop the acquired technology into commercially viable products, estimating the resulting revenue from the projects, and discounting the net cash flows to present value. The revenue and costs projections used to value acquired IPR&D are, as applicable, reduced based on the probability of success of developing a new drug. Additionally, the projections consider the relevant market sizes and growth factors, expected trends in technology, and the nature and expected timing of new product introductions by us and our competitors. The rates utilized to discount the net cash flows to their present value are commensurate with the stage of development of the projects and uncertainties in the economic estimates used in the projections. Upon the acquisition of IPR&D, we complete an assessment of whether our acquisition constitutes the purchase of a single asset or a group of assets. Multiple factors are considered in this assessment, including the nature of the technology acquired, the presence or absence of separate

cash flows, the development process and stage of completion, quantitative significance and the rationale for entering into the transaction. Indefinite-lived assets are maintained on our consolidated balance sheet until either the project underlying it is completed or the asset becomes impaired. Indefinite-lived assets are tested for impairment on an annual basis, or whenever events or changes in circumstances indicate the reduction in the fair value of the IPR&D asset below its respective carrying amount. If we determine that an impairment has occurred, a write-down of the carrying value and an impairment charge to operating expenses in the period the determination is made is recorded. When development of an IPR&D asset is complete, the associated asset is deemed finite-lived and is then amortized based on its respective estimated useful life at that point.

Goodwill

Goodwill represents the difference between the purchase price and the fair value of the identifiable tangible and intangible net assets when accounted for using the purchase method of accounting. Goodwill is not amortized, but is reviewed for impairment. We test goodwill for impairment annually, or whenever events or changes in circumstances

Table of Contents

indicate an impairment may have occurred, by comparing the carrying value to its implied fair value in accordance with ASC 350. Impairment may result from, among other things, deterioration in the performance of the acquired asset, adverse market conditions, adverse changes in applicable laws or regulations and a variety of other circumstances. If we determine that an impairment has occurred, a write-down of the carrying value and an impairment charge to operating expenses in the period the determination is made is recorded. In evaluating the carrying value of goodwill, we must make assumptions regarding estimated future cash flows and other factors. Changes in strategy or market conditions could significantly impact those judgments in the future and require an adjustment to the recorded balances.

Derivative Assets and Liabilities

In June 2015, in connection with the issuance of the 2022 Notes, we entered into the Convertible Note Hedges. Concurrently with entering into the Convertible Note Hedges, we also entered into certain warrant transactions in which we sold Note Hedge Warrants to the Convertible Note Hedge counterparties to acquire 20,249,665 shares of our Class A common stock, subject to customary anti dilution adjustments. These instruments are derivative financial instruments under ASC Topic 815, Derivatives and Hedging.

These derivatives are recorded as assets or liabilities at fair value each reporting period and the fair value is determined using the Black Scholes option pricing model. The changes in fair value are recorded as a component of other (expense) income in the consolidated statements of operations. Significant inputs used to determine the fair value include the price per share of our Class A common stock on the date of valuation, time to maturity of the derivative instruments, the strike prices of the derivative instruments, the risk free interest rate, and the volatility of our Class A common stock. Changes to these inputs could materially affect the valuation of the Convertible Note Hedges and Note Hedge Warrants in future periods.

Revenue Recognition

Our revenues are generated primarily through collaborative arrangements and licensing related to the research and development and commercialization of linaclotide, as well as co-promotion arrangements in the U.S. and product revenue related to the commercial sale of ZURAMPIC in the U.S. The terms of the collaborative research and development, licensing, and co-promotion agreements contain multiple deliverables which may include (i) licenses, (ii) research and development activities, including participation on joint steering committees, (iii) the manufacture of finished drug product, API or development materials for a partner, which are reimbursed at a contractually determined rate, and (iv) co promotion activities by our clinical sales specialists. Non refundable payments to us under these agreements may include (i) up front license fees, (ii) payments for research and development activities, (iii) payments for the manufacture of finished drug product, API or development materials, (iv) payments based upon the achievement of certain milestones, (v) payments for sales detailing, promotional support services and medical education initiatives, and (vi) royalties on product sales. Additionally, we may receive our share of the net profits or bear our share of the net losses from the sale of linaclotide in the U.S. and China through our collaborations with Allergan and AstraZeneca, respectively.

We evaluate revenue from new agreements that have multiple elements under the guidance of ASU No. 2009 13, Multiple Deliverable Revenue Arrangements, or ASU 2009 13. We also evaluate whether amendments to our multiple element arrangements are considered material modifications that are subject to the application of ASU 2009 13. This evaluation requires us to assess all relevant facts and circumstances and to make subjective determinations and judgments. As part of this assessment, we consider whether the modification results in a material change to the arrangement, including whether there is a change in total arrangement consideration that is more than insignificant, whether there are changes in the deliverables included in the arrangement, whether there is a change in the term of the

arrangement and whether there is a significant modification to the delivery schedule for contracted deliverables.

We identify the deliverables included within multiple element agreements and evaluate which deliverables represent separate units of accounting. We account for those components as separate elements when the following criteria are met:

- the delivered items have value to the customer on a stand alone basis; and
- if there is a general right of return relative to the delivered items, delivery or performance of the undelivered items is considered probable and within our control.

Table of Contents

This evaluation requires subjective determinations and requires us to make judgments about the individual deliverables and whether such deliverables are separable from the other aspects of the contractual relationship. In determining the units of accounting, we evaluate certain criteria, including whether the deliverables have standalone value, based on consideration of the relevant facts and circumstances for each arrangement. Factors considered in this determination include the research, manufacturing and commercialization capabilities of the partner and the availability of peptide research and manufacturing expertise in the general marketplace. In addition, we consider whether the collaborator can use the license or other deliverables for their intended purpose without the receipt of the remaining elements, and whether the value of the deliverable is dependent on the undelivered items and whether there are other vendors that can provide the undelivered items.

The consideration received is allocated among the separate units of accounting using the relative selling price method, and the applicable revenue recognition criteria are applied to each of the separate units.

We determine the estimated selling price for deliverables 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. Determining the BESP for a deliverable requires significant judgment. We use BESP to estimate the selling price for licenses to our proprietary technology, since we often do not have VSOE or TPE of selling price for these deliverables. In those circumstances where we utilize BESP to determine the estimated selling price of a license to our proprietary technology, we consider market conditions as well as entity specific factors, including those factors contemplated in negotiating the agreements as well as internally developed models that include assumptions related to the market opportunity, estimated development costs, probability of success and the time needed to commercialize a product candidate pursuant to the license. In validating our BESP, we evaluate whether changes in the key assumptions used to determine the BESP will have a significant effect on the allocation of arrangement consideration between multiple deliverables.

We recognize revenue when there is persuasive evidence that an arrangement exists, services have been rendered or delivery has occurred, the price is fixed or determinable, and collection is reasonably assured.

For certain of our arrangements, particularly our linaclotide license agreement with Allergan for all countries worldwide other than China, Hong Kong, Macau, Japan, and the countries and territories of North America, it is required that taxes be withheld on payments to us. We have adopted a policy to recognize revenue net of these tax withholdings.

Net Profit or Net Loss Sharing

The determination of whether we should recognize revenue on a gross or net basis involves judgment based on the relevant facts and circumstances. In accordance with ASC Topic 808, Collaborative Arrangements, and ASC 605 45, Principal Agent Considerations, we consider the nature and contractual terms of the arrangement and the nature of our business operations to determine the classification of the transactions under our collaboration agreements. We record revenue transactions gross in the consolidated statements of operations if we are deemed the principal in the transaction, which includes being the primary obligor and having the risks and rewards of ownership.

We recognize our share of the pre tax commercial net profit or net loss generated from the sales of LINZESS in the U.S. in the period the product sales are reported by Allergan and related cost of goods sold and selling, general and administrative expenses are incurred by us and our collaboration partner. These amounts are partially determined based on amounts provided by Allergan and involve the use of estimates and judgments, such as product sales allowances and accruals related to prompt payment discounts, chargebacks, governmental and contractual rebates, wholesaler fees, product returns, and co payment assistance costs, which could be adjusted based on actual results in the future. We are highly dependent on Allergan for timely and accurate information regarding any net revenues

realized from sales of LINZESS in the U.S. and the costs incurred in selling it, in order to accurately report our results of operations. For the periods covered in the consolidated financial statements presented, there have been no material changes to prior period estimates of revenues, cost of goods sold or selling, general and administrative expenses associated with the sales of LINZESS in the U.S. However, if we do not receive timely and accurate information or incorrectly estimate activity levels associated with the collaboration at a given point in time, we could be required to record adjustments in future periods.

We record our share of the net profits or net losses from the sales of LINZESS in the U.S. on a net basis and present the settlement payments to and from Allergan as collaboration expense or collaborative arrangements revenue, as

Table of Contents

applicable, as we are not the primary obligor and do not have the risks and rewards of ownership in the collaboration agreement with Allergan for North America. We and Allergan settle the cost sharing quarterly, such that our statement of operations reflects 50% of the pre tax net profit or loss generated from sales of LINZESS in the U.S.

Up Front License Fees

For nonrefundable up-front license fees related to arrangements entered into prior to the adoption of ASU 2009-13, including the $30.0 million up-front license fee under the Astellas license agreement entered into in November 2009, we recognized revenues on a straight-line basis over the contracted or estimated period of performance since the license deliverables were not deemed to have value on a standalone basis under pre ASU 2009-13 guidance and we could not determine the fair value of the undelivered elements. The period of performance over which the revenues are recognized is typically the period over which the research and/or development is expected to occur. Accordingly, we were required to make estimates regarding the drug development and commercialization timelines for compounds being developed pursuant to any applicable agreement. The determination of the length of the period over which to recognize the revenue is subject to judgment and estimation and could have an impact on the amount of revenue recognized in a given period. Quarterly, we reassessed our period of substantial involvement over which we amortized our up front license fees and made adjustments as appropriate. At December 31, 2016, the up-front fees associated with our license arrangement with Astellas were fully amortized as the period of performance had ended. The up-front license fees under the Allergan collaboration for North America and the Allergan collaboration for Europe (previously with Almirall) were fully amortized at December 31, 2015, as the period of performance under those arrangements ended in the three months ended September 30, 2012.

For nonrefundable up-front license fees related to arrangements entered into or materially modified after the adoption ASU 2009-13, we recognize revenue allocated to the license upon delivery, when we believe the license to our intellectual property has stand alone value. This includes the amounts allocated to the license under the AstraZeneca collaboration agreement for linaclotide entered into in October 2012. When we recognize revenue allocated to the license upon delivery under any of our collaborations, we may experience significant fluctuations in our collaborative arrangements revenues from quarter to quarter and year to year depending on the timing of transactions. When we believe the license to our intellectual property does not have stand alone value from the other deliverables to be provided in the arrangement, it is combined with other deliverables and the revenue of the combined unit of accounting is recorded based on the method appropriate for the last delivered item.

Milestones

At the inception of each arrangement that includes pre commercial milestone payments, we evaluate whether each pre commercial milestone is substantive, in accordance with ASU No. 2010 17, Revenue Recognition—Milestone Method, or ASU 2010 17. This evaluation includes an assessment of whether (a) the consideration is commensurate with either (1) the entity's performance to achieve the milestone, or (2) the enhancement of the value of the delivered item(s) as a result of a specific outcome resulting from the entity's performance to achieve the milestone, (b) the consideration relates solely to past performance and (c) the consideration is reasonable relative to all of the deliverables and payment terms within the arrangement. We evaluate factors such as the scientific, clinical, regulatory, commercial and other risks that must be overcome to achieve the respective milestone, the level of effort and investment required and whether the milestone consideration is reasonable relative to all deliverables and payment terms in the arrangement in making this assessment. At December 31, 2016, we had no pre commercial milestones that were deemed substantive. If a substantive pre commercial milestone were achieved and collection of the related receivable was reasonably assured, we would recognize revenue related to the milestone in its entirety in the period in which the milestone was achieved. If we achieve milestones that we consider substantive under any of our collaborations, we may experience significant fluctuations in our collaborative arrangements revenue from quarter to quarter and year to year depending on the timing of achieving such substantive milestones. In those circumstances

where a pre commercial milestone is not substantive, we recognize as revenue on the date the milestone is achieved an amount equal to the applicable percentage of the performance period that had elapsed as of the date the milestone was achieved, with the balance being deferred and recognized over the remaining period of performance.

Commercial milestones are accounted for as royalties and are recorded as revenue upon achievement of the milestone, assuming all other revenue recognition criteria are met.

Table of Contents

Royalties on Product Sales

We receive, or expect to receive in the future, royalty revenues under certain of our license or collaboration agreements. If we do not have any future performance obligations under these license or collaborations agreements, we record these revenues as earned. To the extent we do not have access to the royalty reports from our partners or the ability to accurately estimate the royalty revenue in the period earned, we record such royalty revenues one quarter in arrears.

Product Revenue, Net

Net product revenue is derived from sales of ZURAMPIC in the U.S. Pursuant to the terms and conditions of the Lesinurad TSA, we sell ZURAMPIC principally to a limited number of major wholesalers and selected regional wholesalers through certain of AstraZeneca's existing arrangements, or the Distributors. The Distributors subsequently resell ZURAMPIC to patients and healthcare providers.

We recognize net product revenue from sales of ZURAMPIC in accordance with ASC 605, Revenue Recognition, or ASC 605, when persuasive evidence of an arrangement exists, delivery has occurred and title of the product and associated risk of loss has passed to the customer, the price is fixed or determinable, and collection from the customer has been reasonably assured. ASC 605 requires, among other criteria, that future returns can be reasonably estimated in order to recognize revenue. We recognize revenue on a gross basis as we have concluded that we are the principal in the product revenue transactions for ZURAMPIC, as we hold the general inventory risk, latitude in establishing price, physical loss inventory risk and credit risk.

The first units of ZURAMPIC were shipped to Distributors in September 2016 under the Lesinurad TSA. Due to the early stage of the product launch, we determined that we were not able to reliably make certain estimates, including returns, necessary to recognize product revenue upon shipment to Distributors. As a result, we record net product revenue for ZURAMPIC using a deferred revenue recognition model (sell-through). Under the deferred revenue model, we do not recognize revenue until ZURAMPIC is prescribed to an end-user. During the transition services period, pursuant to the Lesinurad TSA, AstraZeneca invoices Distributors upon shipment of ZURAMPIC on our behalf. We record deferred revenue upon receipt of the quarterly cash payment from AstraZeneca for shipments of ZURAMPIC to Distributors. We had not received any such payments as of December 31, 2016. We recognize net product revenue when ZURAMPIC is prescribed to the end-user, on a first-in, first-out basis using estimated prescription demand and pharmacy demand from third party sources and our analysis of third party market research data, as well as other third party information. Our estimates are subject to the inherent limitations of estimates that rely on third party data, as certain third party information is itself in the form of estimates. We will continue to evaluate when, if ever, we have sufficient volume of historical activity and visibility into the distribution channel, in order to reasonably make all estimates required under ASC 605 to recognize revenue upon shipment to the Distributor.

Our net product revenues for ZURAMPIC represent total revenues less customer credits, including actual returns, rebates, and other discounts. These allowances are recorded for cash consideration given by a vendor to a customer that is presumed to be a reduction of the selling prices of our products or services and, therefore, characterized as a reduction of revenue.

The cost basis of the product we have purchased pursuant to the Lesinurad TSA is included as a component of other current assets on our consolidated balance sheets. Upon recognition of product revenue, the corresponding product cost is recorded as cost of revenues on our consolidated statements of operations.

Other

We produce finished linaclotide drug product, API and development materials for certain of our partners.

We recognize revenue on linaclotide finished drug product, API and development materials when the material has passed all quality testing required for collaborator acceptance, delivery has occurred, title and risk of loss have transferred to the partner, the price is fixed or determinable, and collection is reasonably assured. As it relates to development materials and API produced for Astellas, we are reimbursed at a contracted rate. Such reimbursements are considered as part of revenue generated pursuant to the Astellas license agreement and are presented as collaborative arrangements revenue. Any linaclotide finished drug product, API and development materials currently produced for

Table of Contents

Allergan for the U.S. or AstraZeneca for China, Hong Kong and Macau are recognized in accordance with the cost sharing provisions of the Allergan and AstraZeneca collaboration agreements, respectively. In October 2015, Almirall transferred its exclusive license to develop and commercialize linaclotide in Europe to Allergan, and we separately entered into an amendment to the license agreement with Allergan relating to the development and commercialization of linaclotide in Europe. Pursuant to the terms of the amendment, Allergan assumed responsibility for the manufacturing of linaclotide API for Europe from us, as well as the associated costs. We may experience fluctuations in our collaborative arrangements revenue from quarter to quarter and year to year depending on the timing of such transactions.

The agreements above are more fully described in Note 5, Collaboration, License, Co-promotion and Other Commercial Agreements, in the accompanying notes to our consolidated financial statements appearing elsewhere in this Annual Report on Form 10 K.

Research and Development Expense

All research and development expenses are expensed as incurred. We defer and capitalize nonrefundable advance payments we make for research and development activities until the related goods are received or the related services are performed.

Research and development expenses are comprised of costs incurred in performing research and development activities, including salary, benefits and other employee related expenses; share based compensation expense; laboratory supplies and other direct expenses; facilities expenses; overhead expenses; third party contractual costs relating to nonclinical studies and clinical trial activities and related contract manufacturing expenses, development of manufacturing processes and regulatory registration of third party manufacturing facilities; licensing fees for our product candidates; and other outside expenses.

Clinical trial expenses include expenses associated with contract research organizations, or CROs. The invoicing from CROs for services rendered can lag several months. We accrue the cost of services rendered in connection with CRO activities based on our estimate of site management, monitoring costs, project management costs, and investigator fees. We maintain regular communication with our CRO vendors to gauge the reasonableness of our estimates. Differences between actual clinical trial expenses and estimated clinical trial expenses recorded have not been material and are adjusted for in the period in which they become known. However, if we incorrectly estimate activity levels associated with the CRO services at a given point in time, we could be required to record material adjustments in future periods. Under our Allergan and AstraZeneca linaclotide collaboration agreements for the U.S. and China, Hong Kong and Macau, respectively, we are reimbursed for certain research and development expenses and we net these reimbursements against our research and development expenses as incurred. Amounts owed to Allergan or AstraZeneca for such territories are recorded as incremental research and development expense. Nonrefundable advance payments for research and development activities are capitalized and expensed over the related service period or as goods are received.

Share Based Compensation Expense

We make certain assumptions in order to value and record expense associated with awards made under our share based compensation arrangements. We estimate the fair value of the stock option awards for employees and non employees using the Black Scholes option pricing model. The fair value of our restricted stock unit, or RSU, awards is based on the market value of our Class A common stock on the date of grant. Determining the fair value of share based awards requires the use of highly subjective assumptions, including expected term of the award and expected stock price volatility. For certain of these awards, we determine the appropriate amount to expense based on the anticipated achievement of performance targets, which requires judgment, including forecasting the achievement of future

specified targets. Changes in these assumptions may lead to variability with respect to the amount of expense we recognize in connection with share based payments.

We recognize compensation expense on a straight line basis over the requisite service period based upon stock options that are ultimately expected to vest, and accordingly, such compensation expense is adjusted by the amount of estimated forfeitures. We estimate forfeitures over the requisite service period when recognizing share based compensation expense based on historical rates and forward looking factors; these estimates are adjusted to the extent that actual forfeitures differ, or are expected to materially differ, from our estimates.

Table of Contents

We have also granted time accelerated stock options with terms that allow the acceleration in vesting of the stock options upon the achievement of performance based milestones specified in the grants. Share based compensation expense associated with these time accelerated stock options is recognized over the requisite service period of the awards or the implied service period, if shorter.

While the assumptions used to calculate and account for share based compensation awards represent management's best estimates, these estimates involve inherent uncertainties and the application of management's judgment. As a result, if revisions are made to our underlying assumptions and estimates, our share based compensation expense could vary significantly from period to period.

Business Combinations

We evaluate acquisitions of assets and other similar transactions to assess whether or not the transaction should be accounted for as a business combination by assessing whether or not we have acquired inputs and processes that have the ability to create outputs. If determined to be a business combination, we account for business acquisitions under the acquisition method of accounting as indicated in the Financial Accounting Standards Board, or FASB, issued ASC 805, which requires the acquiring entity in a business combination to recognize the fair value of all assets acquired, liabilities assumed, and any non-controlling interest in the acquiree and establishes the acquisition date as the fair value measurement point. Accordingly, we recognize assets acquired and liabilities assumed in business combinations, including contingent liabilities and non-controlling interest in the acquiree based on the fair value estimates as of the date of acquisition. In accordance with ASC 805, we recognize and measure goodwill as of the acquisition date, as the excess of the fair value of the consideration paid over the fair value of the identified net assets acquired.

The consideration for our business acquisitions include future payments that are contingent upon the occurrence of a particular event or events. The obligations for such contingent consideration payments are recorded at fair value on the acquisition date. The contingent consideration obligations are then evaluated each reporting period. Changes in the fair value of contingent consideration obligations, other than changes due to payments, are recognized as a (gain) loss on fair value remeasurement of contingent consideration in our consolidated statements of operations.

Table of Contents

Results of Operations

The following discussion summarizes the key factors our management believes are necessary for an understanding of our consolidated financial statements.

| | Year Ended December 31, | | |
|---|---|---|---|
| | 2016 | 2015 | 2014 |
| | (in thousands) | | |
| Collaborative arrangements revenue | $ 273,957 | $ 149,555 | $ 76,436 |
| Cost and expenses: | | | |
| Cost of revenues, excluding amortization of acquired intangible asset | 1,868 | 12 | 5,291 |
| Write-down of inventory to net realizable value and loss on non-cancellable purchase commitments | 374 | 17,638 | 20,292 |
| Research and development | 139,492 | 108,746 | 101,890 |
| Selling, general and administrative | 173,281 | 125,247 | 118,333 |
| Amortization of acquired intangible asset | 981 | — | — |
| Loss on fair value remeasurement of contingent consideration | 9,831 | — | — |
| Total cost and expenses | 325,827 | 251,643 | 245,806 |
| Loss from operations | (51,870) | (102,088) | (169,370) |
| Other (expense) income: | | | |
| Interest expense | (39,153) | (31,096) | (21,166) |
| Interest and investment income | 1,169 | 443 | 257 |
| Gain (loss) on derivatives | 8,146 | (9,928) | — |
| Other income | — | — | 661 |
| Other expense, net | (29,838) | (40,581) | (20,248) |
| Net loss | $ (81,708) | $ (142,669) | $ (189,618) |

Year Ended December 31, 2016 Compared to Year Ended December 31, 2015

Revenues

| | Year Ended December 31, | | Change | |
|---|---|---|---|---|
| | 2016 | 2015 | $ | % |
| | (dollars in thousands) | | | |
| Collaborative arrangements revenue | $ 273,957 | $ 149,555 | $ 124,402 | 83 % |

Collaborative Arrangements Revenue. The increase in revenue from collaborative arrangements of approximately $124.4 million for the year ended December 31, 2016 compared to the year ended December 31, 2015 was primarily related to an approximately $84.3 million increase in our share of the net profits from the sale of LINZESS in the U.S.; an approximately $30.0 million increase due to the achievement of two development milestones in 2016 under our license agreement with Astellas; an approximately $9.4 million increase from shipments of linaclotide API to our linaclotide partners; an approximately $1.8 million increase attributable to the recognition of up-front payments and development milestones achieved prior to 2016 under our agreement with Astellas resulting from a revision of the estimated development period for linaclotide in Japan in September 2016; an approximately $1.6 million increase from our co-promotion agreement with Allergan for VIBERZI in the U.S.; an insignificant increase in royalty revenue based on sales of linaclotide in our partnered territories; and an insignificant increase due to the recognition of net product sales of ZURAMPIC in the U.S. in 2016. The increases were partially offset by an approximately $2.0 million decrease in revenue related to our collaboration agreement with AstraZeneca for linaclotide, and an approximately

$0.9 million decrease in revenue related to the Cologuard Co-Promotion Agreement.

Table of Contents

Cost and Expenses

| | Year Ended December 31, | | Change | |
|---|---|---|---|---|
| | 2016 | 2015 | $ | % |
| | (dollars in thousands) | | | |
| Cost and expenses: | | | | |
| Cost of revenues, excluding amortization of acquired intangible asset | $ 1,868 | $ 12 | $ 1,856 | 15,467% |
| Write-down of inventory to net realizable value and loss on non-cancellable purchase commitments | 374 | 17,638 | (17,264) | (98)% |
| Research and development | 139,492 | 108,746 | 30,746 | 28% |
| Selling, general and administrative | 173,281 | 125,247 | 48,034 | 38% |
| Amortization of acquired intangible asset | 981 | — | 981 | 100% |
| Loss on fair value remeasurement of contingent consideration | 9,831 | — | 9,831 | 100% |
| Total cost and expenses | $ 325,827 | $ 251,643 | $ 74,184 | 29% |

Cost of Revenues, excluding amortization of acquired intangible asset. The increase in cost of revenue of approximately $1.9 million for the year ended December 31, 2016 compared to the year ended December 31, 2015 was primarily attributable to higher sales of linaclotide API to our partners and the launch of ZURAMPIC.

Write down of inventory to net realizable value and loss on non cancelable purchase commitments. The decrease in write-down of inventory and loss on non-cancelable purchase commitments of approximately $17.3 million for the year ended December 31, 2016 compared to the year ended December 31, 2015, was primarily related to the write-down of inventory and an accrual for a loss on excess non-cancelable inventory purchase commitments related to linaclotide API recorded during the year ended December 31, 2015, partially offset by a write-down of approximately $0.4 million related to lesinurad prepaid inventory.

Research and Development Expense. The increase in research and development expense of approximately $30.7 million for the year ended December 31, 2016 compared to the year ended December 31, 2015 was primarily related to an increase of approximately $14.5 million in the costs associated with development activities and transitional support services related to lesinurad; an increase of approximately $13.8 million in research costs related to our early stage pipeline candidates; an increase of approximately $9.6 million in net costs related to the collaboration with Allergan for North America; an increase of approximately $5.2 million in compensation, benefits and other employee related expenses primarily associated with increased headcount; and an increase of approximately $4.2 million in operating costs, including facility costs such as rent and amortization of leasehold improvements allocated to research and development, and an increase of approximately $0.2 million related to the development of manufacturing processes and costs associated with linaclotide API prior to meeting our inventory capitalization policy. The increases were partially offset by an approximately $14.1 million decrease in external costs related to the development of linaclotide; a decrease of approximately $2.1 million decrease due to a reallocation of resources relating to quality testing and set-up cost related to the launch and commercialization of ZURAMPIC recorded as selling, general administrative expenses; and an approximately $0.6 million decrease in costs associated with the collaboration agreement with AstraZeneca for China.

Selling, General and Administrative Expense. Selling, general and administrative expenses increased approximately $48.0 million for the year ended December 31, 2016 compared to the year ended December 31, 2015 primarily as a result of an increase in our workforce and infrastructure expenses due to the launch and commercialization of

ZURAMPIC in the U.S. This increase includes an approximately $17.0 million increase in compensation, benefits and other employee-related expenses associated with the increased headcount primarily in our field sales force; an approximately $12.4 million increase in costs associated with selling expenses, marketing programs, and speaker programs; an approximately $8.1 million increase in external consulting costs, recruiting costs and other professional service costs; an approximately $5.3 million increase in costs associated with other infrastructure costs related to lesinurad; an approximately $3.5 million increase in costs related to facilities and information technology infrastructure, including rent; and an approximately $1.7 million increase due to the internal costs relating to quality testing and set-up costs related to the launch and commercialization of ZURAMPIC.

Amortization of Acquired Intangible Asset. The increase in amortization of acquired intangible asset expense of approximately $1.0 million for the year ended December 31, 2016 compared to the year ended December 31, 2015 was

Table of Contents

due to the Lesinurad Transaction that closed in June 2016, in which we acquired an exclusive license in the U.S. to, among other things, the approved product ZURAMPIC. The amount allocated to the ZURAMPIC intangible asset will be amortized on a straight-line basis over its estimated useful life of 13 years, the period of estimated future cash flows.

Loss on Fair Value remeasurement of contingent consideration. The increase in the fair value of the contingent consideration obligation of approximately $9.8 million for the year ended December 31, 2016 compared to the year ended December 31, 2015 was due to the Lesinurad Transaction. The change in the fair value remeasurement of contingent consideration from the date the Lesinurad Transaction closed, on June 2, 2016, to December 31, 2016 was primarily due to the passage of time and changes in the yield curve equivalent to our credit risk, which was the estimated cost of debt financing for similar market participants used in the valuation.

Other (Expense) Income, Net

| | Year Ended December 31, | | Change | |
|---|---|---|---|---|
| | 2016 | 2015 | $ | % |
| | (dollars in thousands) | | | |
| Other (expense) income: | | | | |
| Interest expense | $ (39,153) | $ (31,096) | $ (8,057) | 26 % |
| Interest and investment income | 1,169 | 443 | 726 | 164 % |
| Gain (loss) on derivatives | 8,146 | (9,928) | 18,074 | (182)% |
| Total other expense, net | $ (29,838) | $ (40,581) | $ 10,743 | (26) % |

Interest Expense. Interest expense increased approximately $8.1 million for the year ended December 31, 2016 compared to the year ended December 31, 2015, mainly due to an increase in interest expense of approximately $10.2 million associated with our 2022 Notes as we began incurring interest in June 2015. This increase was partially offset by a decrease of approximately $2.1 million in interest expense associated with the PhaRMA Notes for the year ended December 31, 2016 associated with the decreased principal balance, and a decrease of an insignificant amount due to interest associated with capital leases for the automobiles for our field based sales force and medical science liaisons.

Interest and investment income. Interest and investment income increased approximately $0.7 million for the year ended December 31, 2016 compared to the year ended December 31, 2015, mainly due to an increase of approximately $0.7 million in investment income. This increase is partially offset by an insignificant decrease in interest income on certificate deposits.

Gain (loss) on derivatives. For the year ended December 31, 2016 we recorded a gain on derivatives of approximately $8.1 million resulting from an approximately $46.0 million increase in fair value of the Convertible Note Hedges and an approximately $37.9 million increase in the fair value of the Note Hedge Warrants. For the year ended December 31, 2015 we recorded a loss on derivatives of approximately $9.9 million resulting from an approximately $5.4 million decrease in fair value of the Convertible Note Hedges and an approximately $4.5 million decrease in the fair value of the Note Hedge Warrants.

Year Ended December 31, 2015 Compared to Year Ended December 31, 2014

Revenue

| | Year Ended December 31, | | Change | |
|---|---|---|---|---|
| | 2015 | 2014 | $ | % |
| | (dollars in thousands) | | | |
| Collaborative arrangements revenue | $ 149,555 | $ 76,436 | $ 73,119 | 96 % |

Collaborative Arrangements Revenue. The increase in revenue from collaborative arrangements of approximately $73.1 million for the year ended December 31, 2015 compared to the year ended December 31, 2014 was primarily related to an approximately $85.8 million increase in our share of the net profits from the sale of LINZESS in the U.S.; an approximately $4.4 million increase due to revenues from our co promotion agreement with Exact Sciences for Cologuard in the U.S. entered into in March 2015; an approximately $0.8 million increase in royalty revenue based on sales of linaclotide in our partnered territories; and an approximately $0.2 million increase due to revenues from our

Table of Contents

co promotion agreement with Allergan for VIBERZI in the U.S. entered into in August 2015. The increases were partially offset by an approximately $8.1 million decrease in revenue recognized in connection with the achievement of a development milestone under our Astellas license agreement in 2014; an approximately $7.0 million decrease in revenue from the shipments of linaclotide API to our licensing partners; an approximately $1.9 million decrease in revenue recognized related to the achievement of commercial launch milestones under our license agreement with Almirall in 2014; and an approximately $1.1 million decrease in revenue related to our collaboration agreement with AstraZeneca.

Cost and Expenses

| | Year Ended December 31, | | Change | |
|---|---|---|---|---|
| | 2015 | 2014 | $ | % |
| | (dollars in thousands) | | | |
| Cost and expenses: | | | | |
| Cost of revenues | $ 12 | $ 5,291 | $ (5,279) | (100)% |
| Write-down of inventory to net realizable value and loss on non-cancellable purchase commitments | 17,638 | 20,292 | (2,654) | (13)% |
| Research and development | 108,746 | 101,890 | 6,856 | 7 % |
| Selling, general and administrative | 125,247 | 118,333 | 6,914 | 6 % |
| Total cost and expenses | $ 251,643 | $ 245,806 | $ 5,837 | 2 % |

Cost of Revenues. The decrease in cost of revenue of approximately $5.3 million for the year ended December 31, 2015 compared to the year ended December 31, 2014 was primarily attributable to lower sales of linaclotide API to our licensing partners.

Write down of inventory to net realizable value and loss on non cancelable purchase commitments. The decrease in write down of inventory and loss on non cancelable purchase commitments of approximately $2.7 million for the year ended December 31, 2015 compared to the year ended December 31, 2014 was primarily related to an accrual for a loss on non cancelable inventory purchase commitments recorded in the year ended December 31, 2015, partially offset by a decrease in the amount of inventory written down to estimated net realizable value.

Inventory represents linaclotide API that is available for commercial sale. We evaluate inventory levels quarterly and any inventory that has a cost basis in excess of its expected net realizable value, inventory that becomes obsolete, inventory in excess of expected sales requirements, inventory that fails to meet commercial sale specifications or is otherwise impaired is written down with a corresponding charge to the statement of operations in the period that the impairment is first identified. As part of our net realizable value assessment of our inventory, we assess whether we have any excess non cancelable purchase commitments resulting from our two minimum supply agreements with our suppliers of linaclotide API outside of North America.

We have entered into multiple commercial supply agreements for the purchase of linaclotide API. Two of our API supply agreements for supplying API to our collaboration partners outside of North America contain minimum purchase commitments. Prior to October 2015, we were also responsible for the manufacturing of linaclotide API for Europe. As part of our net realizable value assessment of our inventory, we assess whether we have any excess non cancelable purchase commitments resulting from our minimum supply agreements with our suppliers of linaclotide API.

The determination of the net realizable value of inventory and non cancelable purchase commitments is based on demand forecasts from our partners that are received quarterly, to project the next 24 months of demand and our

internal forecast for projected demand in subsequent years. During the three months ended June 30, 2015, Almirall, our former European partner, reduced its forecasted purchases of linaclotide API for its territory for the subsequent 18 months. In addition, regulatory changes made by the CFDA to the marketing approval process in China resulted in a potentially lengthened approval timeline for the commercialization of linaclotide. The reduced demand from Almirall, and the potential extended timeline for commercialization of linaclotide in China, resulted in lower projected sales of linaclotide API to our partners in Europe and China. As a result, during the three months ended June 30, 2015, we wrote down the balance of our inventory of approximately $5.0 million to zero and accrued approximately $3.2 million for excess non cancelable inventory purchase commitments.

Table of Contents

In October 2015, Almirall transferred its exclusive license to develop and commercialize linaclotide in Europe to Allergan, and we separately entered into an amendment to the license agreement with Allergan relating to the development and commercialization of linaclotide in Europe. Pursuant to the terms of the amendment, Allergan assumed responsibility for the manufacturing of linaclotide API for Europe, as well as the associated costs. Upon the execution of the amendment to the license agreement, we recorded an incremental loss on non cancelable API purchase commitments of approximately $6.9 million related to one of our API supply agreements covering the commercial supply of linaclotide API for the European market. During the three months ended September 30, 2015, we also recorded an incremental loss on non cancelable API purchase commitments related to in process API batches. We have evaluated all remaining minimum purchase commitments under our linaclotide API supply agreements through 2023 and concluded that the approximately $22.3 million of purchase commitments from the second API supply agreement covering the Japan, China, Hong Kong and Macau markets are realizable based on the current forecasts received from our partners in these territories and our internal forecasts. These charges are more fully described in Note 8, Inventory, to our consolidated financial statements appearing elsewhere in this Annual Report on Form 10 K.

During the year ended December 31, 2014, we wrote down approximately $20.3 million in inventory to an estimated net realizable value of approximately $5.0 million. This write down was primarily attributable to Almirall's reduced inventory demand forecasts, mainly due to the suspension of commercialization of CONSTELLA in Germany and a challenging commercial environment throughout Europe.

Research and Development Expense. The increase in research and development expense of approximately $6.9 million for the year ended December 31, 2015 compared to the year ended December 31, 2014 was primarily related to an increase of approximately $19.7 million in external costs related to the development of linaclotide; an increase of approximately $4.2 million in compensation, benefits and other employee related expenses primarily associated with increased headcount; and an increase of approximately $3.2 million in research costs related to our early stage pipeline candidates. The increases were partially offset by a decrease of approximately $12.6 million in costs related to the collaboration with Allergan for North America; a decrease of approximately $3.0 million related to our January 2014 workforce reduction; a decrease of approximately $1.8 million in operating costs, including information technology infrastructure costs and facility costs such as rent and amortization of leasehold improvements allocated to research and development; an approximately $1.6 million decrease in costs associated with the collaboration with AstraZeneca; and a decrease of approximately $1.2 million related to the development of manufacturing processes and costs associated with linaclotide API prior to meeting our inventory capitalization policy.

Selling, General and Administrative Expense. Selling, general and administrative expenses increased approximately $6.9 million for the year ended December 31, 2015 compared to the year ended December 31, 2014 primarily as a result of an approximately $2.9 million increase in costs associated with selling expenses and marketing programs; an approximately $2.7 million increase in external consulting costs, patent related legal costs and other service costs primarily associated with commercial activities to support linaclotide; an approximately $2.1 million increase in compensation, benefits and other employee related expenses; and an approximately $0.4 million increase in selling, general and administrative expenses related to facilities and information technology infrastructure costs, including rent and amortization of leasehold improvements. These increases were partially offset by a decrease in costs of approximately $1.2 million related to our January 2014 workforce reduction.

Other (Expense) Income, Net

| | Year Ended December 31, | | Change | |
|---|---|---|---|---|
| | 2015 | 2014 | $ | % |
| | (dollars in thousands) | | | |
| Other (expense) income: | | | | |
| Interest expense | $ (31,096) | $ (21,166) | $ (9,930) | 47 % |
| Interest and investment income | 443 | 257 | 186 | 72 % |
| Loss on derivatives | (9,928) | — | (9,928) | 100 % |
| Other income | — | 661 | (661) | (100)% |
| Total other (expense) income, net | $ (40,581) | $ (20,248) | $ (20,333) | 100 % |

Interest Expense. Interest expense increased approximately $9.9 million for the year ended December 31, 2015 compared to the year ended December 31, 2014, mainly due to an increase in interest expense of approximately $10.9 million associated with our 2022 Notes. This increase was partially offset by a decrease of approximately

Table of Contents

$0.9 million in interest expense associated with the PhaRMA Notes for the year ended December 31, 2015, and an insignificant amount due to interest associated with capital leases for the automobiles for our field based sales force and medical science liaisons.

Loss on derivatives. The approximately $9.9 million increase in the net loss on derivatives for the year ended December 31, 2015, compared to the year ended December 31, 2014 is due to an approximately $5.4 million decrease in the fair value of the Convertible Note Hedges and an approximately $4.5 million increase in the fair value of the Note Hedge Warrants since their issuance in June 2015.

Other Income. The decrease in other income of approximately $0.7 million for the year ended December 31, 2015 compared to the year ended December 31, 2014 is primarily related to timing of the recognition of tax incentive awards that were recognized in the year ended December 31, 2014. In the year ended December 31, 2012, we were awarded an approximately $1.7 million tax incentive, associated with the Life Sciences Tax Incentive Program from the Massachusetts Life Sciences Center. During the year ended December 31, 2014, we recognized approximately $0.7 million as other income in the consolidated statement of operations, as we believed we had satisfied our job creation commitments related to this award for 2012 and 2013.

Liquidity and Capital Resources

We have incurred losses since our inception in 1998 and, as of December 31, 2016, we had an accumulated deficit of approximately $1.2 billion. We have financed our operations to date primarily through both the private sale of our preferred stock and the public sale of our common stock, including approximately $203.2 million of net proceeds from our initial public offering, or IPO, in February 2010, and approximately $413.4 million of net proceeds from our follow on public offerings; payments received under our strategic collaborative arrangements, including up-front and milestone payments, royalties and our share of net profits, as well as reimbursement of certain expenses; and debt financings, including approximately $11.2 million of net proceeds from the private placement of our 2026 Notes, approximately $167.3 million of net proceeds from the private placement of our PhaRMA Notes in January 2013 (which we redeemed, in full, in connection with the funding in January 2017 of the 2026 Notes), and approximately $324.0 million of net proceeds from the private placement of our 2022 Notes in June 2015. At December 31, 2016, we had approximately $305.2 million of unrestricted cash, cash equivalents and available for sale securities. Our cash equivalents include amounts held in money market funds. Our available for sale securities include amounts held in U.S. Treasury securities and U.S. government sponsored securities. We invest cash in excess of immediate requirements in accordance with our investment policy, which limits the amounts we may invest in any one type of investment and requires all investments held by us to be at least A+ rated, with a remaining maturity when purchased of less than twelve months, so as to primarily achieve liquidity and capital preservation.

During the year ended December 31, 2016, our balances of cash, cash equivalents and available for sale securities decreased approximately $134.2 million. This decrease is primarily due to an up-front payment of $100.0 million to AstraZeneca related to the Lesinurad License, as well as the cash used to operate our business, including payments related to, among other things, research and development and selling, general and administrative expenses as we continued to invest in our research pipeline and support the continued commercialization of LINZESS and the launch of ZURAMPIC in the U.S. We also made principal payments of approximately $26.9 million on our outstanding PhaRMA Notes, invested approximately $4.2 million in capital expenditures, and made payments of approximately $1.9 million on capital lease obligations. These cash outflows were partially offset by approximately $24.8 million in proceeds from the exercise of stock options and the issuance of shares pursuant to our employee stock purchase plan.

Cash Flows From Operating Activities

Net cash used in operating activities totaled approximately $25.4 million for the year ended December 31, 2016. The primary uses of cash were our net loss of approximately $81.7 million and changes in assets and liabilities of approximately $5.0 million resulting primarily from an increase in related party accounts receivable principally attributable to higher amounts due from Allergan as a result of increased profits on the sale of LINZESS in the U.S., a decrease in restricted cash associated with our salesforce vehicle fleet, an increase in accounts payable, related party accounts payable and accrued expenses, an increase in prepaid expenses and other assets, a decrease in deferred revenue, a decrease in deferred rent and an increase in accrued research and development costs. These uses of cash were primarily offset by non cash items of approximately $61.3 million, including approximately $29.2 million in share based compensation expense, approximately $14.8 million in non-cash interest expense, approximately $10.3 million in

Table of Contents

depreciation and amortization expense of property and equipment, approximately $9.8 million due to the non-cash change in fair value of contingent consideration, approximately $3.5 million due to the loss on facility subleases, approximately $1.0 million in amortization of acquired assets, approximately $0.7 million in accretion of discounts and premiums on available for sale securities, and approximately $0.4 million in write-down of prepaid inventory; partially offset by an approximately $8.1 million due to the change in fair value of the Convertible Note Hedges and Note Hedge Warrants, and approximately $0.2 million in gain on disposal of property and equipment.

Net cash used in operating activities totaled approximately $106.9 million for the year ended December 31, 2015. The primary uses of cash were our net loss of approximately $142.7 million and changes in assets and liabilities of approximately $38.2 million resulting primarily from an increase in related party accounts receivable principally attributable to higher amounts due from Allergan as a result of increased profits on the sale of LINZESS in the U.S., an increase in restricted cash associated with our salesforce vehicle fleet, a decrease in accounts payable, related party accounts payable and accrued expenses, a decrease in prepaid expenses and other assets, a decrease in deferred revenue, a decrease in deferred rent and an increase in accrued research and development costs. These uses of cash were primarily offset by non cash items of approximately $74.0 million, including approximately $25.5 million in share based compensation expense, approximately $17.6 million due to the write down of inventory to net realizable value and loss on non cancelable purchase commitments, approximately $11.6 million in depreciation and amortization expense of property and equipment, approximately $8.1 million in non cash interest expense, approximately $9.9 million due to the change in fair value of the Convertible Note Hedges and Note Hedge Warrants, and approximately $1.1 million in accretion of discounts and premiums on available for sale securities.

Net cash used in operating activities totaled approximately $155.6 million for the year ended December 31, 2014. The primary uses of cash were our net loss of approximately $189.6 million and changes in assets and liabilities of approximately $30.1 million resulting primarily from an increase in related party accounts receivable principally due to higher amounts due from Allergan due to increased profits on the sale of LINZESS in the U.S., an increase in purchases of linaclotide API, an increase in prepaid expenses and other assets, and an increase in deferred rent. These uses of cash were partially offset by non cash items of approximately $64.2 million, including approximately $26.2 million in share based compensation expense, approximately $20.3 million due to the write down of inventory to net realizable value, approximately $12.3 million in depreciation and amortization expense of property and equipment, approximately $2.6 million in losses on facility subleases, approximately $1.6 million in non cash interest expense and approximately $1.1 million in accretion of discounts and premiums on available for sale securities.

Cash Flows From Investing Activities

Cash used in investing activities for the year ended December 31, 2016 totaled approximately $177.7 million and resulted primarily from the costs associated with the Lesinurad License consisting of an up-front payment of $100.0 million, the purchase of approximately $311.1 million of available for sale securities and the purchase of approximately $4.2 million of property and equipment, primarily laboratory equipment as well as hardware and software related to our information technology infrastructure. This was partially offset by the sales and maturities of approximately $237.4 million of available for sale securities, and approximately $0.2 million of proceeds from the sale of property and equipment.

Cash used in investing activities for the year ended December 31, 2015 totaled approximately $9.2 million and resulted primarily from the purchase of approximately $282.0 million of available for sale securities and the purchase of approximately $4.0 million of property and equipment, primarily leasehold improvements and laboratory equipment. This was partially offset by the sales and maturities of approximately $276.7 million of available for sale securities and an insignificant amount of proceeds from the sale of property and equipment.

Table of Contents

Cash used in investing activities for the year ended December 31, 2014 totaled approximately $56.6 million and resulted primarily from the purchase of approximately $254.0 million of available for sale securities and the purchase of approximately $3.5 million of property and equipment, primarily manufacturing and laboratory equipment as well as software to improve our information technology infrastructure. This was partially offset by the maturity of approximately $200.9 million in available for sale securities.

Cash Flows From Financing Activities

Cash used in financing activities for the year ended December 31, 2016 totaled approximately $4.2 million and resulted primarily from approximately $26.9 million in cash used for principal payments on our outstanding PhaRMA Notes, approximately $1.9 million in cash used for payments on our capital leases, and approximately $0.2 million in costs associated with the issuance of the 2026 Notes, partially offset by approximately $24.8 million in cash provided by stock option exercises and the issuance of shares under our employee stock purchase plan.

Cash provided by financing activities for the year ended December 31, 2015 totaled approximately $303.1 million and resulted primarily from approximately $324.0 million in net proceeds from the issuance of our 2022 Notes in June 2015, approximately $70.8 million in gross proceeds from the issuance of the Note Hedge Warrants in connection with the 2022 Notes, approximately $14.2 million in cash provided by stock option exercises and the issuance of shares under our employee stock purchase plan, partially offset by approximately $91.9 million related to the purchase of the Convertible Note Hedges in connection with our 2022 Notes, approximately $12.7 million in cash used for principal payments on our outstanding PhaRMA Notes, and approximately $1.3 million in cash used for payments on our capital leases.

Cash provided by financing activities for the year ended December 31, 2014 totaled approximately $210.9 million and resulted primarily from approximately $190.4 million in net proceeds from our follow on public stock offering in the first quarter of 2014 and approximately $22.7 million in cash provided by stock option exercises and the issuance of shares under our employee stock purchase plan, partially offset by approximately $1.2 million in cash used for principal payments on debt and approximately $1.0 million in cash used for payments on our capital leases.

Funding Requirements

We began commercializing LINZESS in the U.S. with our collaboration partner, Allergan, in the fourth quarter of 2012, and we currently derive substantially all of our revenue from this collaboration. Additionally, we began commercializing ZURAMPIC in the U.S. for the treatment of uncontrolled gout in the fourth quarter of 2016. We are also deploying significant resources to advance product opportunities in IBS-C/CIC, uncontrolled gout, uncontrolled GERD, and vascular and fibrotic diseases. Our goal is to become cash flow positive, driven by increased revenue generated through sales of LINZESS and ZURAMPIC, and financial discipline. However, we have not achieved positive cash flows from operations to date.

Under our collaboration with Allergan for North America, total net sales of LINZESS in the U.S., as recorded by Allergan, are reduced by commercial costs incurred by each party, and the resulting amount is shared equally between us and Allergan. Additionally, we receive royalties from Allergan based on sales of linaclotide in its licensed territories outside of the U.S. We believe revenues from our LINZESS partnership for the U.S. with Allergan will continue to constitute a significant portion of our total revenue for the foreseeable future and we cannot be certain that such revenues, as well as the revenues from our other commercial activities including the sales of ZURAMPIC, DUZALLO (if approved) and any other products, will enable us to become cash flow positive, or to do so in the timeframes we expect. We also anticipate that we will continue to incur substantial expenses for the next several years

as we further develop and commercialize linaclotide in the U.S., China and other markets, develop and commercialize lesinurad in the U.S., and continue to invest in our pipeline and potentially other external opportunities. We believe that our cash on hand as of December 31, 2016 will be sufficient to meet our projected operating needs at least through the next twelve months.

Our forecast of the period of time through which our financial resources will be adequate to support our operations, including the underlying estimates regarding the costs to develop our product candidates and obtain regulatory approvals and the costs to commercialize linaclotide in the U.S., China and other markets, and develop and commercialize lesinurad in the U.S., as well as our goal to become cash flow positive, are forward-looking statements that involve risks and uncertainties. Our actual results could vary materially and negatively from these and other

Table of Contents

forward-looking statements as a result of a number of factors, including the factors discussed in the "Risk Factors" section of this Annual Report on Form 10-K. We have based our estimates on assumptions that may prove to be wrong, and we could utilize our available capital resources sooner than we currently expect.

Due to the numerous risks and uncertainties associated with the development and commercialization of our product candidates, we are unable to estimate precisely the amounts of capital outlays and operating expenditures necessary to develop, obtain regulatory approval for, and commercialize linaclotide, lesinurad and our other product candidates, in each case, for all of the markets, indications, populations and formulations for which we believe each is suited. Our funding requirements will depend on many factors, including, but not limited to, the following:

- the revenue generated by sales of LINZESS, CONSTELLA, ZURAMPIC and any other products;
- the rate of progress and cost of our commercialization activities, including the expense we incur in marketing and selling LINZESS, ZURAMPIC and any other products;
- the success of our third-party manufacturing activities;
- the time and costs involved in developing, and obtaining regulatory approvals for, our product candidates, as well as the timing and cost of any post-approval development and regulatory requirements;
- the success of our research and development efforts;
- the emergence of competing or complementary products;
- the costs of filing, prosecuting, defending and enforcing any patent claims and other intellectual property rights;
- the terms and timing of any additional collaborative, licensing or other arrangements that we may establish, including royalties or other payments due or payable under such agreements; and
- the acquisition of businesses, products and technologies and the impact of other strategic transactions, as well as the cost and timing of integrating any such assets into our business operations.

Financing Strategy

We may, from time to time, consider additional funding through a combination of new collaborative arrangements, strategic alliances, and additional equity and debt financings or from other sources. We will continue to manage our

capital structure and to consider all financing opportunities, whenever they may occur, that could strengthen our long term liquidity profile. Any such capital transactions may or may not be similar to transactions in which we have engaged in the past. There can be no assurance that any such financing opportunities will also be available on acceptable terms, if at all.

Contractual Commitments and Obligations

Lease and Commercial Supply Obligations

The following table summarizes our lease and commercial supply obligations at December 31, 2016 (excluding interest, except as otherwise noted):

| | Payments Due by Period | | | | |
|---|---|---|---|---|---|
| | Total | Less Than 1 Year | 1 3 Years | 3 5 Years | More Than 5 Years |
| | (in thousands) | | | | |
| Commercial supply obligations(1) | $ 36,809 | $ 11,417 | $ 10,478 | $ 11,818 | $ 3,096 |
| Capital lease obligations(2) | 6,455 | 6,370 | 85 | — | — |
| Operating lease obligations(3) | 21,329 | 20,498 | 831 | — | — |
| Total contractual obligations | $ 64,593 | $ 38,285 | $ 11,394 | $ 11,818 | $ 3,096 |

Table of Contents

(1) We have multiple commercial supply agreements with contract manufacturing organizations for the purchase of linaclotide finished drug product and API. Two of our API supply agreements for supplying linaclotide API to our collaboration partners outside of North America contain minimum purchase commitments, which are reflected in the table above. As of December 31, 2016, approximately $10.1 million of the commitments included in the table above are recorded as an accrual for excess purchase commitments in our consolidated balance sheet. These commitments are more fully described in Note 12, Commitments and Contingencies, to our consolidated financial statements appearing elsewhere in this Annual Report on Form 10-K. In addition, we and Allergan are jointly obligated to make minimum purchases of linaclotide API for the territories covered by our collaboration with Allergan for North America. Currently, Allergan fulfills all such minimum purchase commitments and, as a result, they are excluded from the table above.

Additionally, the Lesinurad CSA with AstraZeneca provides for commercial supply and samples of ZURAMPIC, and, if approved by the FDA, DUZALLO. The Lesinurad CSA includes certain purchase obligations based on our forecasted demand for commercial product and samples. As of December 31, 2016, we had approximately $6.6 million of such commitments related to lesinurad commercial supply and samples for 2017 and none thereafter.

(2) Our commitment for capital lease obligations principally relates to leased automobiles for our field based sales force and medical science liaisons, and computer and office equipment.

(3) Our commitments for operating leases relate to our lease of office and laboratory space in Cambridge, Massachusetts and our data storage space in Boston, Massachusetts. In the third quarter of 2014, we entered into two arrangements, with the landlord's consent, to sublease a portion of our Cambridge, Massachusetts corporate headquarters, one of which expired during 2016. The future minimum lease payments included in this table do not reflect the $6.1 million of sublease rental income that we are entitled to receive through 2018.

Notes Payable

In January 2013, we closed a private placement of $175.0 million in aggregate principal amount of 11% PhaRMA Notes due 2024. The PhaRMA Notes were redeemed on the Funding Date with proceeds from the 2026 Notes. The redemption is more fully described in Note 20, Subsequent Events, in the accompanying notes to our consolidated financial statements appearing elsewhere in this Annual Report on Form 10-K. The PhaRMA Notes bore an annual interest rate of 11%, with interest payable March 15, June 15, September 15 and December 15 of each year, each an 11% Payment Date, which began on June 15, 2013. On March 15, 2014, we began making quarterly payments on the notes equal to the greater of (i) 7.5% of net sales of LINZESS in the U.S. for the preceding quarter, or the 11% Synthetic Royalty Amount, and (ii) accrued and unpaid interest on the notes, or the 11% Required Interest Amount. Principal on the notes was repaid in an amount equal to the 11% Synthetic Royalty Amount minus the 11% Required Interest Amount, when this was a positive number, until the principal had been paid in full. We made principal payments of $40.7 million through December 31, 2016.

In June 2015, we issued approximately $335.7 million of 2.25% Convertible Senior Notes due June 15, 2022. The 2022 Notes are governed by an indenture between us and U.S. Bank National Association, as the trustee, or the Indenture. The 2022 Notes are senior unsecured obligations and bear interest at a rate of 2.25% per year, payable on June 15 and December 15 of each year, which began on December 15, 2015. The 2022 Notes will mature on June 15, 2022, unless earlier converted or repurchased. The initial conversion rate for the 2022 Notes is 60.3209 shares of Class A common stock (subject to adjustment as provided for in the Indenture) per $1,000 principal amount of the 2022 Notes, which is equal to an initial conversion price of approximately $16.58 per share. In addition, to minimize the impact of potential dilution to our common stock upon conversion of the 2022 Notes, we entered into the Convertible Note Hedges covering 20,249,665 shares of our Class A common stock in connection with the 2022 Notes. Concurrently with entering into the Convertible Note Hedges, we sold Note Hedge Warrants to acquire 20,249,665 shares of our Class A common stock at an initial strike price of approximately $21.50 per share, subject to customary anti dilution adjustments. The following table summarizes our 2022 Notes obligations at December 31, 2016:

| | Payments Due by Period | | | | |
|---|---|---|---|---|---|
| | Total | Less Than 1 Year | 1 3 Years | 3 5 Years | More Than 5 Years |
| | (in thousands) | | | | |
| 2022 Notes (including interest) | 377,242 | 7,553 | 15,106 | 15,106 | 339,476 |

81

Table of Contents

The 2022 Notes, Convertible Note Hedges and Note Hedge Warrants are more fully described in Note 11, Notes Payable, in the accompanying notes to our consolidated financial statements appearing elsewhere in this Annual Report on Form 10-K.

In September 2016, we closed a direct private placement, pursuant to which we subsequently issued $150.0 million in aggregate principal amount of 8.375% notes due 2026 on the Funding Date, January 5, 2017. The proceeds from the issuance of the 2026 Notes were used to redeem the outstanding principal balance of the PhaRMA Notes. The 2026 Notes bear an annual interest rate of 8.375%, with interest payable March 15, June 15, September 15 and December 15 of each year, each an 8.375% Payment Date, which begins on June 15, 2017. Beginning March 15, 2019, we will began making quarterly payments on the 2026 Notes equal to the greater of (i) 7.5% of net sales of linaclotide in the U.S. for the preceding quarter, or the 8.375% Synthetic Royalty Amount, and (ii) accrued and unpaid interest on the notes, or the 8.375% Required Interest Amount. Principal on the 2026 Notes will be repaid in an amount equal to the 8.375% Synthetic Royalty Amount minus the 8.375% Required Interest Amount, when this is a positive number, until the principal has been paid in full. Given the principal payments on the 2026 Notes are based on the net sales of linaclotide in the U.S., which will vary from quarter to quarter, the 2026 Notes may be repaid prior to September 15, 2026, the final legal maturity date. Since we are unable to reliably estimate the exact timing and amounts of the principal payments, as discussed under “Risk Factors” in Item 1A of this Annual Report on Form 10 K, the related commitments are not included in the table above. This transaction is more fully described in Note 11, Notes Payable, and Note 20, Subsequent Events, to our consolidated financial statements appearing elsewhere in this Annual Report on Form 10 K.

Commitments Related to Our Collaboration and License Agreements

Under our collaborative agreements with Allergan for North America and AstraZeneca for China, Hong Kong and Macau, we share with Allergan and AstraZeneca all development and commercialization costs related to linaclotide in the U.S. and for China, Hong Kong and Macau, respectively. The actual amounts that we pay our partners or that partners pay to us will depend on numerous factors outside of our control, including the success of our clinical development efforts with respect to linaclotide, the content and timing of decisions made by the regulators, the reimbursement and competitive landscape around linaclotide and our other product candidates, and other factors described under “Risk Factors” in Item 1A of this Annual Report on Form 10 K.

Under our Lesinurad License, we are undertaking the development and commercialization of lesinurad in the U.S. Pursuant to the terms of the Lesinurad License, we will pay a tiered royalty to AstraZeneca in the single-digits as a percentage of net sales of ZURAMPIC, and if approved DUZALLO, in the U.S., as well as commercial and other milestones of up to $165.0 million over the duration of the agreement. Additionally, AstraZeneca is obligated to conduct certain development activities on our behalf for (i) ZURAMPIC, including the post-marketing requirement activities currently required by the FDA, for which we are obligated to reimburse AstraZeneca up to $100.0 million over up to ten years, and (ii) DUZALLO, for which we will also reimburse AstraZeneca.

In addition, we have other collaboration and license agreements that are not individually significant to our business. Under one such license and collaboration arrangement, we have commitments to make potential future milestone payments totaling $23.0 million, which includes $5.0 million for development milestones and $18.0 million for regulatory milestones. We are also committed to make potential future milestone payments of up to $114.5 million per product to one of our collaboration partners, including $21.5 million for development milestones, $58.0 million for regulatory milestones and $35.0 million for sales based milestones. These milestones primarily include the commencement and results of clinical trials, obtaining regulatory approval in various jurisdictions and the future commercial success of development programs, the outcome and timing of which are difficult to predict and subject to significant uncertainty. In addition to the milestones discussed above, we are obligated to pay royalties on future sales, which are contingent on generating levels of sales of future products that have not been achieved and may never be

achieved. Since we are unable to reliably estimate the timing and amounts of such milestone and royalty payments, or whether they will occur at all, these contingent payments have been excluded from the table above. Our license and collaboration agreements are more fully described in Note 5, Collaboration, License, Co promotion and Other Commercial Agreements, in the accompanying notes to our consolidated financial statements appearing elsewhere in this Annual Report on Form 10 K.

Table of Contents

Tax related Obligations

We exclude liabilities or obligations pertaining to uncertain tax positions from our summary of contractual commitments and obligations as we cannot make a reliable estimate of the period of cash settlement with the respective taxing authorities. As of December 31, 2016, we have approximately $26.4 million of uncertain tax positions, and we cannot reasonably estimate the potential adjustment to our net operating loss carryforward. These uncertain tax positions are more fully described in Note 15, Income Taxes, in the accompanying notes to our consolidated financial statements appearing elsewhere in this Annual Report on Form 10 K.

Other Funding Commitments

As of December 31, 2016, we have several ongoing studies in various clinical trial stages. Our most significant clinical trial expenditures are to CROs. The contracts with CROs generally are cancellable, with notice, at our option and do not have any significant cancellation penalties. These items are not included in the table above.

Off Balance Sheet Arrangements

We do not have any relationships with unconsolidated entities or financial partnerships, such as entities often referred to as structured finance or special purpose entities, that would have been established for the purpose of facilitating off balance sheet arrangements (as that term is defined in Item 303(a)(4)(ii) of Regulation S K) or other contractually narrow or limited purposes. As such, we are not exposed to any financing, liquidity, market or credit risk that could arise if we had engaged in those types of relationships. We enter into guarantees in the ordinary course of business related to the guarantee of our own performance and the performance of our subsidiaries.

New Accounting Pronouncements

For a discussion of new accounting pronouncements refer to Note 2, Summary of Significant Accounting Policies, to our consolidated financial statements appearing elsewhere in this Annual Report on Form 10 K.

Item 7A. Quantitative and Qualitative Disclosures about Market Risk

Interest Rate Risk

We are exposed to market risk related to changes in interest rates. We invest our cash in a variety of financial instruments, principally securities issued by the U.S. government and its agencies and money market instruments. The goals of our investment policy are preservation of capital, fulfillment of liquidity needs and fiduciary control of cash and investments. We also seek to maximize income from our investments without assuming significant risk.

Our primary exposure to market risk is interest income sensitivity, which is affected by changes in the general level of interest rates, particularly because our investments are in short term marketable securities. Due to the short term duration of our investment portfolio and the low risk profile of our investments, an immediate 1% change in interest rates would not have a material effect on the fair market value of our portfolio. Accordingly, we would not expect our operating results or cash flows to be affected to any significant degree by the effect of a sudden change in market interest rates on our investment portfolio.

We do not believe our cash, cash equivalents and available for sale securities have significant risk of default or illiquidity. While we believe our cash, cash equivalents and available for sale securities do not contain excessive risk, we cannot provide absolute assurance that in the future our investments will not be subject to adverse changes in market value. In addition, we maintain significant amounts of cash, cash equivalents and available for sale securities at

one or more financial institutions that are in excess of federally insured limits. Given the potential instability of financial institutions, we cannot provide assurance that we will not experience losses on these deposits.

Our capital lease obligations, 2026 Notes and 2022 Notes bear interest at a fixed rate and therefore have minimal exposure to changes in interest rates; however, because these interest rates are fixed, we may be paying a higher interest rate, relative to market, in the future if our credit rating improves or other circumstances change.

Table of Contents

Equity Price Risk

2022 Notes

Our 2022 Notes include conversion and settlement provisions that are based on the price of our Class A common stock at conversion or at maturity of the 2022 Notes. The amount of cash we may be required to pay is determined by the price of our Class A common stock. The fair value of our 2022 Notes is dependent on the price and volatility of our Class A common stock and will generally increase or decrease as the market price of our Class A common stock changes.

The 2022 Notes are convertible into Class A common stock at an initial conversion rate of 60.3209 shares of Class A common stock (subject to adjustment as provided for in the Indenture) per $1,000 principal amount of the 2022 Notes, which is equal to an initial conversion price of approximately $16.58 per share. The 2022 Notes will mature on June 15, 2022 unless earlier converted or repurchased. The 2022 Notes bear cash interest at an annual rate of 2.25%, payable on June 15 and December 15 of each year, which began on December 15, 2015. As of December 31, 2016, the fair value of the 2022 Notes was estimated by us to be $384.2 million. The 2022 Notes are more fully described in Note 6, Fair Value of Financial Instruments, and Note 11, Notes Payable, in the accompanying notes to our consolidated financial statements appearing elsewhere in this Annual Report on Form 10 K.

Convertible Note Hedge and Warrant Transactions with Respect to 2022 Notes

To minimize the impact of potential dilution to our common stock upon conversion of the 2022 Notes, we entered into Convertible Note Hedges. Concurrently with entering into the Convertible Note Hedges, we entered into warrant transactions whereby we sold Note Hedge Warrants to acquire, subject to customary adjustments, 20,249,665 shares of our Class A common stock at an initial strike price of approximately $21.50 per share, subject to adjustment. The Convertible Note Hedges and Note Hedge Warrants are more fully described in Note 11, Notes Payable, in the accompanying notes to our consolidated financial statements appearing elsewhere in this Annual Report on Form 10 K.

Foreign Currency Risk

We have no significant operations outside the U.S. and we do not expect to be impacted significantly by foreign currency fluctuations.

Effects of Inflation

We do not believe that inflation and changing prices over the years ended December 31, 2016, 2015 and 2014 had a significant impact on our results of operations.

Item 8. Consolidated Financial Statements and Supplementary Data

Our consolidated financial statements, together with the independent registered public accounting firm report thereon, appear at pages F 1 through F 58, of this Annual Report on Form 10 K.

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

None.

Item 9A. Controls and Procedures

Evaluation of Disclosure Controls and Procedures

As required by Rule 13a 15(b) of the Exchange Act, our management, including our principal executive officer and our principal financial officer, conducted an evaluation as of the end of the period covered by this Annual Report on Form 10 K of the effectiveness of the design and operation of our disclosure controls and procedures. Based on that evaluation, our principal executive officer and principal financial officer concluded that our disclosure controls and procedures are effective at the reasonable assurance level in ensuring that information required to be disclosed by us in the reports that we file or submit under the Exchange Act is recorded, processed, summarized and reported within the

Table of Contents

time periods specified in the SEC's rules and forms. Disclosure controls and procedures include, without limitation, controls and procedures designed to ensure that information required to be disclosed by us in the reports we file under the Exchange Act is accumulated and communicated to our management, including our principal executive officer and principal financial officer, as appropriate to allow timely decisions regarding required disclosure.

Management's Report on Internal Control Over Financial Reporting

Our management is responsible for establishing and maintaining adequate internal control over our financial reporting. Internal control over financial reporting is defined in Rules 13a 15(f) and 15d 15(f) under the Exchange Act as the process designed by, or under the supervision of, our Chief Executive Officer and Chief Financial Officer, and effected by our board of directors, management and other personnel, to provide reasonable assurance regarding the reliability of our financial reporting and the preparation of our financial statements for external purposes in accordance with generally accepted accounting principles, and 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 assets;
(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 are being made only in accordance with the authorizations of management and directors; and
(3) provide reasonable assurance regarding the prevention or timely detection of unauthorized acquisition, use or disposition of assets that could have a material effect on our financial statements.

Under the supervision and with the participation of our management, including our Chief Executive Officer and Chief Financial Officer, we conducted an evaluation of the effectiveness of our internal control over financial reporting based on the framework provided in Internal Control—Integrated Framework issued by the Committee of Sponsoring Organizations of the Treadway Commission (2013 framework). Based on this evaluation, our management concluded that our internal control over financial reporting was effective as of December 31, 2016.

The effectiveness of our internal control over financial reporting as of December 31, 2016 has been audited by Ernst and Young LLP, an independent registered public accounting firm, as stated in their report, which is included herein.

Changes in Internal Control

As required by Rule 13a 15(d) of the Exchange Act, our management, including our principal executive officer and our principal financial officer, conducted an evaluation of the internal control over financial reporting to determine whether any changes occurred during the quarter ended December 31, 2016 that have materially affected, or are reasonably likely to materially affect, our internal control over financial reporting. Based on that evaluation, our principal executive officer and principal financial officer concluded no such changes during the quarter ended December 31, 2016 materially affected, or were reasonably likely to materially affect, our internal control over financial reporting.

Table of Contents

Report of Independent Registered Public Accounting Firm

The Board of Directors and Shareholders of Ironwood Pharmaceuticals, Inc.

We have audited Ironwood 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). Ironwood 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 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, Ironwood 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 consolidated balance sheets of Ironwood Pharmaceuticals, Inc. as of December 31, 2016 and 2015, and the related consolidated statements of operations, comprehensive loss, stockholders' equity, and cash flows for each of the three years in the period ended December 31, 2016 of Ironwood Pharmaceuticals, Inc. and our report dated February 22, 2017 expressed an unqualified opinion thereon.

/s/ Ernst & Young LLP

Boston, Massachusetts
February 22, 2017

86

Table of Contents

Item 9B. Other Information

None.

Table of Contents

PART III

Item 10. Directors, Executive Officers and Corporate Governance

We have adopted a code of business conduct and ethics applicable to our directors, executive officers and all other employees. A copy of that code is available on our corporate website at http://www.ironwoodpharma.com. Any amendments to the code of business conduct and ethics, and any waivers thereto involving our executive officers, also will be available on our corporate website. A printed copy of these documents will be made available upon request. The content on our website is not incorporated by reference into this Annual Report on Form 10 K.

Certain information regarding our executive officers is set forth at the end of Part I, Item 1 of this Form 10 K under the heading, “Executive Officers of the Registrant.” The other information required by this item is incorporated by reference from our proxy statement for our 2017 Annual Meeting of Stockholders.

Item 11. Executive Compensation

The information required by this item is incorporated by reference from our proxy statement for our 2017 Annual Meeting of Stockholders.

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

The information relating to security ownership of certain beneficial owners of our common stock and information relating to the security ownership of our management required by this item is incorporated by reference from our proxy statement for our 2017 Annual Meeting of Stockholders.

The table below sets forth information with regard to securities authorized for issuance under our equity compensation plans as of December 31, 2016. As of December 31, 2016, we had four active equity compensation plans, each of which was approved by our stockholders:

•Our Amended and Restated 2002 Stock Incentive Plan;

•Our Amended and Restated 2005 Stock Incentive Plan;

•Our Amended and Restated 2010 Employee, Director and Consultant Equity Incentive Plan; and

•Our Amended and Restated 2010 Employee Stock Purchase Plan.

| Plan Category | Number of securities to be issued upon exercise of outstanding options, warrants and rights (1) (a) | Weighted-average exercise price of outstanding options, warrants, and rights (2) (b) | Number of securities remaining available for future issuance under equity compensation plans (excluding securities reflected in column (a)) (c) |
|---|---|---|---|
| Equity compensation plans approved by security holders | 21,754,116 | 11.92 | 12,959,613 |
| Equity compensation plans not approved by | — | — | — |

| | | | |
|---|---|---|---|
| security holders | | | |
| Total | 21,754,116 | $ 11.92 | 12,959,613 |

(1) Amount includes the number of shares subject to issuance upon exercise of 20,454,659 outstanding stock options and vesting of 1,299,457 restricted stock units.
(2) Amount includes all outstanding stock options but does not include restricted stock units, which do not have an exercise price.

Table of Contents

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

The information required by this item is incorporated by reference from our proxy statement for our 2017 Annual Meeting of Stockholders.

Item 14. Principal Accountant Fees and Services

The information required by this item is incorporated by reference from our proxy statement for our 2017 Annual Meeting of Stockholders.

Table of Contents

PART IV

Item 15. Exhibits and Financial Statement Schedules

1. List of documents filed as part of this report
1. Consolidated Financial Statements listed under Part II, Item 8 and included herein by reference.
2. Consolidated Financial Statement Schedules

No schedules are submitted because they are not applicable, not required or because the information is included in the Consolidated Financial Statements or Notes to Consolidated Financial Statements.

3. Exhibits

| | | Incorporated by reference herein | |
|---|---|---|---|
| Number | Description | Form | Date |
| 3.1 | Eleventh Amended and Restated Certificate of Incorporation | Annual Report on Form 10 K (File No. 001 34620) | March 30, 2010 |
| 3.2 | Fifth Amended and Restated Bylaws | Annual Report on Form 10 K (File No. 001 34620) | March 30, 2010 |
| 4.1 | Specimen Class A common stock certificate | Registration Statement on Form S 1, as amended (File No. 333 163275) | January 20, 2010 |
| 4.2 | Eighth Amended and Restated Investors' Rights Agreement, dated as of September 1, 2009, by and among Ironwood Pharmaceuticals, Inc., the Founders and the Investors named therein | Registration Statement on Form S 1, as amended (File No. 333 163275) | November 20, 2009 |
| 4.3 | Indenture, dated as of June 15, 2015, by and between Ironwood Pharmaceuticals, Inc. and U. S. Bank National Association (including the form of the 2.25% Convertible Senior Note due 2022) | Form 8 K (File No. 001 34620) | June 15, 2015 |
| 4.4 | Indenture, dated as of September 23, 2016, by and between Ironwood Pharmaceuticals, Inc. and U.S. Bank National Association (including the form of the 8.375% Notes due 2026) | Form 8 K (File No. 001 34620) | September 26, 2016 |
| 10.1# | Amended and Restated 2002 Stock Incentive Plan and form agreements thereunder | Registration Statement on Form S 1, as amended (File No. 333 163275) | December 23, 2009 |
| 10.2# | Amended and Restated 2005 Stock Incentive Plan and form agreements thereunder | Registration Statement on Form S 1, as amended (File No. 333 163275) | January 29, 2010 |
| 10.3# | Amended and Restated 2010 Employee, Director and Consultant Equity Incentive Plan | Registration Statement on Form S 8, as amended (File No. 333 184396) | October 12, 2012 |

Table of Contents

| | | Incorporated by reference herein | |
|---|---|---|---|
| Number | Description | Form | Date |
| 10.3.1# | Form of Stock Option Agreement under the Amended and Restated 2010 Employee, Director and Consultant Equity Incentive Plan | Annual Report on Form 10 K (File No. 001 34620) | February 18, 2015 |
| 10.3.2# | Form of Non employee Director Restricted Stock Agreement under the Amended and Restated 2010 Employee, Director and Consultant Equity Incentive Plan | Annual Report on Form 10 K (File No. 001 34620) | February 18, 2015 |
| 10.3.3# | Form of Restricted Stock Unit Agreement under the Amended and Restated 2010 Employee, Director and Consultant Equity Incentive Plan | Annual Report on Form 10 K (File No. 001 34620) | February 18, 2015 |
| 10.4# | Amended and Restated 2010 Employee Stock Purchase Plan | Annual Report on Form 10 K (File No. 001 34620) | February 21, 2013 |
| 10.5# | Change of Control Severance Benefit Plan, as amended and restated | Quarterly Report on Form 10 Q (File No. 001 34620) | April 29, 2014 |
| 10.6# | Form of Executive Severance Agreement | Annual Report on Form 10 K (File No. 001 34620) | February 18, 2015 |
| 10.7# | Director Compensation Plan effective January 1, 2014 | Annual Report on Form 10 K (File No. 001 34620) | February 7, 2014 |
| 10.8# | Form of Indemnification Agreement with Directors and Officers | Registration Statement on Form S 1, as amended (File No. 333 163275) | December 23, 2009 |
| 10.9# | Consulting Agreement, dated as of December 16, 2014, by and between Christopher Walsh and Ironwood Pharmaceuticals, Inc. | Annual Report on Form 10 K (File No. 001 34620) | February 18, 2015 |
| 10.10# | Consulting Agreement, dated December 3, 2014, by and between Lawrence S. Olanoff and Ironwood Pharmaceuticals, Inc. | Quarterly Report on Form 10 Q (File No. 001 34620) | May 6, 2015 |
| 10.11+ | Collaboration Agreement, dated as of September 12, 2007, as amended on November 3, 2009, by and between Forest Laboratories, Inc. and Ironwood Pharmaceuticals, Inc. | Registration Statement on Form S 1, as amended (File No. 333 163275) | February 2, 2010 |
| 10.11.1 | Amendment No. 2 to the Collaboration Agreement, dated as of January 8, 2013, by and between Forest Laboratories, Inc. and Ironwood Pharmaceuticals, Inc. | Annual Report on Form 10 K (File No. 001 34620) | February 21, 2013 |
| 10.12+ | License Agreement, dated as of April 30, 2009, by and between Allergan Pharmaceuticals International Ltd. (formerly with Almirall, S.A.) and Ironwood Pharmaceuticals, Inc. | Registration Statement on Form S 1, as amended (File No. 333 163275) | February 2, 2010 |

Table of Contents

| | | Incorporated by reference herein | |
|---|---|---|---|
| Number | Description | Form | Date |
| 10.12.1+ | Amendment No. 1 to License Agreement, dated as of June 11, 2013, by and between Allergan Pharmaceuticals International Ltd. (formerly with Almirall, S.A.) and Ironwood Pharmaceuticals, Inc. | Quarterly Report on Form 10 Q (File No. 001 34620) | August 8, 2013 |
| 10.12.2+ | Amendment to the License Agreement, dated as of October 26, 2015, by and between Allergan Pharmaceuticals International Ltd. and Ironwood Pharmaceuticals, Inc. | Annual Report on Form 10 K (File No. 001 34620) | February 19, 2016 |
| 10.13+ | Novation Agreement, dated as of October 26, 2015, by and among Almirall, S.A., Allergan Pharmaceuticals International Ltd. and Ironwood Pharmaceuticals, Inc. | Annual Report on Form 10 K (File No. 001 34620) | February 19, 2016 |
| 10.14+ | License Agreement, dated as of November 10, 2009, by and among Astellas Pharma Inc. and Ironwood Pharmaceuticals, Inc. | Registration Statement on Form S 1, as amended (File No. 333 163275) | February 2, 2010 |
| 10.15+ | Collaboration Agreement, dated as of October 23, 2012, by and between AstraZeneca AB and Ironwood Pharmaceuticals, Inc. | Annual Report on Form 10 K (File No. 001 34620) | February 21, 2013 |
| 10.16+ | License Agreement, dated as of April 26, 2016, by and between Ardea Biosciences, Inc. and Ironwood Pharmaceuticals, Inc | Quarterly Report on Form 10 Q (File No. 001 34620) | August 8, 2016 |
| 10.17+ | Commercial Supply Agreement, dated as of June 23, 2010, by and among PolyPeptide Laboratories, Inc. and Polypeptide Laboratories (SWEDEN) AB, Forest Laboratories, Inc. and Ironwood Pharmaceuticals, Inc. | Quarterly Report on Form 10 Q (File No. 001 34620) | August 10, 2010 |
| 10.18+ | Commercial Supply Agreement, dated as of March 28, 2011, by and among Corden Pharma Colorado, Inc. (f/k/a Roche Colorado Corporation), Ironwood Pharmaceuticals, Inc. and Forest Laboratories, Inc. | Quarterly Report on Form 10 Q (File No. 001 34620) | May 13, 2011 |
| 10.18.1+ | Amendment No. 3 to Commercial Supply Agreement, dated as of November 26, 2013, by and between Corden Pharma Colorado, Inc. (f/k/a Roche Colorado Corporation), Ironwood Pharmaceuticals, Inc. and Forest Laboratories, Inc. | Annual Report on Form 10 K (File No. 001 34620) | February 7, 2014 |

Table of Contents

| | | Incorporated by reference herein | |
|---|---|---|---|
| Number | Description | Form | Date |
| 10.19+ | Commercial Supply Agreement, dated as of April 26, 2016, by and between AstraZeneca Pharmaceuticals LP and Ironwood Pharmaceuticals, Inc. | Quarterly Report on Form 10 Q (File No. 001 34620) | August 8, 2016 |
| 10.20 | Lease for facilities at 301 Binney St., Cambridge, MA, dated as of January 12, 2007, as amended on April 9, 2009, by and between Ironwood Pharmaceuticals, Inc. and BMR Rogers Street LLC | Registration Statement on Form S 1, as amended (File No. 333 163275) | December 23, 2009 |
| 10.20.1 | Second Amendment to Lease for facilities at 301 Binney St., Cambridge, MA, dated as of February 9, 2010, by and between Ironwood Pharmaceuticals, Inc. and BMR-Rogers Street LLC | Annual Report on Form 10-K (File No. 001-34620) | March 30, 2010 |
| 10.20.2 | Third Amendment to Lease for facilities at 301 Binney St., Cambridge, MA, dated as of July 1, 2010, by and between Ironwood Pharmaceuticals, Inc. and BMR Rogers Street LLC | Annual Report on Form 10 K (File No. 001 34620) | March 30, 2011 |
| 10.20.3 | Fourth Amendment to Lease for facilities at 301 Binney St., Cambridge, MA, dated as of February 3, 2011, by and between Ironwood Pharmaceuticals, Inc. and BMR Rogers Street LLC | Annual Report on Form 10 K (File No. 001 34620) | March 30, 2011 |
| 10.20.4 | Fifth Amendment to Lease for facilities at 301 Binney St., Cambridge, MA, dated as of October 18, 2011, by and between Ironwood Pharmaceuticals, Inc. and BMR Rogers Street LLC | Annual Report on Form 10 K (File No. 001 34620) | February 29, 2012 |
| 10.20.5 | Sixth Amendment to Lease for facilities at 301 Binney St., Cambridge, MA, dated as of July 19, 2012, by and between Ironwood Pharmaceuticals, Inc. and BMR Rogers Street LLC | Annual Report on Form 10 K (File No. 001 34620) | February 21, 2013 |
| 10.20.6 | Seventh Amendment to Lease for facilities at 301 Binney St., Cambridge, MA, dated as of October 30, 2012, by and between Ironwood Pharmaceuticals, Inc. and BMR Rogers Street LLC | Annual Report on Form 10 K (File No. 001 34620) | February 21, 2013 |
| 10.20.7 | Eighth Amendment to Lease for facilities at 301 Binney St., Cambridge, MA, dated as of July 8, 2014, by and between Ironwood Pharmaceuticals, Inc. and BMR Rogers Street LLC | Annual Report on Form 10 K (File No. 001 34620) | February 18, 2015 |

Table of Contents

| | | Incorporated by reference herein | |
|---|---|---|---|
| Number | Description | Form | Date |
| 10.20.8 | Ninth Amendment to Lease for facilities at 301 Binney St., Cambridge, MA, dated as of October 27, 2014, by and between Ironwood Pharmaceuticals, Inc. and BMR Rogers Street LLC | Annual Report on Form 10 K (File No. 001 34620) | February 18, 2015 |
| 10.20.9 | Tenth Amendment to Lease for facilities at 301 Binney St., Cambridge, MA, dated as of January 21, 2015, by and between Ironwood Pharmaceuticals, Inc. and BMR Rogers Street LLC | Annual Report on Form 10 K (File No. 001 34620) | February 18, 2015 |
| 10.20.10* | Eleventh Amendment to Lease for facilities at 301 Binney St., Cambridge, MA, dated as of June 30, 2016, by and between Ironwood Pharmaceuticals, Inc. and BMR Rogers Street LLC | | |
| 10.20.11 | Sublease, dated as of July 1, 2014, by and between Biogen Idec MA Inc. and Ironwood Pharmaceuticals, Inc. to Lease for facilities at 301 Binney St., Cambridge, MA, as amended, by and between Ironwood Pharmaceuticals, Inc. and BMR Rogers Street LLC | Annual Report on Form 10 K (File No. 001 34620) | February 18, 2015 |
| 10.21 | Base Call Option Transaction Confirmation, dated as of June 10, 2015, between Ironwood Pharmaceuticals, Inc. and JPMorgan Chase Bank, National Association, London Branch | Quarterly Report on Form 10 Q (File No. 001 34620) | August 7, 2015 |
| 10.22 | Base Call Option Transaction Confirmation, dated as of June 10, 2015, between Ironwood Pharmaceuticals, Inc. and Credit Suisse Capital LLC, through its agent Credit Suisse Securities (USA) LLC | Quarterly Report on Form 10 Q (File No. 001 34620) | August 7, 2015 |
| 10.23 | Base Warrants Confirmation, dated as of June 10, 2015, between Ironwood Pharmaceuticals, Inc. and JPMorgan Chase Bank, National Association, London Branch | Quarterly Report on Form 10 Q (File No. 001 34620) | August 7, 2015 |
| 10.24 | Base Warrants Confirmation, dated as of June 10, 2015, between Ironwood Pharmaceuticals, Inc. and Credit Suisse Capital LLC, through its agent Credit Suisse Securities (USA) LLC | Quarterly Report on Form 10 Q (File No. 001 34620) | August 7, 2015 |
| 10.25 | Additional Call Option Transaction Confirmation, dated as of June 22, 2015, between Ironwood Pharmaceuticals, Inc. and JPMorgan Chase Bank, National Association, London Branch | Quarterly Report on Form 10 Q (File No. 001 34620) | August 7, 2015 |

Table of Contents

| | | Incorporated by reference herein | |
|---|---|---|---|
| Number | Description | Form | Date |
| 10.26 | Additional Call Option Transaction Confirmation, dated as of June 22, 2015, between Ironwood Pharmaceuticals, Inc. and Credit Suisse Capital LLC, through its agent Credit Suisse Securities (USA) LLC | Quarterly Report on Form 10 Q (File No. 001 34620) | August 7, 2015 |
| 10.27 | Additional Warrants Confirmation, dated as of June 22, 2015, between Ironwood Pharmaceuticals, Inc. and JPMorgan Chase Bank, National Association, London Branch | Quarterly Report on Form 10 Q (File No. 001 34620) | August 7, 2015 |
| 10.28 | Additional Warrants Confirmation, dated as of June 22, 2015, between Ironwood Pharmaceuticals, Inc. and Credit Suisse Capital LLC, through its agent Credit Suisse Securities (USA) LLC | Quarterly Report on Form 10 Q (File No. 001 34620) | August 7, 2015 |
| 21.1* | Subsidiaries of Ironwood Pharmaceuticals, Inc. | | |
| 23.1* | Consent of Independent Registered Public Accounting Firm | | |
| 31.1* | Certification of Chief Executive Officer pursuant to Rules 13a 14 or 15d 14 of the Exchange Act | | |
| 31.2* | Certification of Chief Financial Officer pursuant to Rules 13a 14 or 15d 14 of the Exchange Act | | |
| 32.1‡ | Certification of Chief Executive Officer pursuant to Rules 13a 14(b) or 15d 14(b) of the Exchange Act and 18 U.S.C. Section 1350 | | |
| 32.2‡ | Certification of Chief Financial Officer pursuant to Rules 13a 14(b) or 15d 14(b) of the Exchange Act and 18 U.S.C. Section 1350 | | |
| 101.INS* | XBRL Instance Document | | |
| 101.SCH* | XBRL Taxonomy Extension Schema Document | | |
| 101.CAL* | XBRL Taxonomy Extension Calculation Linkbase Document | | |
| 101.LAB* | XBRL Taxonomy Extension Label Linkbase Database | | |
| 101.PRE* | XBRL Taxonomy Extension Presentation Linkbase Document | | |
| 101.DEF* | XBRL Taxonomy Extension Definition Linkbase Document | | |

*Filed herewith.

‡Furnished herewith.

Table of Contents

+Confidential treatment granted under 17 C.F.R. §§200.80(b)(4) and 230.406. The confidential portions of this exhibit have been omitted and are marked accordingly. The confidential portions have been provided separately to the SEC pursuant to the confidential treatment request.

#Management contract or compensatory plan, contract, or arrangement.

(b) Exhibits.

The exhibits required by this Item are listed under Item 15(a)(3).

(c) Financial Statement Schedules.

The financial statement schedules required by this Item are listed under Item 15(a)(2).

Table of Contents

SIGNATURES

Pursuant to the requirements of Section 13 or 15(d) of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned, thereunto duly authorized, in the City of Cambridge, Commonwealth of Massachusetts, on the 22nd day of February 2017.

Ironwood
Pharmaceuticals, Inc.
By: /s/ Peter M. Hecht
Peter M. Hecht
Chief Executive Officer

Pursuant to the requirements of Section 13 or 15(d) of the Securities Exchange Act of 1934, this report has been signed below by the following persons on behalf of the registrant and in the capacities and on the date indicated.

| Signature | Title | Date |
|---|---|---|
| /s/ Peter M. Hecht<br>Peter M. Hecht | Chief Executive Officer and Director (Principal Executive Officer) | February 22, 2017 |
| /s/ Thomas Graney<br>Thomas Graney | Chief Financial Officer (Principal Financial Officer) | February 22, 2017 |
| /s/ Gina Consylman<br>Gina Consylman | Vice President, Finance and Chief Accounting Officer (Principal Accounting Officer) | February 22, 2017 |
| /s/ Terrance G. McGuire<br>Terrance G. McGuire | Chairman of the Board | February 22, 2017 |
| /s/ Andrew Dreyfus<br>Andrew Dreyfus | Director | February 22, 2017 |
| /s/ Marsha H. Fanucci<br>Marsha H. Fanucci | Director | February 22, 2017 |
| /s/ Julie H. McHugh<br>Julie H. McHugh | Director | February 22, 2017 |
| /s/ Lawrence S. Olanoff<br>Lawrence S. Olanoff | Director | February 22, 2017 |
| /s/ Edward P. Owens<br>Edward P. Owens | Director | February 22, 2017 |
| /s/ Amy W. Schulman | Director | |

| | | |
|---|---|---|
| Amy W. Schulman | | February 22, 2017 |
| /s/ Christopher T. Walsh<br>Christopher T. Walsh | Director | February 22, 2017 |
| /s/ Douglas E. Williams<br>Douglas E. Williams | Director | February 22, 2017 |

Table of Contents

Index to Consolidated Financial Statements of

Ironwood Pharmaceuticals, Inc.

Table of Contents

REPORT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

To the Board of Directors and Shareholders of

Ironwood Pharmaceuticals, Inc.

We have audited the accompanying consolidated balance sheets of Ironwood Pharmaceuticals, Inc. as of December 31, 2016 and 2015, and the related consolidated statements of operations, 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 consolidated financial position of Ironwood Pharmaceuticals, Inc. at December 31, 2016 and 2015, and the consolidated 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), Ironwood 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 February 22, 2017 expressed an unqualified opinion thereon.

/s/ Ernst & Young LLP

Boston, Massachusetts
February 22, 2017

Table of Contents

Ironwood Pharmaceuticals, Inc.

Consolidated Balance Sheets

(In thousands, except share and per share amounts)

| | December 31, 2016 | December 31, 2015 |
|---|---|---|
| ASSETS | | |
| Current assets: | | |
| Cash and cash equivalents | $ 54,004 | $ 261,287 |
| Available-for-sale securities | 251,212 | 178,107 |
| Accounts receivable | 933 | 2,884 |
| Related party accounts receivable, net | 63,921 | 51,634 |
| Inventory | 1,081 | — |
| Prepaid expenses and other current assets | 9,030 | 6,293 |
| Total current assets | 380,181 | 500,205 |
| Restricted cash | 8,247 | 8,747 |
| Property and equipment, net | 20,512 | 21,075 |
| Convertible note hedges | 132,521 | 86,466 |
| Intangible assets, net | 166,119 | — |
| Goodwill | 785 | — |
| Other assets | 1,456 | 2,628 |
| Total assets | $ 709,821 | $ 619,121 |
| LIABILITIES AND STOCKHOLDERS' EQUITY | | |
| Current liabilities: | | |
| Accounts payable | $ 17,702 | $ 8,586 |
| Related party accounts payable, net | 1 | 3 |
| Accrued research and development costs | 6,937 | 4,245 |
| Accrued expenses and other current liabilities | 38,301 | 23,301 |
| Current portion of capital lease obligations | 6,227 | 2,631 |
| Current portion of deferred rent | 7,719 | 5,544 |
| Current portion of deferred revenue | — | 7,191 |
| Current portion of PhaRMA notes payable | — | 24,964 |
| Current portion of contingent consideration | 14,244 | — |
| Total current liabilities | 91,131 | 76,465 |
| Capital lease obligations, net of current portion | 82 | 306 |
| Deferred rent, net of current portion | 557 | 6,395 |
| Deferred revenue, net of current portion | — | 1,798 |
| Contingent consideration, net of current portion | 63,416 | — |
| Note hedge warrants | 113,237 | 75,328 |
| Convertible senior notes | 234,243 | 220,620 |
| PhaRMA notes payable, net of current portion | 132,249 | 132,964 |
| Other liabilities | 8,190 | 10,120 |
| Commitments and contingencies | | |
| Stockholders’ equity: | | |

| | | |
|---|---|---|
| Preferred stock, $0.001 par value, 75,000,000 shares authorized, no shares issued and outstanding | — | — |
| Class A common stock, $0.001 par value, 500,000,000 shares authorized and 132,631,387 and 127,371,478 shares issued and outstanding at December 31, 2016 and December 31, 2015, respectively | 133 | 127 |
| Class B common stock, $0.001 par value, 100,000,000 shares authorized and 14,784,077 shares issued, 14,484,077 shares outstanding, and 15,870,356 shares issued and outstanding at December 31, 2016 and December 31, 2015, respectively | 15 | 16 |
| Additional paid-in capital | 1,258,398 | 1,205,183 |
| Accumulated deficit | (1,191,823) | (1,110,115) |
| Accumulated other comprehensive loss | (7) | (86) |
| Total stockholders' equity | 66,716 | 95,125 |
| Total liabilities and stockholders' equity | $ 709,821 | $ 619,121 |

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

Table of Contents

Ironwood Pharmaceuticals, Inc.

Consolidated Statements of Operations

(In thousands, except per share amounts)

| | Years Ended December 31, | | |
|---|---|---|---|
| | 2016 | 2015 | 2014 |
| Collaborative arrangements revenue | $ 273,957 | $ 149,555 | $ 76,436 |
| Cost and expenses: | | | |
| Cost of revenues, excluding amortization of acquired intangible asset | 1,868 | 12 | 5,291 |
| Write-down of inventory to net realizable value and loss on non-cancellable purchase commitments | 374 | 17,638 | 20,292 |
| Research and development | 139,492 | 108,746 | 101,890 |
| Selling, general and administrative | 173,281 | 125,247 | 118,333 |
| Amortization of acquired intangible asset | 981 | — | — |
| Loss on fair value remeasurement of contingent consideration | 9,831 | — | — |
| Total cost and expenses | 325,827 | 251,643 | 245,806 |
| Loss from operations | (51,870) | (102,088) | (169,370) |
| Other (expense) income: | | | |
| Interest expense | (39,153) | (31,096) | (21,166) |
| Interest and investment income | 1,169 | 443 | 257 |
| Gain (loss) on derivatives | 8,146 | (9,928) | — |
| Other income | — | — | 661 |
| Other expense, net | (29,838) | (40,581) | (20,248) |
| Net loss | $ (81,708) | $ (142,669) | $ (189,618) |
| Net loss per share—basic and diluted | $ (0.56) | $ (1.00) | $ (1.39) |
| Weighted average number of common shares used in net loss per share—basic and diluted: | 144,928 | 142,155 | 136,811 |

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

Table of Contents

Ironwood Pharmaceuticals, Inc.

Consolidated Statements of Comprehensive Loss

(In thousands)

| | Years Ended December 31, | | |
|---|---|---|---|
| | 2016 | 2015 | 2014 |
| Net loss | $ (81,708) | $ (142,669) | $ (189,618) |
| Other comprehensive income (loss): | | | |
| Unrealized gains (losses) on available-for-sale securities | 79 | (67) | (21) |
| Total other comprehensive income (loss) | 79 | (67) | (21) |
| Comprehensive loss | $ (81,629) | $ (142,736) | $ (189,639) |

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

Table of Contents

Ironwood Pharmaceuticals, Inc.

Consolidated Statements of Stockholders' Equity

(In thousands, except share amounts)

| | Class A common stock | | Class B common stock | | Additional paid-in | Accumulated | Accumulated other comprehensive income | Total Stockholders' |
|---|---|---|---|---|---|---|---|---|
| | Shares | Amount | Shares | Amount | capital | deficit | (loss) | equity |
| Balance at December 31, 2013 | 102,803,093 | $ 103 | 18,362,037 | $ 18 | $ 815,930 | $ (777,828) | $ 2 | $ 38,225 |
| Issuance of common stock upon exercise of stock options and employee stock purchase plan | 1,705,752 | 2 | 1,876,880 | 2 | 23,328 | — | — | 23,332 |
| Issuance of common stock awards | 290,843 | — | — | — | 22 | — | — | 22 |
| Issuance of common stock upon public offering, net of offering costs of $10.8 million | 15,784,325 | 16 | — | — | 190,412 | — | — | 190,428 |
| Conversion of Class B common stock to Class A common stock | 4,331,645 | 4 | (4,331,645) | (4) | — | — | — | — |
| Share-based compensation expense related to issuance of stock options to non-employees | — | — | — | — | 2,618 | — | — | 2,618 |
| Share-based compensation expense related to share-based awards to employees and employee stock purchase plan | — | — | — | — | 23,566 | — | — | 23,566 |
| Restricted common shares subject to repurchase | — | — | — | — | | — | — | |
| | — | — | — | — | — | — | (21) | (21) |

| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| Unrealized losses on available-for-sale securities | | | | | | | | |
| Net loss | — | — | — | — | — | (189,618) | — | (189,618) |
| Balance at December 31, 2014 | 124,915,658 | 125 | 15,907,272 | 16 | 1,055,876 | (967,446) | (19) | 88,552 |
| Issuance of common stock upon exercise of stock options and employee stock purchase plan | 972,325 | 1 | 1,293,032 | 1 | 13,619 | — | — | 13,621 |
| Issuance of common stock awards | 153,547 | — | — | — | 24 | — | — | 24 |
| Conversion of Class B common stock to Class A common stock | 1,329,948 | 1 | (1,329,948) | (1) | — | — | — | — |
| Share-based compensation expense related to share-based awards to employees and employee stock purchase plan | — | — | — | — | 25,448 | — | — | 25,448 |
| Equity component of convertible debt | — | — | — | — | 114,199 | — | — | 114,199 |
| Equity component of deferred financing costs for convertible debt | — | — | — | — | (3,983) | — | — | (3,983) |
| Unrealized losses on available-for-sale securities | — | — | — | — | — | — | (67) | (67) |
| Net loss | — | — | — | — | — | (142,669) | — | (142,669) |
| Balance at December 31, 2015 | 127,371,478 | 127 | 15,870,356 | 16 | 1,205,183 | (1,110,115) | (86) | 95,125 |
| Issuance of common stock upon exercise of stock options and employee stock purchase plan | 1,813,018 | 3 | 1,867,111 | 2 | 23,996 | — | — | 24,001 |
| Issuance of common stock awards | 193,501 | — | — | — | 20 | — | — | 20 |
| Conversion of Class B common | 3,253,390 | 3 | (3,253,390) | (3) | — | — | — | — |

| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| stock to Class A common stock | | | | | | | | |
| Share-based compensation expense related to share-based awards to non-employees | — | — | — | — | 529 | — | — | 529 |
| Share-based compensation expense related to share-based awards to employees and employee stock purchase plan | — | — | — | — | 28,670 | — | — | 28,670 |
| Unrealized gains on available-for-sale securities | — | — | — | — | — | — | 79 | 79 |
| Net loss | — | — | — | — | — | (81,708) | — | (81,708) |
| Balance at December 31, 2016 | 132,631,387 | $ 133 | 14,484,077 | $ 15 | $ 1,258,398 | $ (1,191,823) | $ (7) | $ 66,716 |

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

Table of Contents

Ironwood Pharmaceuticals, Inc.

Consolidated Statements of Cash Flows

(In thousands)

| | Year Ended December 31, | | |
|---|---|---|---|
| | 2016 | 2015 | 2014 |
| Cash flows from operating activities: | | | |
| Net loss | $ (81,708) | $ (142,669) | $ (189,618) |
| Adjustments to reconcile net loss to net cash used in operating activities: | | | |
| Depreciation and amortization | 10,279 | 11,630 | 12,331 |
| Amortization of acquired intangible asset | 981 | — | — |
| (Gain) loss on disposal of property and equipment | (204) | (196) | 119 |
| Share-based compensation expense | 29,219 | 25,469 | 26,184 |
| Change in fair value of note hedge warrants | 37,909 | 4,479 | — |
| Change in fair value of convertible note hedges | (46,055) | 5,449 | — |
| Write-down of inventory to net realizable value and loss on non-cancellable purchase commitments | 374 | 17,638 | 20,292 |
| Loss on facility subleases | 3,480 | 296 | 2,573 |
| Accretion of discount/premium on investment securities | 667 | 1,114 | 1,085 |
| Non-cash interest expense | 14,812 | 8,102 | 1,566 |
| Non-cash change in fair value of contingent consideration | 9,831 | — | — |
| Changes in assets and liabilities: | | | |
| Accounts receivable and related party accounts receivable | (10,336) | (28,679) | (23,680) |
| Restricted cash | 500 | (600) | — |
| Prepaid expenses and other current assets | (3,069) | 2,568 | (3,947) |
| Inventory | — | — | (3,078) |
| Other assets | 1,644 | 414 | (2,876) |
| Accounts payable, related party accounts payable and accrued expenses | 19,683 | (1,551) | 1,425 |
| Accrued research and development costs | 2,692 | 671 | 162 |
| Deferred revenue | (8,989) | (7,191) | 744 |
| Deferred rent | (7,143) | (3,871) | 1,811 |
| Other liabilities | — | — | (661) |
| Net cash used in operating activities | (25,433) | (106,927) | (155,568) |
| Cash flows from investing activities: | | | |
| Purchases of available-for-sale securities | (311,116) | (281,958) | (253,995) |
| Sales and maturities of available-for-sale securities | 237,423 | 276,707 | 200,964 |
| Purchases of property and equipment | (4,206) | (4,049) | (3,538) |
| Payment for acquisition of lesinurad license | (100,000) | — | — |
| Proceeds from sale of property and equipment | 225 | 147 | — |
| Net cash used in investing activities | (177,674) | (9,153) | (56,569) |
| Cash flows from financing activities: | | | |
| Proceeds from issuance of convertible senior notes | — | 335,699 | — |

| | | | |
|---|---|---|---|
| Proceeds from issuance of common stock | — | — | 190,428 |
| Costs associated with issuance of 2026 notes | (246) | — | — |
| Proceeds from issuance of note hedge warrants | — | 70,849 | — |
| Purchase of convertible note hedges | — | (91,915) | — |
| Costs associated with issuance of convertible senior notes | — | (11,730) | — |
| Proceeds from exercise of stock options and employee stock purchase plan | 24,841 | 14,196 | 22,741 |
| Payments on capital leases | (1,903) | (1,317) | (1,062) |
| Principal payments on PhaRMA notes | (26,868) | (12,712) | (1,163) |
| Net cash (used in) provided by financing activities | (4,176) | 303,070 | 210,944 |
| Net (decrease) increase in cash and cash equivalents | (207,283) | 186,990 | (1,193) |
| Cash and cash equivalents, beginning of period | 261,287 | 74,297 | 75,490 |
| Cash and cash equivalents, end of period | $ 54,004 | $ 261,287 | $ 74,297 |
| Supplemental cash flow disclosure: | | | |
| Cash paid for interest | $ 24,473 | $ 22,742 | $ 19,606 |
| Non-cash investing activities | | | |
| Contingent consideration | $ 67,885 | $ — | $ — |
| Purchases under capital leases | $ 6,277 | $ 2,957 | $ 766 |
| Disposals under capital leases | $ (1,001) | $ (2,529) | $ — |
| Fixed asset purchases in accounts payable and accrued expenses | $ 353 | $ 98 | $ 1,592 |

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

Table of Contents

Ironwood Pharmaceuticals, Inc.

Notes to Consolidated Financial Statements

1. Nature of Business

Ironwood Pharmaceuticals, Inc. (the "Company") is a commercial biotechnology company leveraging its proven development and commercial capabilities as it seeks to bring multiple medicines to patients. The Company is advancing innovative product opportunities in areas of large unmet need, including irritable bowel syndrome with constipation ("IBS-C"), and chronic idiopathic constipation ("CIC"), hyperuricemia associated with uncontrolled gout, uncontrolled gastroesophageal reflux disease ("uncontrolled GERD"), and vascular and fibrotic diseases.

The Company's first commercial product, linaclotide, is available to adult men and women suffering from IBS-C or CIC in the United States (the "U.S."), under the trademarked name LINZESS®, and is available to adult men and women suffering from IBS-C in certain European countries under the trademarked name CONSTELLA®. The Company and its U.S. partner Allergan plc (together with its affiliates, "Allergan"), began commercializing LINZESS in the U.S. in December 2012. Under the Company's collaboration with Allergan for North America, total net sales of LINZESS in the U.S., as recorded by Allergan, are reduced by commercial costs incurred by each party, and the resulting amount is shared equally between the Company and Allergan. The Company's former European partner, Almirall, S.A. ("Almirall"), began commercializing CONSTELLA in Europe for the symptomatic treatment of moderate to severe IBS-C in adults in the second quarter of 2013. In October 2015, Almirall transferred its exclusive license to develop and commercialize linaclotide in Europe to Allergan, and the Company and Allergan entered into an amendment to the European license agreement. Currently, CONSTELLA is commercially available in a number of European countries, including the United Kingdom, Italy and Spain. In January 2017, the Company and Allergan entered into an amendment to the European license agreement, pursuant to which the license granted to Allergan was extended to a territory consisting of all countries worldwide not previously covered by the European license agreement, other than China, Hong Kong, Macau, Japan, and the countries and territories of North America. On a country-by-country and product-by-product basis in such additional territory, Allergan will pay the Company an annual royalty as a percentage of net sales of products containing linaclotide as an active ingredient (Note 20).

In December 2013 and February 2014, linaclotide was approved in Canada and Mexico, respectively, as a treatment for adult men and women suffering from IBS-C or CIC. Allergan has exclusive rights to commercialize linaclotide in Canada as CONSTELLA and in Mexico as LINZESS. In May 2014, CONSTELLA became commercially available in Canada and in June 2014, LINZESS became commercially available in Mexico. Astellas Pharma Inc. ("Astellas"), the Company's partner in Japan, is developing linaclotide for the treatment of patients with IBS-C and chronic constipation in Japan. In December 2016, Astellas secured approval of linaclotide for the treatment of adults with IBS-C in Japan. In October 2012, the Company entered into a collaboration agreement with AstraZeneca AB (together with its affiliates, "AstraZeneca"), to co-develop and co-commercialize linaclotide in China, Hong Kong and Macau, with AstraZeneca having primary responsibility for the local operational execution. In December 2015, the Company and AstraZeneca filed for approval with the China Food and Drug Administration ("CFDA"), to market linaclotide in China.

The Company and Allergan are also advancing two linaclotide colonic release formulations. Linaclotide colonic release-1 (“CR1”), is a second generation product candidate with the potential to improve abdominal pain relief in adult IBS-C patients. Linaclotide colonic release-2 (“CR2”), is a product candidate with the potential to improve abdominal pain in patients with additional gastrointestinal (“GI”), disorders where lower abdominal pain is a predominant symptom such as non-constipation subtypes of IBS. Further, the Company and Allergan are exploring ways to enhance the clinical profile of LINZESS by studying linaclotide in additional indications and populations to assess its potential to treat various GI conditions. Linaclotide is being developed and commercialized in other parts of the world by certain of the Company’s partners.

The Company is also advancing another GI development program, IW-3718, a gastric retentive formulation of a bile acid sequestrant with the potential to provide symptomatic relief in patients with uncontrolled GERD.

In April 2016, the Company discontinued development of IW-9179 for gastroparesis, as top-line data from its exploratory Phase IIa clinical study indicated that IW-9179 did not meaningfully reduce the severity of symptoms in

Table of Contents

patients with diabetic gastroparesis. In July 2016, the Company discontinued advancing IW-9179 for the treatment of functional dyspepsia and is no longer advancing the program.

In June 2016, the Company closed a transaction with AstraZeneca (the "Lesinurad Transaction") pursuant to which the Company received an exclusive license to develop, manufacture, and commercialize in the U.S. products containing lesinurad as an active ingredient (the "Lesinurad License"), including ZURAMPIC® and DUZALLOTM. Lesinurad 200mg tablets were approved as ZURAMPIC by the U.S. Food and Drug Administration ("FDA") in December 2015 for use in combination with a xanthine oxidase inhibitor ("XOI") for the treatment of hyperuricemia associated with uncontrolled gout. In October 2016, ZURAMPIC became commercially available in the U.S. The Company is developing DUZALLO, a fixed-dose combination product of lesinurad and allopurinol, an XOI, which is included under the Lesinurad License. In January 2017, the FDA accepted for review a new drug application ("NDA"), for DUZALLO for the treatment of hyperuricemia in patients with uncontrolled gout.

The Company periodically enters into co-promotion agreements to maximize salesforce efficiency. The Company and Exact Sciences Corp. ("Exact Sciences") entered into an agreement (the "Cologuard Co-Promotion Agreement") to co-promote Cologuard®, the first and only FDA-approved noninvasive stool DNA screening test for colorectal cancer in March 2015. The parties co-promoted Cologuard through July 2016 and the Cologuard Co-Promotion Agreement was terminated in August 2016. Under the terms of the Cologuard Co-Promotion Agreement, the Company will continue to receive royalty payments through July 2017. In August 2015, the Company and Allergan entered into an agreement for the co-promotion of VIBERZI™ (eluxadoline) in the U.S., Allergan's treatment for adults suffering from IBS with diarrhea ("IBS-D").

In January 2017, the Company and Allergan entered into a commercial agreement under which the adjustments to the Company's or Allergan's share of the net profits under the share adjustment provision of the collaboration agreement for linaclotide in North America are eliminated, in full, in 2018 and all subsequent years (Note 20).

These agreements are more fully described in Note 4, Business Combinations, and Note 5, Collaboration, License, Co promotion and Other Commercial Agreements, to these consolidated financial statements.

In June 2015, the Company issued approximately $335.7 million in aggregate principal amount of 2.25% Convertible Senior Notes due 2022 (the "2022 Notes"). The Company received net proceeds of approximately $324.0 million from the sale of the 2022 Notes, after deducting fees and expenses of approximately $11.7 million. In September 2016, the Company closed a direct private placement, pursuant to which the Company subsequently issued $150.0 million in aggregate principal amount of 8.375% notes due 2026 (the "2026 Notes") on January 5, 2017 (the "Funding Date"). The proceeds from the issuance of the 2026 Notes were used to redeem the outstanding principal balance of the 11% PhaRMA Notes due 2024 (the "PhaRMA Notes"), on the Funding Date. These transactions are more fully described in Note 11, Notes Payable, to these consolidated financial statements.

The Company was incorporated in Delaware on January 5, 1998 as Microbia, Inc. On April 7, 2008, the Company changed its name to Ironwood Pharmaceuticals, Inc. To date, the Company has dedicated a majority of its activities to the research, development and commercialization of linaclotide, as well as to the research and development of its other product candidates. The Company has incurred significant operating losses since its inception in 1998. As of December 31, 2016, the Company had an accumulated deficit of approximately $1.2 billion.

2. Summary of Significant Accounting Policies

Principles of Consolidation

The accompanying consolidated financial statements include the accounts of Ironwood Pharmaceuticals, Inc. and its wholly owned subsidiaries, Ironwood Pharmaceuticals Securities Corporation and Ironwood Pharmaceuticals GmbH. All intercompany transactions and balances are eliminated in consolidation.

Segment Information

Operating segments are components of an enterprise for which separate financial information is available and is evaluated regularly by the Company’s chief operating decision maker in deciding how to allocate resources and in assessing performance. The Company currently operates in one reportable business segment—human therapeutics.

Table of Contents

Use of Estimates

The preparation of consolidated financial statements in accordance with U.S. generally accepted accounting principles requires the Company's management to make estimates and judgments that may affect the reported amounts of assets and liabilities and disclosure of contingent assets and liabilities at the date of the consolidated financial statements, and the amounts of revenues and expenses during the reported periods. On an on-going basis, the Company's management evaluates its estimates, judgments and methodologies. Significant estimates and assumptions in the consolidated financial statements include those related to revenue recognition, including returns, rebates, and other pricing adjustments; available-for-sale securities; inventory valuation, and related reserves; impairment of long-lived assets; initial valuation procedures for the issuance of convertible notes; fair value of derivatives; balance sheet classification of notes payable and convertible notes; income taxes, including the valuation allowance for deferred tax assets; research and development expenses; goodwill; contingent consideration; acquired intangible assets; contingencies and share-based compensation. The Company bases its estimates on historical experience and on various other assumptions that are believed to be reasonable, the results of which form the basis for making judgments about the carrying values of assets and liabilities. Actual results may differ materially from these estimates under different assumptions or conditions. Changes in estimates are reflected in reported results in the period in which they become known.

Cash and Cash Equivalents

The Company considers all highly liquid investment instruments with a remaining maturity when purchased of three months or less to be cash equivalents. Investments qualifying as cash equivalents primarily consist of money market funds and U.S. government sponsored securities. The carrying amount of cash equivalents approximates fair value. The amount of cash equivalents included in cash and cash equivalents was approximately $32.5 million and approximately $258.2 million at December 31, 2016 and 2015, respectively.

Restricted Cash

The Company is contingently liable under unused letters of credit with a bank, related to the Company's facility lease and automobile lease agreements, in the amount of approximately $8.2 million and approximately $8.7 million as of December 31, 2016 and 2015, respectively. As a result, the Company has restricted cash of approximately $8.2 million and approximately $8.7 million as of December 31, 2016 and 2015, respectively, securing these letters of credit. The cash will be restricted until the termination or modification of the lease arrangements.

Available for Sale Securities

The Company classifies all short term investments with a remaining maturity when purchased of greater than three months as available for sale. Available for sale securities are recorded at fair value, with the unrealized gains and losses reported in other comprehensive income (loss). The amortized cost of debt securities in this category is adjusted for the amortization of premiums and accretion of discounts to maturity. Such amortization is included in interest and investment income. Realized gains and losses, interest, dividends, and declines in value judged to be other than temporary on available for sale securities are included in interest and investment income.

The cost of securities sold is based on the specific identification method for purposes of recording realized gains and losses. To determine whether an other than temporary impairment exists, the Company considers whether it has the ability and intent to hold the investment until a market price recovery, and whether evidence indicating the recoverability of the cost of the investment outweighs evidence to the contrary. There were no other than temporary impairments for the years ended December 31, 2016, 2015 or 2014.

Inventory

Inventory is stated at the lower of cost or net realizable value with cost determined under the first in, first out basis in accordance with Accounting Standards Update ("ASU") No. 2015-11, Inventory (Topic 330): Simplifying the Measurement of Inventory ("ASU 2015-11").

The Company evaluates inventory levels quarterly and any inventory that has a cost basis in excess of its expected net realizable value, inventory that becomes obsolete, inventory in excess of expected sales requirements,

Table of Contents

inventory that fails to meet commercial sale specifications or is otherwise impaired is written down with a corresponding charge to the statement of operations in the period that the impairment is first identified. The Company also assesses, on a quarterly basis, whether it has any excess non-cancelable purchase commitments resulting from its minimum supply agreements with its suppliers. The Company relies on data from several sources to estimate the net realizable value of inventory and non-cancelable purchase commitments, including partner forecasts of projected inventory purchases that are received quarterly, the Company's internal forecasts and related process, historical sales by geographic region, and the status of and progress toward commercialization of linaclotide in partnered territories.

The Company capitalizes inventories manufactured in preparation for initiating sales of a product candidate when the related product candidate is considered to have a high likelihood of regulatory approval and the related costs are expected to be recoverable through sales of the inventories. In determining whether or not to capitalize such inventories, the Company evaluates, among other factors, information regarding the product candidate's safety and efficacy, the status of regulatory submissions and communications with regulatory authorities and the outlook for commercial sales, including the existence of current or anticipated competitive drugs and the availability of reimbursement. In addition, the Company evaluates risks associated with manufacturing the product candidate, including the ability of the Company's third party suppliers to complete the validation batches, and the remaining shelf life of the inventories.

Costs associated with developmental products prior to satisfying the inventory capitalization criteria are charged to research and development expense as incurred.

Concentrations of Suppliers

The Company relies on third party manufacturers and its collaboration partners to manufacture the linaclotide active pharmaceutical ingredient ("API"), linaclotide drug product and lesinurad drug product.

Currently, there are two third party manufacturers approved for the production of the linaclotide API in three facilities. Each of Allergan and Astellas is responsible for drug product manufacturing of linaclotide into finished product for its respective territory. Under the Company's linaclotide collaboration with AstraZeneca, the Company is responsible for drug product and finished goods manufacturing for China, Hong Kong and Macau. The Company also has an agreement with another independent third party to serve as a second source of API manufacturing of linaclotide for its partnered territories.

In connection with the Lesinurad License with AstraZeneca, the Company and AstraZeneca entered into a commercial supply agreement (the "Lesinurad CSA"), pursuant to which the Company relies exclusively on AstraZeneca for the commercial manufacture and supply of ZURAMPIC and, if approved, DUZALLO.

If any of the Company's suppliers were to limit or terminate production or otherwise fail to meet the quality or delivery requirements needed to satisfy the supply commitments, the process of locating and qualifying alternate sources could require up to several months, during which time the Company's production could be delayed. Such delays could have a material adverse effect on the Company's business, financial position and results of operations.

Accounts Receivable and Related Valuation Account

The Company makes judgments as to its ability to collect outstanding receivables and provides an allowance for receivables when collection becomes doubtful. Provisions are made based upon a specific review of all significant outstanding invoices and the overall quality and age of those invoices not specifically reviewed. The Company's receivables primarily relate to amounts reimbursed under its collaboration, license and co-promotion agreements. The Company believes that credit risks associated with these partners are not significant. To date, the Company has not

had any write-offs of bad debt, and the Company did not have an allowance for doubtful accounts as of December 31, 2016 and 2015.

In connection with the Lesinurad License, the Company and AstraZeneca entered into a transitional service agreement, ("the Lesinurad TSA"), pursuant to which AstraZeneca is providing certain support services, including development, regulatory and commercial services, to the Company for ZURAMPIC until such activities under the Lesinurad TSA are transferred to the Company. Under the Lesinurad TSA, AstraZeneca is facilitating the collections of sales of ZURAMPIC in the U.S. While under the Lesinurad TSA, the receivables due from AstraZeneca for sales of

Table of Contents

ZURAMPIC in the U.S. are net against payables due to AstraZeneca for costs incurred in connection with the lesinurad activities, resulting in a net payable at December 31, 2016.

Concentrations of Credit Risk

Financial instruments that subject the Company to credit risk primarily consist of cash and cash equivalents, restricted cash, available for sale securities, and accounts receivable. The Company maintains its cash and cash equivalent balances with high quality financial institutions and, consequently, the Company believes that such funds are subject to minimal credit risk. The Company's available for sale investments primarily consist of U.S. Treasury securities and certain U.S. government sponsored securities and potentially subject the Company to concentrations of credit risk. The Company has adopted an investment policy which limits the amounts the Company may invest in any one type of investment, and requires all investments held by the Company to be at least A+ rated, thereby reducing credit risk exposure.

Accounts receivable, including related party accounts receivable, primarily consist of amounts due under the linaclotide collaboration agreement with Allergan for North America and the linaclotide license agreement with Astellas for Japan (Note 5) for which the Company does not obtain collateral. Accounts receivable or payable to or from Allergan are presented as related party transactions on the consolidated balance sheets as Allergan owns common stock of the Company.

The percentages of revenue recognized from significant customers of the Company in the years ended December 31, 2016, 2015 and 2014 as well as the account receivable balances, net of any payables due, at December 31, 2016 and 2015 are included in the following table:

| | Accounts Receivable | | Revenue | | |
|---|---|---|---|---|---|
| | December 31, | | Year Ended December 31, | | |
| | 2016 | 2015 | 2016 | 2015 | 2014 |
| Collaborative Partner: | | | | | |
| Linaclotide Agreements: | | | | | |
| Allergan (North America and Europe)(1) | 99 % | 95 % | 82 % | 90 % | 62 % |
| Almirall (Europe) (1) | — % | — % | — % | — % | 10 % |
| Astellas (Japan) | — % | 2 % | 16 % | 5 % | 23 % |

(1) In October 2015, Almirall transferred its exclusive license to develop and commercialize linaclotide in Europe to Allergan.

For the years ended December 31, 2016, 2015 and 2014, no additional customers accounted for more than 10% of the Company's revenue.

Property and Equipment

Property and equipment, including leasehold improvements, are recorded at cost, and are depreciated when placed into service using the straight line method based on their estimated useful lives as follows:

| Asset Description | Estimated Useful Life (In Years) |
|---|---|
| Manufacturing equipment | 10 |
| Laboratory equipment | 5 |
| Computer and office equipment | 3 |
| Furniture and fixtures | 7 |
| Software | 3 |

Included in property and equipment are certain costs of software obtained for internal use. Costs incurred during the preliminary project stage are expensed as incurred, while costs incurred during the application development stage are capitalized and amortized over the estimated useful life of the software. The Company also capitalizes costs related to specific upgrades and enhancements when it is probable the expenditures will result in additional functionality. Maintenance and training costs related to software obtained for internal use are expensed as incurred.

Table of Contents

Leasehold improvements are amortized over the shorter of the estimated useful life of the asset or the lease term. Capital lease assets are amortized over the lease term. However, if ownership was transferred by the end of the capital lease, or there was a bargain purchase option, such capital lease assets would be amortized over the useful life that would be assigned if such assets were owned.

Costs for capital assets not yet placed into service have been capitalized as construction in progress, and will be depreciated in accordance with the above guidelines once placed into service. Maintenance and repair costs are expensed as incurred.

Finite and Indefinite-Lived Intangible Assets

The Company records the fair value of purchased intangible assets with finite useful lives as of the transaction date of a business combination. Purchased intangible assets with finite useful lives are amortized to their estimated residual values over their estimated useful lives. The Company evaluates the finite-lived intangible assets for impairment whenever events or changes in circumstances indicate the reduction in the fair value below their respective carrying amounts. If the Company determines that an impairment has occurred, a write-down of the carrying value and an impairment charge to operating expenses in the period the determination is made is recorded. In addition, the remaining estimated useful life of the finite-lived intangible asset would be reassessed.

In accordance with Accounting Standards Codification ("ASC") Topic 350, Intangibles – Goodwill and Other ("ASC 350"), during the period that an asset is considered indefinite-lived, such as in-process research and development ("IPR&D"), it will not be amortized. Acquired IPR&D represents the fair value assigned to research and development assets that have not reached technological feasibility. The value assigned to acquired IPR&D is determined by estimating the costs to develop the acquired technology into commercially viable products, estimating the resulting revenue from the projects, and discounting the net cash flows to present value. The revenue and costs projections used to value acquired IPR&D are, as applicable, reduced based on the probability of success of developing a new drug. Additionally, the projections consider the relevant market sizes and growth factors, expected trends in technology, and the nature and expected timing of new product introductions by the Company and its competitors. The rates utilized to discount the net cash flows to their present value are commensurate with the stage of development of the projects and uncertainties in the economic estimates used in the projections. Upon the acquisition of IPR&D, the Company completes an assessment of whether its acquisition constitutes the purchase of a single asset or a group of assets. Multiple factors are considered in this assessment, including the nature of the technology acquired, the presence or absence of separate cash flows, the development process and stage of completion, quantitative significance and the rationale for entering into the transaction. Indefinite-lived assets are maintained on the Company's consolidated balance sheet until either the project underlying it is completed or the asset becomes impaired. Indefinite-lived assets are tested for impairment on an annual basis, or whenever events or changes in circumstances indicate the reduction in the fair value of the IPR&D asset below its respective carrying amount. If the Company determines that an impairment has occurred, a write-down of the carrying value and an impairment charge to operating expenses in the period the determination is made is recorded. When development of an IPR&D asset is complete the associated asset is deemed finite-lived and is then amortized based on its respective estimated useful life at that point.

Goodwill

Goodwill represents the difference between the purchase price and the fair value of the identifiable tangible and intangible net assets when accounted for using the purchase method of accounting. Goodwill is not amortized, but is reviewed for impairment. The Company tests its goodwill for impairment annually, or whenever events or changes in circumstances indicate an impairment may have occurred, by comparing its carrying value to its implied fair value in accordance with ASC 350. Impairment may result from, among other things, deterioration in the performance of the acquired asset, adverse market conditions, adverse changes in applicable laws or regulations and a variety of other circumstances. If the Company determines that an impairment has occurred, a write-down of the carrying value and an impairment charge to operating expenses in the period the determination is made is recorded. In evaluating the carrying value of goodwill, the Company must make assumptions regarding estimated future cash flows and other factors. Changes in strategy or market conditions could significantly impact those judgments in the future and require an adjustment to the recorded balances.

Table of Contents

Impairment of Long Lived Assets

The Company regularly reviews the carrying amount of its long lived assets to determine whether indicators of impairment may exist, which warrant adjustments to carrying values or estimated useful lives. If indications of impairment exist, projected future undiscounted cash flows associated with the asset are compared to the carrying amount to determine whether the asset's value is recoverable. If the carrying value of the asset exceeds such projected undiscounted cash flows, the asset will be written down to its estimated fair value. There were no significant impairments of long lived assets for the years ended December 31, 2016, 2015, or 2014.

Income Taxes

The Company provides for income taxes under the liability method. Deferred tax assets and liabilities are determined based on differences between financial reporting and tax bases of assets and liabilities and are measured using the enacted tax rates in effect when the differences are expected to reverse. Deferred tax assets are reduced by a valuation allowance to reflect the uncertainty associated with their ultimate realization.

The Company accounts for uncertain tax positions recognized in the consolidated financial statements in accordance with the provisions of ASC Topic 740, Income Taxes, by prescribing a more-likely-than-not threshold for financial statement recognition and measurement of a tax position taken or expected to be taken in a tax return. When uncertain tax positions exist, the Company recognizes the tax benefit of tax positions to the extent that the benefit will more likely than not be realized. The determination as to whether the tax benefit will more likely than not be realized is based upon the technical merits of the tax position as well as consideration of the available facts and circumstances. The Company evaluates uncertain tax positions on a quarterly basis and adjusts the level of the liability to reflect any subsequent changes in the relevant facts surrounding the uncertain positions. Any changes to these estimates, based on the actual results obtained and/or a change in assumptions, could impact the Company's income tax provision in future periods. Interest and penalty charges, if any, related to unrecognized tax benefits would be classified as a provision for income tax in the Company's consolidated statement of operations.

Deferred Financing Costs

Deferred financing costs include costs directly attributable to the Company's offerings of its equity securities and its debt financings. Costs attributable to equity offerings are charged against the proceeds of the offering once the offering is completed. Costs attributable to debt financings are deferred and amortized over the term of the debt using the effective interest rate method. A portion of the deferred financing cost incurred in connection with the 2022 Notes was deemed to relate to the equity component and was allocated to additional paid in capital. In accordance with ASU No. 2015-03, Simplifying the Presentation of Debt Issuance Costs ("ASU 2015-03"), the Company presents debt issuance costs on the balance sheet as a direct deduction from the associated debt liability. The 2026 Notes, 2022 Notes and PhaRMA Notes are more fully described in Note 11, Notes Payable, to these consolidated financial statements.

Derivative Assets and Liabilities

In June 2015, in connection with the issuance of the 2022 Notes, the Company entered into convertible note hedge transactions (the "Convertible Note Hedges"). Concurrently with entering into the Convertible Note Hedges, the Company also entered into certain warrant transactions in which it sold note hedge warrants (the "Note Hedge Warrants") to the Convertible Note Hedge counterparties to acquire 20,249,665 shares of the Company's Class A common stock, subject to customary anti-dilution adjustments (Note 11). These instruments are derivative financial instruments under ASC Topic 815, Derivatives and Hedging ("ASC 815").

These derivatives are recorded as assets or liabilities at fair value each reporting period and the fair value is determined using the Black-Scholes option-pricing model. The changes in fair value are recorded as a component of other (expense) income in the consolidated statements of operations. Significant inputs used to determine the fair value include the price per share of the Company's Class A common stock on the date of valuation, time to maturity of the derivative instruments, the strike prices of the derivative instruments, the risk free interest rate, and the volatility of the Company's Class A common stock. Changes to these inputs could materially affect the valuation of the Convertible Note Hedges and Note Hedge Warrants in future periods.

Table of Contents

Revenue Recognition

The Company's revenues are generated primarily through collaborative arrangements and licensing related to the research and development and commercialization of linaclotide, as well as co-promotion arrangements in the U.S. and product revenue related to the commercial sale of ZURAMPIC in the U.S. The terms of the collaborative research and development, licensing, and co-promotion agreements contain multiple deliverables which may include (i) licenses, (ii) research and development activities, including participation on joint steering committees, (iii) the manufacture of finished drug product, API, or development materials for a partner which are reimbursed at a contractually determined rate, and (iv) co-promotion activities by the Company's clinical sales specialists. Non-refundable payments to the Company under these agreements may include (i) up-front license fees, (ii) payments for research and development activities, (iii) payments for the manufacture of finished drug product, API, or development materials, (iv) payments based upon the achievement of certain milestones, (v) payments for sales detailing, promotional support services and medical education initiatives, and (vi) royalties on product sales. Additionally, the Company may receive its share of the net profits or bear its share of the net losses from the sale of linaclotide in the U.S. and for China, Hong Kong and Macau through its collaborations with Allergan and AstraZeneca, respectively.

At December 31, 2016, the Company had collaboration agreements with Allergan (North America) and AstraZeneca (China, Hong Kong and Macau), as well as license agreements with Allergan (Europe) and Astellas (Japan) to develop and commercialize linaclotide. The Company also had an exclusive license agreement with AstraZeneca to develop, manufacture, and commercialize products containing lesinurad as an active agreement in the U.S. Additionally, the Company had a co-promotion agreement with Allergan for VIBERZI. Under the terms of the Company's co-promotion agreement with Exact Sciences, which was terminated in August 2016, the Company will continue to receive royalty payments through July 2017.

The Company recognizes revenue when there is persuasive evidence that an arrangement exists, services have been rendered or delivery has occurred, the price is fixed or determinable, and collection is reasonably assured.

For certain of the Company's arrangements, particularly the linaclotide license agreement with Allergan for all countries worldwide other than China, Hong Kong, Macau, Japan, and the countries and territories of North America, it is required that taxes be withheld on payments to the Company. The Company has adopted a policy to recognize revenue net of these tax withholdings.

Agreements Entered into Prior to January 1, 2011

For arrangements that include multiple deliverables and were entered into prior to January 1, 2011, the Company follows the provisions of ASC Topic 605-25, Revenue Recognition—Multiple-Element Arrangements (''ASC 605-25''), in accounting for these agreements. Under ASC 605 25, the Company was required to identify the deliverables included within the agreement and evaluate which deliverables represent separate units of accounting. Collaborative research and development and licensing agreements that contained multiple deliverables were divided into separate units of accounting when the following criteria were met:

- Delivered element(s) had value to the collaborator on a standalone basis,
- There was objective and reliable evidence of the fair value of the undelivered obligation(s), and
- If the arrangement included a general right of return relative to the delivered item(s), delivery or performance of the undelivered item(s) was considered probable and substantially within the Company's control.

The Company allocated arrangement consideration among the separate units of accounting either on the basis of each unit's respective fair value or using the residual method, and applied the applicable revenue recognition criteria to each of the separate units. If the separation criteria were not met, revenue of the combined unit of accounting was recorded based on the method appropriate for the last delivered item.

Table of Contents

Up Front License Fees

Prior to the adoption of ASU 2009-13, the Company recognized revenue from nonrefundable, up-front license fees on a straight-line basis over the contracted or estimated period of performance, which is typically the period over which the research and development is expected to occur or manufacturing services are expected to be provided. Accordingly, the Company was required to make estimates regarding the drug development and commercialization timelines for drugs and drug candidates being developed pursuant to any applicable agreement. The determination of the length of the period over which to recognize the revenue is subject to judgment and estimation and impacted the amount of revenue recognized in each period. Quarterly, the Company reassessed its period of substantial involvement over which the Company amortized its up-front license fees and made adjustments as appropriate. At December 31, 2016, the up-front fees associated with the Company's license agreement with Astellas were fully amortized as the period of performance had ended. The up-front license fees under the Allergan collaboration for North America and the Allergan collaboration for Europe (previously with Almirall) were fully amortized at December 31, 2015, as the period of performance under those arrangements ended in the three months ended September 30, 2012.

Agreements Entered into or Materially Modified on or after January 1, 2011

The Company evaluates revenue from new multiple element agreements entered into on or after January 1, 2011 under ASU No. 2009 13, Multiple-Deliverable Revenue Arrangements ("ASU 2009 13"). The Company also evaluates whether amendments to its multiple element arrangements are considered material modifications that are subject to the application of ASU 2009 13. This evaluation requires management to assess all relevant facts and circumstances and to make subjective determinations and judgments. As part of this assessment, the Company considers whether the modification results in a material change to the arrangement, including whether there is a change in total arrangement consideration that is more than insignificant, whether there are changes in the deliverables included in the arrangement, whether there is a change in the term of the arrangement and whether there is a significant modification to the delivery schedule for contracted deliverables.

When evaluating multiple element arrangements under ASU 2009 13, the Company considers whether the deliverables under the arrangement represent separate units of accounting. This evaluation requires subjective determinations and requires management to make judgments about the individual deliverables and whether such deliverables are separable from the other aspects of the contractual relationship. In determining the units of accounting, management evaluates certain criteria, including whether the deliverables have standalone value, based on the consideration of the relevant facts and circumstances for each arrangement. Factors considered in this determination include the research, manufacturing and commercialization capabilities of the partner and the availability of relevant research and manufacturing expertise in the general marketplace. In addition, the Company considers whether the collaborator can use the license or other deliverables for their intended purpose without the receipt of the remaining elements, and whether the value of the deliverable is dependent on the undelivered items and whether there are other vendors that can provide the undelivered items.

The consideration received is allocated among the separate units of accounting using the relative selling price method, and the applicable revenue recognition criteria are applied to each of the separate units.

The Company determines the estimated selling price for deliverables 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. Determining the BESP for a deliverable requires significant judgment. The Company uses BESP to estimate the selling price for licenses to the Company's proprietary technology, since the Company often does not have VSOE or TPE of selling price for these deliverables. In those circumstances where the Company utilizes BESP to determine the estimated selling price of a license to the Company's proprietary technology, the Company considers market conditions as well as entity specific factors,

including those factors contemplated in negotiating the agreements as well as internally developed models that include assumptions related to the market opportunity, estimated development costs, probability of success and the time needed to commercialize a product candidate pursuant to the license. In validating the Company's BESP, the Company evaluates whether changes in the key assumptions used to determine the BESP will have a significant effect on the allocation of arrangement consideration between multiple deliverables.

Table of Contents

At December 31, 2016, the Company's collaboration agreement with AstraZeneca for linaclotide and co-promotion agreements with Allergan for VIBERZI and Exact Sciences for Cologuard in the U.S. are each being accounted for under ASU 2009-13.

Up Front License Fees

When management believes the license to its intellectual property has stand-alone value, the Company generally recognizes revenue attributed to the license upon delivery. When management believes the license to its intellectual property does not have stand alone value from the other deliverables to be provided in the arrangement, it is combined with other deliverables and the revenue of the combined unit of accounting is recorded based on the method appropriate for the last delivered item.

Milestones

At the inception of each arrangement that includes pre-commercial milestone payments, the Company evaluates whether each pre-commercial milestone is substantive, in accordance with ASU No. 2010-17, Revenue Recognition—Milestone Method ("ASU 2010-17"), adopted on January 1, 2011. This evaluation includes an assessment of whether (a) the consideration is commensurate with either (1) the entity's performance to achieve the milestone, or (2) the enhancement of the value of the delivered item(s) as a result of a specific outcome resulting from the entity's performance to achieve the milestone, (b) the consideration relates solely to past performance and (c) the consideration is reasonable relative to all of the deliverables and payment terms within the arrangement. The Company evaluates factors such as the scientific, clinical, regulatory, commercial and other risks that must be overcome to achieve the respective milestone, the level of effort and investment required and whether the milestone consideration is reasonable relative to all deliverables and payment terms in the arrangement in making this assessment. At December 31, 2016, the Company had no pre-commercial milestones that were deemed substantive. If a substantive pre-commercial milestone were achieved and collection of the related receivable was reasonably assured, the Company would recognize revenue related to the milestone in its entirety in the period in which the milestone was achieved. If the Company were to achieve milestones that are considered substantive under any of the Company's collaborations, the Company may experience significant fluctuations in collaborative arrangements revenue from quarter to quarter and year to year depending on the timing of achieving such substantive milestones. In those circumstances where a pre-commercial milestone is not substantive, the Company recognizes as revenue on the date the milestone is achieved an amount equal to the applicable percentage of the performance period that had elapsed as of the date the milestone was achieved, with the balance being deferred and recognized over the remaining period of performance.

Commercial milestones are accounted for as royalties and are recorded as revenue upon achievement of the milestone, assuming all other revenue recognition criteria are met.

Net Profit or Net Loss Sharing

In accordance with ASC 808 Topic, Collaborative Arrangements, and ASC 605 45, Principal Agent Considerations, the Company considers the nature and contractual terms of the arrangement and the nature of the Company's business operations to determine the classification of the transactions under the Company's collaboration agreements. The Company records revenue transactions gross in the consolidated statements of operations if it is deemed the principal in the transaction, which includes being the primary obligor and having the risks and rewards of ownership.

The Company recognizes its share of the pre tax commercial net profit or net loss generated from the sales of LINZESS in the U.S. in the period the product sales are reported by Allergan and related cost of goods sold and selling, general and administrative expenses are incurred by the Company and its collaboration partner. These

amounts are partially determined based on amounts provided by Allergan and involve the use of estimates and judgments, such as product sales allowances and accruals related to prompt payment discounts, chargebacks, governmental and contractual rebates, wholesaler fees, product returns, and co payment assistance costs, which could be adjusted based on actual results in the future. The Company is highly dependent on Allergan for timely and accurate information regarding any net revenues realized from sales of LINZESS in the U.S. and the costs incurred in selling it, in order to accurately report its results of operations. For the periods covered in the consolidated financial statements presented, there have been no material changes to prior period estimates of revenues, cost of goods sold or selling, general and administrative expenses associated with the sales of LINZESS in the U.S. However, if the Company does not receive timely and accurate

Table of Contents

information or incorrectly estimates activity levels associated with the collaboration at a given point in time, the Company could be required to record adjustments in future periods.

The Company records its share of the net profits or net losses from the sales of LINZESS in the U.S. on a net basis and presents the settlement payments to and from Allergan as collaboration expense or collaborative arrangements revenue, as applicable, as the Company is not the primary obligor and does not have the risks and rewards of ownership in the collaboration agreement with Allergan for North America. The Company and Allergan settle the cost sharing quarterly, such that the Company's statement of operations reflects 50% of the pre tax net profit or loss generated from sales of LINZESS in the U.S.

Royalties on Product Sales

The Company receives or expects to receive in the future royalty revenues under certain of the Company's license or collaboration agreements. If the Company does not have any future performance obligations under these license or collaborations agreements, the Company records these revenues as earned. To the extent the Company does not have access to the royalty reports from the Company's partners or the ability to accurately estimate the royalty revenue in the period earned, the Company records such royalty revenues one quarter in arrears.

Product Revenue, Net

Net product revenue is derived from sales of ZURAMPIC in the U.S. Pursuant to the terms and conditions of the Lesinurad TSA, the Company sells ZURAMPIC principally to a limited number of major wholesalers and selected regional wholesalers through certain of AstraZeneca's existing arrangements (the "Distributors"). The Distributors subsequently resell ZURAMPIC to patients and healthcare providers.

The Company recognizes net product revenue from sales of ZURAMPIC in accordance with ASC 605, Revenue Recognition ("ASC 605"), when persuasive evidence of an arrangement exists, delivery has occurred and title of the product and associated risk of loss has passed to the customer, the price is fixed or determinable, and collection from the customer has been reasonably assured. ASC 605 requires, among other criteria, that future returns can be reasonably estimated in order to recognize revenue. The Company recognizes revenue on a gross basis as it has concluded that it is the principal in the product revenue transactions for ZURAMPIC, as it holds the general inventory risk, latitude in establishing price, physical loss inventory risk and credit risk.

The first units of ZURAMPIC were shipped to Distributors in September 2016 under the Lesinurad TSA. Due to the early stage of the product launch, the Company determined that it was not able to reliably make certain estimates, including returns, necessary to recognize product revenue upon shipment to Distributors. As a result, the Company records net product revenue for ZURAMPIC using a deferred revenue recognition model (sell-through). Under the deferred revenue model, the Company does not recognize revenue until ZURAMPIC is prescribed to an end-user. During the transition services period, pursuant to the Lesinurad TSA, AstraZeneca invoices Distributors upon shipment of ZURAMPIC on behalf of the Company. The Company records deferred revenue upon receipt of the quarterly cash payment from AstraZeneca for shipments of ZURAMPIC to Distributors. No such payments had been received by the Company as of December 31, 2016. The Company recognizes net product revenue when ZURAMPIC is prescribed to the end-user, on a first-in, first-out basis using estimated prescription demand and pharmacy demand from third party sources and the Company's analysis of third party market research data, as well as other third party information. The Company's estimates are subject to the inherent limitations of estimates that rely on third party data, as certain third party information is itself in the form of estimates. The Company will continue to evaluate when, if ever, it has sufficient volume of historical activity and visibility into the distribution channel, in order to reasonably make all estimates required under ASC 605 to recognize revenue upon shipment to the Distributor (Note 5).

The Company's net product revenues for ZURAMPIC represent total revenues less customer credits, including actual returns, rebates, and other discounts. These allowances are recorded for cash consideration given by a vendor to a customer that is presumed to be a reduction of the selling prices of the Company's products or services and, therefore, characterized as a reduction of revenue.

The cost basis of the product purchased by the Company pursuant to the Lesinurad TSA is included as a component of other current assets. Upon recognition of product revenue, the corresponding product cost is recorded as cost of revenues on the Company's consolidated statements of operations.

Table of Contents

Other

The Company produces linaclotide finished drug product, API and development materials for certain of its partners.

The Company recognizes revenue on linaclotide finished drug product, API and development materials when the material has passed all quality testing required for collaborator acceptance, delivery has occurred, title and risk of loss have transferred to the partner, the price is fixed or determinable, and collection is reasonably assured. As it relates to development materials and API produced for Astellas, the Company is reimbursed at a contracted rate. Such reimbursements are considered as part of revenue generated pursuant to the Astellas license agreement and are presented as collaborative arrangements revenue. Any linaclotide finished drug product, API and development materials currently produced for Allergan for the U.S. or AstraZeneca for China, Hong Kong and Macau are recognized in accordance with the cost-sharing provisions of the Allergan and AstraZeneca collaboration agreements, respectively. In October 2015, Almirall transferred its exclusive license to develop and commercialize linaclotide in Europe to Allergan, and the Company separately entered into an amendment to the license agreement with Allergan relating to the development and commercialization of linaclotide in Europe. Pursuant to the terms of the amendment, Allergan assumed responsibility for the manufacturing of linaclotide API for Europe from the Company, as well as the associated costs (Note 5).

Cost of Revenues

Cost of collaborative arrangements revenue related to linaclotide collaboration and license agreements is recognized upon shipment of linaclotide API to certain of the Company’s licensing partners outside of the U.S. and consists of the internal and external costs of producing such API. In addition to the cost of collaborative arrangement revenue related to linaclotide API, the Company records cost of product revenue for sales of ZURAMPIC in the U.S. Cost of product revenue related to the sales of ZURAMPIC includes the cost of producing finished goods that correspond with product revenue for the reporting period, as well as certain period costs related to freight, packaging, stability and quality testing, and customer acquisition.

During the year ended December 31, 2015, the Company recorded expenses of approximately $17.6 million for the write-down of inventory and an accrual for excess non-cancelable inventory purchase commitments related to linaclotide API. During the year ended December 31, 2014, the Company wrote-down approximately $20.3 million in inventory to an estimated net realizable value of approximately $5.0 million. The write-down of inventory to net realizable value and the loss on non-cancelable inventory purchase commitments for the years ended December 31, 2015 and December 31, 2014 were recorded as a separate line item in the Company’s consolidated statement of operations. These charges are more fully described in Note 8, Inventory, to these consolidated financial statements.

Research and Development Costs

The Company expenses research and development costs to operations as incurred. The Company defers and capitalizes nonrefundable advance payments made by the Company for research and development activities until the related goods are received or the related services are performed.

Research and development expenses are comprised of costs incurred in performing research and development activities, including salary, benefits and other employee-related expenses; share-based compensation expense; laboratory supplies and other direct expenses; facilities expenses; overhead expenses; third-party contractual costs relating to nonclinical studies and clinical trial activities and related contract manufacturing expenses, development of manufacturing processes and regulatory registration of third-party manufacturing facilities; licensing fees for the

Company’s product candidates; and other outside expenses.

Table of Contents

The Company has collaboration agreements with Allergan for the U.S. and AstraZeneca for China, Hong Kong and Macau pursuant to which it shares research and development expenses related to linaclotide. The Company records expenses incurred under the linaclotide collaboration arrangements for such work as research and development expense. Because the collaboration arrangements are cost sharing arrangements, the Company concluded that when there is a period during the collaboration arrangements during which the Company is owed payment from Allergan or AstraZeneca for such territories, the Company records the reimbursement by Allergan or AstraZeneca for their share of the development effort as a reduction of research and development expense. Amounts owed to Allergan or AstraZeneca for such territories are recorded as incremental research and development expense.

Selling, General and Administrative Expenses

The Company expenses selling, general and administrative costs to operations as incurred. Selling, general and administrative expense consists primarily of compensation, benefits and other employee-related expenses for personnel in the Company's administrative, finance, legal, information technology, business development, commercial, sales, marketing, communications and human resource functions. Other costs include the legal costs of pursuing patent protection of the Company's intellectual property, general and administrative related facility costs, insurance costs and professional fees for accounting and legal services.

Under the linaclotide collaboration agreements with Allergan for the U.S. and AstraZeneca for China, Hong Kong and Macau, the Company is reimbursed for certain selling, general and administrative expenses and it nets these reimbursements against selling, general and administrative expenses as incurred. Payments to Allergan or AstraZeneca for such territories are recorded as incremental selling, general and administrative expense.

Share-Based Compensation

The Company's share-based compensation programs grant awards which have included stock awards, restricted stock awards ("RSAs"), restricted stock units ("RSUs"), and stock options. Share-based compensation is recognized as an expense in the financial statements based on the grant date fair value over the requisite service period. For awards that vest based on service conditions, the Company uses the straight-line method to allocate compensation expense to reporting periods. The grant date fair value of options granted is calculated using the Black-Scholes option-pricing model, which requires the use of subjective assumptions including volatility, expected term, and expected forfeitures, among others. The fair value of the Company's RSUs is based on the market value of the Company's Class A common stock on the date of grant. Compensation expense for RSUs is recognized on a straight-line basis over the applicable service period.

The Company records the expense for stock option grants subject to performance based milestone vesting using the accelerated attribution method over the remaining service period when management determines that achievement of the milestone is probable. Management evaluates when the achievement of a performance based milestone is probable based on the relative satisfaction of the performance conditions as of the reporting date.

The Company records the expense of stock options granted for services rendered by non employees based on the estimated fair value of the stock option using the Black Scholes option pricing model. The fair value of unvested non employee stock option awards is remeasured at each reporting period and expensed over the vesting term of the underlying stock options.

While the assumptions used to calculate and account for share-based compensation awards represent management's best estimates, these estimates involve inherent uncertainties and the application of management's judgment. As a result, if revisions are made to our underlying assumptions and estimates, the Company's share-based compensation expense could vary significantly from period to period.

Patent Costs

The Company incurred and recorded as operating expense legal and other fees related to patents of approximately $2.3 million, approximately $2.2 million, and approximately $1.3 million for the years ended December 31, 2016, 2015 and 2014, respectively. These costs were charged to selling, general and administrative expenses as incurred.

Table of Contents

Business Combinations

The Company evaluates acquisitions of assets and other similar transactions to assess whether or not the transaction should be accounted for as a business combination by assessing whether or not the Company has acquired inputs and processes that have the ability to create outputs. If determined to be a business combination, the Company accounts for business acquisitions under the acquisition method of accounting as indicated in the Financial Accounting Standards Board ("FASB") issued ASC Topic 805, Business Combinations, ("ASC 805") which requires the acquiring entity in a business combination to recognize the fair value of all assets acquired, liabilities assumed, and any non-controlling interest in the acquiree and establishes the acquisition date as the fair value measurement point. Accordingly, the Company recognizes assets acquired and liabilities assumed in business combinations, including contingent liabilities and non-controlling interest in the acquiree based on the fair value estimates as of the date of acquisition. In accordance with ASC 805, the Company recognizes and measures goodwill as of the acquisition date, as the excess of the fair value of the consideration paid over the fair value of the identified net assets acquired.

The consideration for the Company's business acquisitions includes future payments that are contingent upon the occurrence of a particular event or events. The obligations for such contingent consideration payments are recorded at fair value on the acquisition date. The contingent consideration obligations are then evaluated each reporting period. Changes in the fair value of contingent consideration obligations, other than changes due to payments, are recognized as a (gain) loss on fair value remeasurement of contingent consideration in the consolidated statements of operations.

Net Income (Loss) Per Share

The Company calculates basic net income (loss) per common share and diluted net income (loss) per common share by dividing the net income (loss) by the weighted average number of common shares outstanding during the period. Diluted net income (loss) per common share is computed by dividing net income (loss) by the diluted number of shares outstanding during the period. Except where the result would be antidilutive to net income (loss), diluted net income (loss) per common share is computed assuming the conversion of the 2022 Notes, the exercise of outstanding common stock options and the vesting of RSUs and restricted stock (using the treasury stock method), as well as their related income tax effects. The Company allocates undistributed earnings between the classes of common stock on a one to one basis when computing net income (loss) per share. As a result, basic and diluted net income (loss) per Class A and Class B shares are equivalent.

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 and currently consists of net loss and changes in unrealized gains and losses on available for sale securities.

Subsequent Events

The Company considers events or transactions that have occurred after the balance sheet date of December 31, 2016, but prior to the filing of the financial statements with the Securities and Exchange Commission to provide additional evidence relative to certain estimates or to identify matters that require additional recognition or disclosure. Subsequent events have been evaluated through the filing of the financial statements accompanying this Annual Report on Form 10-K.

New Accounting Pronouncements

From time to time, new accounting pronouncements are issued by the FASB or other standard setting bodies that are adopted by the Company as of the specified effective date. Except as set forth below, the Company did not adopt any new accounting pronouncements during the year ended December 31, 2016 that had a material effect on its consolidated financial statements.

In May 2014, the FASB issued ASU No. 2014-09, Revenue from Contracts with Customers ("ASU 2014-09"), which supersedes the revenue recognition requirements in ASC 605, and most industry-specific guidance. The new standard requires that an entity recognize revenue to depict the transfer of promised goods or services to customers in an amount that reflects the consideration to which the Company expects to be entitled in exchange for those goods or

Table of Contents

services. The update also requires additional disclosure about the nature, amount, timing and uncertainty of revenue and cash flows arising from customer contracts, including significant judgments and changes in judgments and assets recognized from costs incurred to obtain or fulfill a contract. ASU 2014-09 is effective for fiscal years, and interim periods within those years, beginning after December 15, 2017 and should be applied retrospectively to each prior reporting period presented or retrospectively with the cumulative effect of initially applying this update recognized at the date of initial application. Early adoption is permitted beginning after December 15, 2016, including interim reporting periods within those years. In April 2016, the FASB issued ASU No. 2016-10, Revenue from Contracts with Customers: Identifying Performance Obligations and Licensing ("ASU 2016-10"), which clarifies certain aspects of identifying performance obligations and licensing implementation guidance. In May 2016, the FASB issued ASU No. 2016-12, Revenue from Contracts with Customers: Narrow-Scope Improvements and Practical Expedients ("ASU 2016-12"), related to disclosures of remaining performance obligations, as well as other amendments to guidance on collectability, non-cash consideration and the presentation of sales and other similar taxes collected from customers. These standards have the same effective date and transition date as ASU 2014-09. The Company is analyzing the potential impact that ASU 2014-09, ASU 2016-10 and ASU 2016-12 may have on its financial position and results of operations. This analysis of the Company's collaborative arrangements and license agreements includes, but is not limited to, reviewing variable consideration as it relates to its agreements, assessing potential disclosures and evaluating the impact of each potential method of adoption on the Company's consolidated financial statements. In addition, the Company continues to monitor additional changes, modifications, clarifications or interpretations undertaken by the FASB, which may impact its conclusions.

In August 2014, the FASB issued ASU No. 2014-15, Presentation of Financial Statements - Going Concern: Disclosure of Uncertainties about an Entity's Ability to Continue as a Going Concern ("ASU 2014-15"). ASU 2014-15 is intended to define management's responsibility to evaluate whether there is substantial doubt about an organization's ability to continue as a going concern and to provide related footnote disclosures, if required. ASU 2014-15 is effective for annual reporting periods ending after December 15, 2016, and applies to annual and interim periods thereafter. The Company adopted this standard during the three months ended December 31, 2016. The Company determined there was not substantial doubt about the organization's ability to continue as a going concern.

In April 2015, the FASB issued ASU No. 2015-05, Customer's Accounting for Fees Paid in a Cloud Computing Arrangement, which amends ASC 350. Under this standard, if a cloud computing arrangement includes a software license, the software license element of the arrangement should be accounted for consistent with the acquisition of other software licenses. If a cloud computing arrangement does not include a software license, the arrangement should be accounted for as a service contract. The amendments are effective for fiscal years, and interim periods within those years, beginning after December 15, 2015 and may be applied on either a prospective or retrospective basis. The Company adopted this standard during the three months ended March 31, 2016. The adoption of this standard did not have a material impact on the Company's financial position or results of operations for the year ended and as of December 31, 2016.

In July 2015, the FASB issued ASU No. 2015-11, Inventory (Topic 330): Simplifying the Measurement of Inventory. ASU 2015-11 requires that for entities that measure inventory using the first-in, first-out method, inventory should be measured at the lower of cost and net realizable value. The standard defines net realizable value as the estimated selling prices in the ordinary course of business, less reasonably predictable costs of completion, disposal and transportation. The standard is effective for fiscal years, and interim periods within those years, beginning after December 15, 2016. Early adoption is permitted. The Company adopted this standard during the three months ended December 31, 2016. The adoption of this standard did not have a material impact on the Company's financial position or results of operations for the year ended and as of December 31, 2016.

In February 2016, the FASB issued ASU No. 2016-02, Leases ("ASU 2016-02"), which supersedes the lease accounting requirements in ASC Topic 840, Leases, and most industry-specific guidance. ASU 2016-02 requires the

identification of arrangements that should be accounted for as leases by lessees. In general, for lease arrangements exceeding a 12-month term, these arrangements must now be recognized as assets and liabilities on the balance sheet of the lessee. Under ASU 2016-02, a right-of-use asset and lease obligation will be recorded for all leases, whether operating or financing, while the income statement will reflect lease expense for operating leases and amortization and interest expense for financing leases. The balance sheet amount recorded for existing leases at the date of adoption of ASU 2016-02 must be calculated using the applicable incremental borrowing rate at the date of adoption. In addition, ASU 2016-02 requires the use of modified retrospective method, which will require adjustment to all comparative periods presented in the consolidated financial statements. ASU 2016-02 is effective for fiscal years beginning after

Table of Contents

December 15, 2018, including interim periods within those fiscal years. Early adoption is permitted. The Company is evaluating the potential impact that ASU 2016-02 may have on the Company's financial position or results of operations for the year ended and as of December 31, 2016.

In March 2016, the FASB issued ASU No. 2016-09, Compensation - Stock Compensation, which amends ASC Topic 718, Compensation - Stock Compensation ("ASU 2016-09"). ASU 2016-09 identifies areas for simplification involving several aspects of accounting for share-based payment transactions, including the income tax consequences, classification of awards as either equity or liabilities, an option to recognize gross stock compensation expense with actual forfeitures recognized as they occur, as well as certain classifications on the statement of cash flows. The amendments are effective for annual periods beginning after December 15, 2016, and interim periods within those annual periods. Early adoption is permitted. The Company adopted this standard during the three months ended December 31, 2016. The adoption of this standard did not have a material impact on the Company's financial position or results of operations for the year ended and as of December 31, 2016.

In August 2016, the FASB issued ASU No. 2016-15, Statement of Cash Flows (Topic 230): Classification of Certain Cash Receipts and Cash Payments ("ASU 2016-15"). The new standard clarifies certain aspects of the statement of cash flows, including the classification of debt prepayment or debt extinguishment costs, contingent consideration payments made after a business combination, proceeds from the settlement of insurance claims, and distributions received from equity method investees and beneficial interests in securitization transactions. The new standard also clarifies that an entity should determine each separately identifiable source or use within the cash receipts and cash payments on the basis of the nature of the underlying cash flows. In situations in which cash receipts and payments have aspects of more than one class of cash flows and cannot be separated by source or use, the appropriate classification should depend on the activity that is likely to be the predominant source or use of cash flows for the item. The amendments are effective for annual periods beginning after December 15, 2017, and interim periods within those annual periods. Early adoption is permitted. The Company adopted this standard during the three months ended December 31, 2016. The adoption of this standard did not have a material impact on the Company's financial position or results of operations for the year ended and as of December 31, 2016.

In October 2016, the FASB issued ASU No. 2016-16, Accounting for Income Taxes: Intra-Entity Asset Transfers of Assets Other than Inventory ("ASU 2016-16"). ASU 2016-16 eliminates the ability to defer the tax expense related to intra-entity asset transfers other than Inventory. Under the new standard, entities should recognize the income tax consequences on an intra-entity transfer of an asset other than inventory when the transfer occurs. ASU 2016-16 is effective for fiscal periods beginning after December 15, 2018. Early adoption is permitted. The Company is evaluating the potential impact that the adoption of ASU 2016-16 will have on the Company's financial position or results of operations. The standard does not have a material impact on the Company's financial position or results of operations for the year ended and as of December 31, 2016.

In October 2016, the FASB issued No. ASU 2016-17, Consolidation Topic 810: Interests held through Related Parties that are under Common Control ("ASU 2016-17"), which amends how a decision maker is required to consider indirect interests in a variable interest entity held through an entity under common control. ASU 2016-17 is effective for fiscal years beginning after December 15, 2016, and interim periods within those years. Early adoption is permitted. The Company adopted this standard during the three months ended December 31, 2016. The adoption of this standard did not have a material impact on the Company's financial position or results of operations for the year ended and as of December 31, 2016.

In October 2016, the FASB ASU 2016-18, Statement of Cash Flows (Topic 230) Restricted Cash ("ASU 2016-18"), which requires that a statement of cash flows explain the change during the period in the total of cash, cash equivalents, and restricted cash or restricted cash equivalents. Therefore, amounts described as restricted cash and restricted cash equivalents should be included with cash and cash equivalents when reconciling the

beginning-of-period and end-of-period total amounts shown on the statement of cash flows. ASU 2016-18 is effective for fiscal years beginning after December 15, 2017, and interim periods within those years. Early adoption is permitted. The Company is evaluating the potential impact that the adoption of ASU 2016-18 will have on the Company's financial position or results of operations.

In January 2017, the FASB ASU No. 2017-01, Business Combinations (Topic 805): Clarifying the Definition of a Business ("ASU 2017-01"), to clarify the definition of a business by adding guidance to assist entities with evaluating whether transactions should be accounted for as acquisitions or disposals of assets versus businesses. ASU 2017-01 is

Table of Contents

effective for fiscal years beginning after December 15, 2017, and interim periods within those fiscal years. Early adoption is permitted. The Company is evaluating the potential impact that the adoption of ASU 2016-16 will have on the Company's financial position or results of operations.

No other accounting standards known by the Company to be applicable to it that have been issued or proposed by the FASB or other standard-setting bodies and that do not require adoption until a future date are expected to have a material impact on the Company's consolidated financial statements upon adoption.

3. Net Loss Per Share

The following table sets forth the computation of basic and diluted net loss per common share (in thousands, except per share amounts):

| | Year Ended December 31, | | |
|---|---|---|---|
| | 2016 | 2015 | 2014 |
| Numerator: | | | |
| Net Loss | $ (81,708) | $ (142,669) | $ (189,618) |
| Denominator: | | | |
| Weighted average number of common shares used in net loss per share — basic and diluted | 144,928 | 142,155 | 136,811 |
| Net loss per share — basic and diluted | $ (0.56) | $ (1.00) | $ (1.39) |

In June 2015, in connection with the issuance of approximately $335.7 million in aggregate principal amount of the 2022 Notes, the Company entered into the Convertible Note Hedges. The Convertible Note Hedges are generally expected to reduce the potential dilution to the Company's Class A common stockholders upon a conversion of the 2022 Notes and/or offset any cash payments the Company is required to make in excess of the principal amount of converted 2022 Notes in the event that the market price per share of the Company's Class A common stock, as measured under the terms of the Convertible Note Hedges, is greater than the conversion price of the 2022 Notes (Note 11). The Convertible Note Hedges are not considered for purposes of calculating the number of diluted weighted average shares outstanding, as their effect would be antidilutive.

Concurrently with entering into the Convertible Note Hedges, the Company also issued Note Hedge Warrants to the Convertible Note Hedge counterparties to acquire 20,249,665 shares of the Company's Class A common stock, subject to customary anti-dilution adjustments. The Note Hedge Warrants could have a dilutive effect on the Company's Class A common stock to the extent that the market price per share of the Class A common stock exceeds the applicable strike price of such warrants (Note 11). The Note Hedge Warrants are not considered for purposes of calculating the number of diluted weighted averages shares outstanding, as their effect would be antidilutive.

The following potentially dilutive securities have been excluded from the computation of diluted weighted average shares outstanding as their effect would be anti dilutive (in thousands):

| | Year Ended December 31, | | |
|---|---|---|---|
| | 2016 | 2015 | 2014 |
| Options to purchase common stock | 20,455 | 20,567 | 19,958 |
| Shares subject to repurchase | 94 | 74 | 99 |
| Unvested shares from early option exercises | 300 | — | — |
| Restricted stock units | 1,299 | 900 | — |
| Note hedge warrants | 20,250 | 20,250 | — |

| | | | |
|---|---|---|---|
| 2022 Notes | 20,250 | 20,250 | — |
| | 62,648 | 62,041 | 20,057 |

An insignificant number of shares issuable under the Company's employee stock purchase plan were excluded from the calculation of diluted weighted average shares outstanding because their effects would be anti-dilutive.

Table of Contents

4. Business Combinations

The Company closed the Lesinurad Transaction on June 2, 2016 (the "Acquisition Date") with AstraZeneca pursuant to which the Company received an exclusive license to develop, manufacture and commercialize in the U.S. products containing lesinurad as an active ingredient, including ZURAMPIC (the "Products"). Subject to the terms of the Lesinurad License, AstraZeneca is obligated to conduct certain development activities on the Company's behalf for (i) ZURAMPIC, including the post-marketing activities currently required by the FDA, for which the Company is obligated to reimburse AstraZeneca up to $100.0 million over up to ten years, and (ii) DUZALLO, for which the Company will also reimburse AstraZeneca. In connection with the Lesinurad License, the Company and AstraZeneca entered into the Lesinurad CSA, pursuant to which the Company relies exclusively on AstraZeneca for the commercial manufacture and supply of ZURAMPIC and, if approved, DUZALLO, and the Lesinurad TSA, pursuant to which AstraZeneca is providing certain support services, including development, regulatory and commercial services, to the Company for ZURAMPIC until such activities under the Lesinurad TSA are transferred to the Company. The Company may obtain production techniques from AstraZeneca via a manufacturing technology transfer available under the Lesinurad CSA upon provision of six-months' notice. The Company is responsible for commercialization of the Products in the U.S., and any additional development of the Products for commercialization in the U.S. In addition, under the terms of the Lesinurad License, the Company will have the right of first negotiation and right of last refusal with AstraZeneca for the right to commercialize, develop and manufacture for commercialization in the U.S., products for the prevention or treatment of gout that include verinurad as at least one of its active ingredients.

The Company concluded that the Lesinurad Transaction included inputs and processes that have the ability to create outputs and accordingly accounted for the transaction as a business combination in accordance with ASC 805. As such, the assets acquired and liabilities assumed were recorded at fair value, with the remaining purchase price recorded as goodwill.

The purchase price consists of the up-front payment to AstraZeneca of $100.0 million, which was made in June 2016, and the fair value of contingent consideration of approximately $67.9 million. In addition to the up-front payment, the Company will also pay a tiered royalty to AstraZeneca in the single-digits as a percentage of net sales of the Products in the U.S., as well as commercial and other milestones of up to $165.0 million over the duration of the Lesinurad License. As of the Acquisition Date, the contingent consideration fair value of approximately $67.9 million was calculated using a discounted cash flow estimate of expected future milestone and royalty payments to AstraZeneca based on the Company's internally forecasted net product revenue of ZURAMPIC and, if approved, DUZALLO. The fair value of contingent consideration in the purchase price includes initial measurement period adjustments further described below, as of the Acquisition Date. The Company also paid approximately $1.6 million in transaction-related costs, including external consulting fees, which were expensed as incurred as selling, general and administrative expenses.

The Company preliminarily valued the acquired assets and liabilities based on their estimated fair value as of the Acquisition Date upon closing the Lesinurad Transaction. The preliminary fair values included in the Company's consolidated balance sheets as of December 31, 2016 are based on the Company's best estimates. Certain of these

estimates have been adjusted as additional information has become available related to conditions that existed as of the Acquisition Date. During the three months ended December 31, 2016, the Company recorded approximately $19.8 million in adjustments to the preliminary Acquisition Date valuation of the acquired assets and liabilities. These adjustments primarily related to changes in estimated cash flows associated with the commercialization of ZURAMPIC and if approved, DUZALLO. As a result of the adjustments to the Acquisition Date valuation of the acquired assets and liabilities recorded during the three months ended December 31, 2016, the fair value of the IPR&D - DUZALLO increased by approximately $126.0 million, the fair value of the developed technology – ZURAMPIC decreased by approximately $145.9 million, goodwill increased by an insignificant amount and contingent consideration decreased by approximately $19.8 million. The Company will continue to evaluate all information available, including the results of multiple ongoing market research projects, and further adjustments to the respective fair values of these items may be made if additional information becomes available regarding conditions that existed at the time of the acquisition, but such adjustments may be made no later than June 1, 2017. The completion of the valuation of the acquired assets and liabilities may result in additional adjustments to the carrying value of assets and liabilities, revision to the useful life of the finite intangible asset, the determination of any residual amount that will be allocated to goodwill and the related tax effects. The related amortization of acquired finite-lived intangible asset is also subject to revision based on the final valuation.

Table of Contents

The following table presents the allocation of the purchase consideration for the Lesinurad Transaction as of the Acquisition Date, including the contingent consideration (in thousands) and approximately $19.8 million in measurement period adjustments recorded during the three months ended December 31, 2016:

| As of the Acquisition Date: | |
|---|---|
| Cash portion of consideration | $ 100,000 |
| Contingent consideration | 67,885 |
| Total purchase consideration | $ 167,885 |

| As of the Acquisition Date: | |
|---|---|
| Developed technology — ZURAMPIC | $ 22,000 |
| IPR&D - DUZALLO | 145,100 |
| Goodwill | 785 |
| Net assets acquired | $ 167,885 |

The fair value of the IPR&D - DUZALLO was determined using a probability adjusted discounted cash flow approach, including assumptions of projected revenues, operating expenses and a discount rate of 14.0% applied to the projected cash flows. The remaining cost of development for this asset was approximately $13.9 million as of the Acquisition Date, with an expected completion date of no later than December 31, 2017. Through December 31, 2016, the Company continued to incur costs related to DUZALLO.

The fair value of the developed technology - ZURAMPIC intangible asset was determined using a probability adjusted discounted cash flow approach, including assumptions of projected revenues, operating expenses and a discount rate of 12.5% applied to the projected cash flows. The Company considers the developed technology - ZURAMPIC intangible asset acquired to be developed technology, as it was approved by the FDA for commercialization as of the Acquisition Date. The Company believes the assumptions are representative of those a market participant would use in estimating fair value. The developed technology - ZURAMPIC intangible asset is finite lived. The amount allocated to the developed technology - ZURAMPIC intangible asset is being amortized on a straight-line basis to amortization of acquired intangible assets within the Company’s consolidated statements of operations over its estimated useful life of approximately 13 years, the period of estimated future cash flows from the Acquisition Date. The Company believes that the straight-line method of amortization represents the pattern in which the economic benefits of the intangible asset are consumed. As of December 31, 2016, the Company recognized accumulated amortization of approximately $1.0 million with respect to the developed technology - ZURAMPIC intangible asset. The estimated future amortization of developed technology – ZURAMPIC intangible asset is expected to be as follows (in thousands):

| | As of December 31, 2016 |
|---|---|
| 2017 | $ 1,682 |
| 2018 | 1,682 |
| 2019 | 1,682 |
| 2020 | 1,682 |

| | | |
|---|---|---|
| 2021 and thereafter | | 14,291 |
| Total | $ | 21,019 |

The amount allocated to the IPR&D- DUZALLO is considered to be indefinite-lived until the completion or abandonment of the associated research and development efforts. As of December 31, 2016, there was no impairment related to the IPR&D- DUZALLO or the developed technology - ZURAMPIC intangible asset.

The Company allocated the excess of the purchase price over the identifiable intangible assets to goodwill. Such goodwill is not deductible for tax purposes and represents the value placed on entering new markets, expanding market share and operating synergies. As of December 31, 2016, there was no impairment of goodwill. All goodwill has been assigned to the Company’s single reporting unit, which is the single operating segment human therapeutics.

These fair value measurements were based on significant inputs not observable in the market and thus represent Level 3 fair value measurements (Note 6).

As of December 31, 2016, the estimated fair value of the Company’s contingent consideration liability increased by approximately $9.8 million to approximately $77.7 million, compared to the Acquisition Date estimated

Table of Contents

fair value primarily due to the passage of time and changes in the yield curve equivalent to the Company's credit risk, which was the estimated cost of debt financing for similar market participants used in the valuation.

5. Collaboration, License, Co-Promotion and Other Commercial Agreements

For the year ended December 31, 2016, the Company had linaclotide collaboration agreements with Allergan for North America and AstraZeneca for China, Hong Kong and Macau, as well as linaclotide license agreements with Allergan for the European territory (formerly with Almirall) and Astellas for Japan. The Company also had a co-promotion agreement with Exact Sciences to co-promote Cologuard in the U.S., which was terminated in August 2016, and a co-promotion agreement with Allergan to co-promote VIBERZI in the U.S. Additionally, the Company had the Lesinurad License with AstraZeneca for the development, manufacture and commercialization in the U.S. of products containing lesinurad. The following table provides amounts included in the Company's consolidated statements of operations as collaborative arrangements revenue attributable to transactions from these arrangements (in thousands):

| | Collaborative Arrangements Revenue Year Ended December 31, | | |
|---|---|---|---|
| | 2016 | 2015 | 2014 |
| Linaclotide Agreements: | | | |
| Allergan (North America) | $ 223,362 | $ 134,335 | $ 47,682 |
| Allergan (Europe)(1) | 406 | — | — |
| AstraZeneca (China, Hong Kong and Macau) | 370 | 2,370 | 3,417 |
| Almirall (Europe) (1) | 3 | 540 | 7,587 |
| Astellas (Japan) | 44,430 | 7,696 | 17,750 |
| Co-Promotion Agreements: | | | |
| Exact Sciences (Cologuard) (2) | 3,513 | 4,437 | — |
| Allergan (VIBERZI) | 1,764 | 177 | — |
| Product Revenue - ZURAMPIC | 109 | — | — |
| Total collaborative arrangements revenue | $ 273,957 | $ 149,555 | $ 76,436 |

(1) In October 2015, Almirall transferred its exclusive license to develop and commercialize linaclotide in Europe to Allergan.

(2) In August 2016, the Company terminated the Cologuard Co-Promotion Agreement.

Linaclotide Agreements

Collaboration Agreement for North America with Allergan

In September 2007, the Company entered into a collaboration agreement with Allergan to develop and commercialize linaclotide for the treatment of IBS-C, CIC and other GI conditions in North America. Under the terms of this collaboration agreement, the Company shares equally with Allergan all development costs as well as net profits or losses from the development and sale of linaclotide in the U.S. The Company receives royalties in the mid-teens percent based on net sales in Canada and Mexico. Allergan is solely responsible for the further development, regulatory approval and commercialization of linaclotide in those countries and funding any costs. The collaboration agreement for North America also includes contingent milestone payments, as well as a contingent equity investment, based on the achievement of specific development and commercial milestones. At December 31, 2016, $205.0 million in license fees and all six development milestone payments had been received by the Company, as well as a

$25.0 million equity investment in the Company's capital stock (Note 17). The Company can also achieve up to $100.0 million in a sales related milestone if certain conditions are met, which will be recognized as collaborative arrangements revenue as earned.

As a result of the research and development cost sharing provisions of the linaclotide collaboration for North America, the Company offset approximately $7.3 million, approximately $16.9 million, and approximately $4.3 million against research and development costs during the years ended December 31, 2016, 2015 and 2014, respectively, to reflect the obligations of each party under the collaboration to bear half of the development costs incurred. In addition, in March 2015, the Company and Allergan agreed to share certain costs relating to the manufacturing of linaclotide API and certain other manufacturing activities for the North American territory. This arrangement resulted in net amounts

Table of Contents

received from Allergan of approximately $4.3 million for costs incurred in prior periods, which were recorded by the Company as a reduction in research and development expenses during the year ended December 31, 2015.

The Company and Allergan began commercializing LINZESS in the U.S. in December 2012. The Company receives 50% of the net profits and bears 50% of the net losses from the commercial sale of LINZESS in the U.S.; provided, however, that if either party provides fewer calls on physicians in a particular year than it is contractually required to provide, such party's share of the net profits will be adjusted as set forth in the collaboration agreement for North America. During the years ended December 31, 2016 and 2015, certain of these adjustments to the share of the net profits were reduced or eliminated in connection with the co-promotion activities under the Company's agreement with Allergan to co-promote VIBERZI in the U.S., as described below in Co-Promotion Agreement with Allergan for VIBERZI. Additionally, certain of these adjustments to the share of the net profits are eliminated, in full, in 2018 and all subsequent years under the terms of the Company's commercial agreement with Allergan entered into in January 2017 under which the Company will promote Allergan's DELZICOL and CANASA products (Note 20). Net profits or net losses consist of net sales of LINZESS to third-party customers and sublicense income in the U.S. less the cost of goods sold as well as selling, general and administrative expenses. LINZESS net sales are calculated and recorded by Allergan and may include gross sales net of discounts, rebates, allowances, sales taxes, freight and insurance charges, and other applicable deductions. The Company records its share of the net profits or net losses from the sale of LINZESS on a net basis and presents the settlement payments to and from Allergan as collaboration expense or collaborative arrangements revenue, as applicable.

The Company recognized collaborative arrangements revenue from the Allergan collaboration agreement for North America during the years ended December 31, 2016, 2015 and 2014 as follows (in thousands):

| | Year Ended December 31, | | |
|---|---|---|---|
| | 2016 | 2015 | 2014 |
| Collaborative arrangements revenue related to sales of LINZESS in the U.S. | $ 217,726 | $ 133,425 | $ 47,618 |
| Sale of API | 4,482 | — | — |
| Royalty revenue | 1,154 | 910 | 64 |
| Total collaborative arrangements revenue | $ 223,362 | $ 134,335 | $ 47,682 |

The collaborative arrangements revenue recognized in the years ended December 31, 2016, 2015 and 2014 primarily represents the Company's share of the net profits and net losses on the sale of LINZESS in the U.S. In addition, during the year ended December 31, 2016, the Company recorded collaboration revenue of approximately $4.5 million related to the sale of API to Allergan under the terms of the linaclotide collaboration for North America. The Company recorded no collaboration revenue related to the sale of API to Allergan during the years ended December 31, 2015, and 2014.

The following table presents the amounts recorded by the Company for commercial efforts related to LINZESS in the U.S. in the years ended December 31, 2016, 2015 and 2014 (in thousands):

| | Year Ended December 31, | | |
|---|---|---|---|
| | 2016 | 2015 | 2014 |
| Collaborative arrangements revenue related to sales of LINZESS in the U.S.(1)(2) | $ 217,726 | $ 133,425 | $ 47,618 |
| Selling, general and administrative costs incurred by the Company(1) | (35,197) | (32,028) | (31,646) |
| The Company's share of net profit | $ 182,529 | $ 101,397 | $ 15,972 |

(1) Includes only collaborative arrangement revenue or selling, general and administrative costs attributable to the cost sharing arrangement with Allergan.
(2) Certain of the unfavorable adjustments to the Company's share of the LINZESS net profits were reduced or eliminated in connection with the co-promotion activities under the Company's agreement with Allergan to co-promote VIBERZI in the U.S., as described below in Co-Promotion Agreement with Allergan for VIBERZI.

In May 2014, CONSTELLA became commercially available in Canada and in June 2014, LINZESS became commercially available in Mexico. In October 2015, Almirall and Allergan terminated the sublicense arrangement with respect to Mexico, returning the exclusive rights to commercialize CONSTELLA in Mexico to Allergan. CONSTELLA

Table of Contents

continues to be available to adult IBS-C patients in Mexico. The Company records royalties on sales of CONSTELLA in Canada and LINZESS in Mexico one quarter in arrears as it does not have access to the royalty reports from its partner or the ability to estimate the royalty revenue in the period earned. The Company recognized approximately $1.2 million, approximately $0.9 million, and an insignificant amount of royalty revenues from Canada and Mexico during the years ended December 31, 2016, 2015 and 2014, respectively.

License Agreement for the European Territory with Allergan (formerly with Almirall through October 2015)

In April 2009, the Company entered into a license agreement with Almirall (the “European License Agreement”) to develop and commercialize linaclotide in Europe (including the Commonwealth of Independent States and Turkey) for the treatment of IBS-C, CIC and other GI conditions. Under the terms of the European License Agreement, Almirall was responsible for the expenses associated with the development and commercialization of linaclotide in the European territory and the Company was required to participate on a joint development committee over linaclotide’s development period and a joint commercialization committee while the product was being commercialized.

Pursuant to the terms of the European License Agreement, in May 2009 the Company received approximately $38.0 million, net of foreign tax withholdings, as a non-refundable up-front payment from Almirall. In November 2009, the Company achieved a development milestone triggering an equity investment and received $15.0 million from Almirall for the purchase of 681,819 shares of convertible preferred stock (Note 17).

In addition, the European License Agreement with Almirall included contingent milestone payments that could total up to $40.0 million upon achievement of specific development and commercial launch milestones. In November 2010, the Company achieved a development milestone, which resulted in an approximately $19.0 million payment, representing a $20.0 million milestone, net of foreign withholding taxes. This development milestone was recognized as collaborative arrangements revenue through September 2012, the period over which linaclotide was developed under the European License Agreement with Almirall. Commercial milestone payments under the European License Agreement with Almirall, as modified, consisted of approximately $4.0 million which became due upon the first commercial launch in four of the five major European Union (“E.U.”) countries set forth in the agreement, which includes approximately $2.0 million during the second quarter of 2013 and approximately $1.0 million during each of the first and second quarters of 2014. In connection with the achievement of these milestones, the Company received approximately $3.9 million, net of foreign tax withholdings, which includes approximately $1.9 million during the second quarter of 2013 and approximately $1.0 million during each of the first and second quarters of 2014. The European License Agreement with Almirall also included escalating royalties based on sales of linaclotide in the low twenties percent reduced by the transfer price paid for the API included in the product actually sold in the Almirall territory and other contractual deductions.

In October 2015, Almirall transferred its exclusive license to develop and commercialize linaclotide in Europe to Allergan. Additionally, in October 2015, the Company and Allergan separately entered into an amendment to the European License Agreement relating to the development and commercialization of linaclotide in Europe. Pursuant to the terms of the amendment, (i) the remaining sales-based milestones payable to the Company under the European License Agreement were modified to increase the total milestone payments such that, when aggregated with the remaining commercial launch milestones, they could total up to $42.5 million, (ii) the royalties payable to the Company during the term of the European License Agreement were modified such that the royalties based on sales volume in Europe begin in the mid-single digit percent and escalate to the upper-teens percent by calendar year 2019, and (iii) Allergan assumed responsibility for the manufacturing of linaclotide API for Europe from the Company, as well as the associated costs. Furthermore, with the Company no longer responsible for the manufacturing of linaclotide API for Europe, the royalties under the European License Agreement are no longer reduced by the transfer price paid for the API included in the product actually sold by Allergan in Europe in any given period. The Company concluded that the 2015 amendment to the European License Agreement was not a modification to the linaclotide

collaboration agreement with Allergan for North America.

The commercial launch and sales based milestones under the European License Agreement are recognized as revenue as earned. The Company recognized approximately $0.4 million and approximately $0.5 million in royalty revenue during the years ended December 31, 2016 and 2015, respectively. The Company recognized approximately $7.6 million in total collaborative arrangements revenue from the European License Agreement during the year ended December 31, 2014, including approximately $5.1 million from the sale of API to Almirall, approximately $1.9 million in commercial launch milestones, and approximately $0.6 million in royalty revenue. The Company records royalties on

Table of Contents

sales of CONSTELLA one quarter in arrears as it does not have access to the royalty reports from Allergan or the ability to estimate the royalty revenue in the period earned.

In January 2017, the Company and Allergan entered into an amendment to the European License Agreement (Note 20).

License Agreement for Japan with Astellas

In November 2009, the Company entered into a license agreement with Astellas, as amended, to develop and commercialize linaclotide for the treatment of IBS C, CIC and other GI conditions in Japan. Astellas is responsible for all activities relating to development, regulatory approval and commercialization in Japan as well as funding the associated costs and the Company is required to participate on a joint development committee over linaclotide's development period.

In 2009, Astellas paid the Company a non refundable, up front licensing fee of $30.0 million, which was recognized as collaborative arrangements revenue on a straight line basis over the Company's estimate of the period over which linaclotide was developed under the license agreement. In March 2013 and September 2016, the Company revised its estimate of the development period from 115 months to 85 months and from 85 months to 82 months, respectively, based on the Company's assessment of regulatory approval timelines for Japan. During the year ended December 31, 2016, the Company recognized approximately $6.3 million of revenue related to the up-front licensing fee. The revenue recognized during the year ended December 31, 2016 includes approximately $1.9 million of revenue attributable to a revision to the estimated development period in March 2013 and an additional approximately $1.3 million of revenue attributable to a revision to the estimated development period in September 2016. During the years ended December 31, 2015 and 2014, the Company recognized approximately $5.1 million of revenue in each period related to the up-front licensing fee, including approximately $1.9 million of revenue in each period attributable to the March 2013 revision to the estimated development period.

The agreement also includes three development milestone payments that totaled up to $45.0 million, none of which the Company considers substantive. The first milestone payment, consisting of $15.0 million upon enrollment of the first study subject in a Phase III study for linaclotide in Japan, was achieved in November 2014 and was recognized as revenue through December 31, 2016, including approximately $2.7 million, approximately $2.1 million and approximately $10.2 million during the years ended December 31, 2016, 2015 and 2014, respectively. In February 2016, Astellas filed an NDA with the Japanese Ministry of Health, Labor and Welfare seeking approval of linaclotide for the treatment of adults with IBS-C in Japan. In connection with this filing, a second milestone payment, consisting of $15.0 million, was achieved and was recognized as revenue during the year ended December 31, 2016. The third development milestone payment consisting of $15.0 million upon approval of an NDA by the Japanese Ministry of Health, Labor and Welfare to market linaclotide in Japan was also earned and recognized as revenue during the year ended December 31, 2016. In addition, the Company will receive royalties which escalate based on sales volume, beginning in the low twenties percent, less the transfer price paid for the API included in the product actually sold and other contractual deductions.

During the years ended December 31, 2016, 2015 and 2014, the Company recognized approximately $44.4 million, approximately $7.7 million, and approximately $17.7 million, respectively, in collaborative arrangements revenue from the Astellas license agreement, including approximately $5.4 million, approximately $0.5 million, and approximately $2.4 million, respectively, from the sale of API to Astellas.

Collaboration Agreement for China, Hong Kong and Macau with AstraZeneca

In October 2012, the Company entered into a collaboration agreement with AstraZeneca (the "AstraZeneca Collaboration Agreement") to co develop and co commercialize linaclotide in China, Hong Kong and Macau (the "License Territory"). The collaboration provides AstraZeneca with an exclusive nontransferable license to exploit the underlying technology in the License Territory. The parties share responsibility for continued development and commercialization of linaclotide under a joint development plan and a joint commercialization plan, respectively, with AstraZeneca having primary responsibility for the local operational execution.

The parties agreed to an Initial Development Plan ("IDP") which includes the planned development of linaclotide in China, including the lead responsibility for each activity and the related internal and external costs. The

Table of Contents

IDP indicates that AstraZeneca is responsible for a multinational Phase III clinical trial (the "Phase III Trial"), the Company is responsible for nonclinical development and supplying clinical trial material and both parties are responsible for the regulatory submission process. The IDP indicates that the party specifically designated as being responsible for a particular development activity under the IDP shall implement and conduct such activities. The activities are governed by a Joint Development Committee ("JDC"), with equal representation from each party. The JDC is responsible for approving, by unanimous consent, the joint development plan and development budget, as well as approving protocols for clinical studies, reviewing and commenting on regulatory submissions, and providing an exchange of data and information.

The AstraZeneca Collaboration Agreement will continue until there is no longer a development plan or commercialization plan in place, however, it can be terminated by AstraZeneca at any time upon 180 days' prior written notice. Under certain circumstances, either party may terminate the AstraZeneca Collaboration Agreement in the event of bankruptcy or an uncured material breach of the other party. Upon certain change in control scenarios of AstraZeneca, the Company may elect to terminate the AstraZeneca Collaboration Agreement and may re acquire its product rights in a lump sum payment equal to the fair market value of such product rights.

In connection with the AstraZeneca Collaboration Agreement, the Company and AstraZeneca also executed a co-promotion agreement (the "Co-Promotion Agreement"), pursuant to which the Company utilized its existing sales force to co-promote NEXIUM® (esomeprazole magnesium), one of AstraZeneca's products, in the U.S. The Co-Promotion Agreement expired in May 2014.

There are no refund provisions in the AstraZeneca Collaboration Agreement and the Co Promotion Agreement (together, the "AstraZeneca Agreements").

Under the terms of the AstraZeneca Collaboration Agreement, the Company received a $25.0 million non refundable up-front payment upon execution. The Company is also eligible for $125.0 million in additional commercial milestone payments contingent on the achievement of certain sales targets. The parties will also share in the net profits and losses associated with the development and commercialization of linaclotide in the License Territory, with AstraZeneca receiving 55% of the net profits or incurring 55% of the net losses until a certain specified commercial milestone is achieved, at which time profits and losses will be shared equally thereafter.

Activities under the AstraZeneca Agreements were evaluated in accordance with ASC Topic 605-25, Revenue Recognition—Multiple-Element Arrangements, or ASC 605-25, to determine if they represented a multiple element revenue arrangement. The Company identified the following deliverables in the AstraZeneca Agreements:

- an exclusive license to develop and commercialize linaclotide in the License Territory (the "License Deliverable"),
- research, development and regulatory services pursuant to the IDP, as modified from time to time (the "R&D Services"),
- JDC services,
- obligation to supply clinical trial material, and
- co promotion services for AstraZeneca's product (the "Co Promotion Deliverable").

The License Deliverable is nontransferable and has certain sublicense restrictions. The Company determined that the License Deliverable had standalone value as a result of AstraZeneca's internal product development and commercialization capabilities, which would enable it to use the License Deliverable for its intended purposes without the involvement of the Company. The remaining deliverables were deemed to have standalone value based on their nature and all deliverables met the criteria to be accounted for as separate units of accounting under ASC 605 25. Factors considered in this determination included, among other things, whether any other vendors sell the items separately and if the customer could use the delivered item for its intended purpose without the receipt of the remaining deliverables.

Table of Contents

The Company identified the supply of linaclotide drug product for commercial requirements and commercialization services as contingent deliverables because these services are contingent upon the receipt of regulatory approval to commercialize linaclotide in the License Territory, and there were no binding commitments or firm purchase orders pending for commercial supply at the inception of the AstraZeneca Collaboration Agreement. As these deliverables are contingent, and are not at an incremental discount, they are not evaluated as deliverables at the inception of the arrangement. These contingent deliverables will be evaluated and accounted for separately as each related contingency is resolved. As of December 31, 2016, no contingent deliverables were provided by the Company under the AstraZeneca Agreements.

In August 2014, the Company and AstraZeneca, through the JDC, modified the IDP and development budget to include approximately $14.0 million in additional activities over the remaining development period, to be shared by the Company and AstraZeneca under the terms of the AstraZeneca Collaboration Agreement. These additional activities serve to support the continued development of linaclotide in the License Territory, including the Phase III Trial. Pursuant to the terms of the modified IDP and development budget, certain of the Company's deliverables were modified, specifically the R&D Services and the obligation to supply clinical trial material. The modification did not, however, have a material impact on the Company's consolidated financial statements.

The total amount of the non contingent consideration allocable to the AstraZeneca Agreements was approximately $34.0 million ("Arrangement Consideration") which includes the $25.0 million non refundable up-front payment and approximately $9.0 million representing 55% of the costs for clinical trial material supply services and research, development and regulatory activities allocated to the Company in the IDP or as approved by the JDC in subsequent periods.

The Company allocated the Arrangement Consideration to the non-contingent deliverables based on management's best estimated selling price ("BESP") of each deliverable using the relative selling price method, as the Company did not have vendor-specific objective evidence or third-party evidence of selling price for such deliverables. Of the total Arrangement Consideration, approximately $29.7 million was allocated to the License Deliverable, approximately $1.8 million to the R&D Services, approximately $0.1 million to the JDC services, approximately $0.3 million to the clinical trial material supply services, and approximately $2.1 million to the Co-Promotion Deliverable in the relative selling price model, at the time of the material modification.

Because the Company shares development costs with AstraZeneca, payments from AstraZeneca with respect to both research and development and selling, general and administrative costs incurred by the Company prior to the commercialization of linaclotide in the License Territory are recorded as a reduction in expense, in accordance with the Company's policy, which is consistent with the nature of the cost reimbursement. Development costs incurred by the Company that pertain to the joint development plan and subsequent amendments to the joint development plan, as approved by the JDC, are recorded as research and development expense as incurred. Payments to AstraZeneca are recorded as incremental research and development expense.

The Company completed its obligations related to the License Deliverable upon execution of the AstraZeneca Agreements; however, the revenue recognized in the statement of operations was limited to the non-contingent portion of the License Deliverable consideration in accordance with ASC 605-25. During the years ended December 31, 2016, 2015 and 2014, the Company recognized approximately $0.4 million, approximately $2.2 million and approximately $2.5 million, respectively, in collaborative arrangements revenue related to the License Deliverable in connection with the modification to the IDP and development budget in August 2014, as such this portion of the Arrangement Consideration was no longer contingent.

The Company also performs R&D Services and JDC services, and supplies clinical trial materials during the estimated development period. All Arrangement Consideration allocated to such services is being recognized as a reduction of

research and development costs, using the proportional performance method, by which the amounts are recognized in proportion to the costs incurred. As a result of the cost sharing arrangements under the collaboration, the Company recognized an insignificant reduction in research and development costs during the year ended December 31, 2016. During the years ended December 31, 2015 and 2014, the Company recognized approximately $0.7 million and approximately $2.4 million in incremental research and development costs, respectively. The amount allocated to the Co-Promotion Deliverable was recognized as collaborative arrangements revenue using the proportional performance method, which approximates recognition on a straight-line basis beginning on the date that the Company began to co-promote AstraZeneca's product through December 31, 2013 (the earliest cancellation date). As of December 31, 2013,

Table of Contents

the Company completed its obligation related to the Co-Promotion Deliverable; however, the revenue recognized in the statement of operations was limited to the non-contingent consideration in accordance with ASC 605-25. During the years ended December 31, 2016, 2015 and 2014, the Company recognized an insignificant amount, approximately $0.2 million and approximately $0.9 million, respectively, as collaborative arrangements revenue related to this deliverable, as this portion of the Arrangement Consideration was no longer contingent.

The Company reassesses the periods of performance for each deliverable at the end of each reporting period.

Milestone payments received from AstraZeneca upon the achievement of sales targets will be recognized as earned.

Co-Promotion Agreements

Co-Promotion Agreement with Exact Sciences Corp. for Cologuard

In March 2015, the Company and Exact Sciences entered into an agreement to co-promote Exact Sciences' Cologuard, the first and only FDA-approved noninvasive stool DNA screening test for colorectal cancer (the "Exact Sciences Co-Promotion Agreement"). The Exact Sciences Co-Promotion Agreement was terminated by the parties in August 2016. Under the terms of the non-exclusive Exact Sciences Co-Promotion Agreement, the Company's sales team promoted and educated health care practitioners regarding Cologuard through July 2016, with LINZESS remaining the Company's first-position product. Exact Sciences maintained responsibility for all other aspects of the commercialization of Cologuard outside of the co-promotion. Under the terms of the Exact Sciences Co-Promotion Agreement, the Company is compensated primarily via royalties earned on the net sales of Cologuard generated from the healthcare practitioners on whom the Company called with such royalties being payable through July 2017. There are no refund provisions in the Exact Sciences Co-Promotion Agreement. Through December 31, 2016, the Company received approximately $3.4 million in connection with the Exact Sciences Co-Promotion Agreement.

Activities under the Exact Sciences Co-Promotion Agreement were evaluated in accordance with ASC 605-25, to determine if they represented a multiple element revenue arrangement. The Company identified the following deliverables in the Exact Sciences Co-Promotion Agreement through July 31, 2016: (i) second position sales detailing, (ii) promotional support services, and (iii) medical education services. Each of the deliverables was deemed to have standalone value based on their nature and all deliverables met the criteria to be accounted for as separate units of accounting under ASC 605-25. The Company determined that the BESP for each of the three deliverables approximated the value allocated to the deliverables under the agreement. The revenue related to each deliverable is recognized as collaborative arrangements revenue in the Company's consolidated statement of operations, in accordance with ASC 605-25, during the period earned. During the years ended December 31, 2016 and 2015, the Company recognized approximately $3.5 million and approximately $4.4 million as collaborative arrangements revenue related to this arrangement.

Co-Promotion Agreement with Allergan for VIBERZI

In August 2015, the Company and Allergan entered into an agreement for the co-promotion of VIBERZI in the U.S., Allergan's treatment for adults suffering from IBS-D (the "VIBERZI Co-Promotion Agreement"). Under the terms of the VIBERZI Co-Promotion Agreement, the Company's clinical sales specialists are detailing VIBERZI to the approximately 25,000 health care practitioners to whom they detail LINZESS. Allergan is responsible for all costs and activities relating to the commercialization of VIBERZI outside of the co-promotion.

Under the terms of the VIBERZI Co-Promotion Agreement, the Company's promotional efforts are compensated based on the volume of calls delivered by the Company's sales force, with the terms of the agreement reducing or eliminating certain of the unfavorable adjustments to the Company's share of net profits stipulated by the linaclotide

collaboration agreement with Allergan for North America, provided that the Company provides a minimum number of VIBERZI calls on physicians. The Company has the potential to achieve milestone payment of up to $10.0 million based on the net sales of VIBERZI in each of 2017 and 2018, and is also compensated via reimbursements for medical education initiatives.

The Company’s promotional efforts under the non-exclusive co-promotion began when VIBERZI became commercially available in December 2015, and will continue until December 31, 2017, unless earlier terminated by

Table of Contents

either party pursuant to the provisions of the VIBERZI Co-Promotion Agreement. Either party may also terminate the VIBERZI Co-Promotion Agreement in the event of an uncured material breach by the other party, withdrawal of necessary approvals by the FDA, for convenience, or bankruptcy or insolvency of the other party. Allergan may terminate the VIBERZI Co-Promotion Agreement if the Company does not provide the minimum number of calls on physicians for VIBERZI.

Activities under the VIBERZI Co-Promotion Agreement were evaluated in accordance with ASC 605-25 to determine if they represented a multiple element revenue arrangement. The Company concluded that the VIBERZI Co-Promotion Agreement does not represent a material modification to the linaclotide collaboration agreement with Allergan for North America, as it is not material to the total arrangement consideration under the collaboration agreement, does not significantly modify the existing deliverables, and does not significantly change the term of the agreement. The Company identified the following deliverables in the VIBERZI Co-Promotion Agreement: (i) second position sales detailing of VIBERZI, and (ii) medical education services. Each of the deliverables was deemed to have standalone value based on their nature and both deliverables met the criteria to be accounted for as separate units of accounting under ASC 605-25. The Company determined the BESP for each of the deliverables approximated the value allocated to the deliverables under the agreement. As consideration is earned over the term of the agreement, the revenue will be allocated to each deliverable based on the relative selling price, using management's BESP, and recognized as collaborative arrangements revenue in the Company's consolidated statement of operations, in accordance with ASC 605-25, during the quarter earned.

Under the linaclotide collaboration agreement for North America with Allergan, if either party provides fewer calls on physicians in a particular year than it is contractually required to provide, such party's share of the net profits will be adjusted as set forth in the agreement; however, certain of these adjustments to the share of the net profits may be reduced or eliminated in connection with the co-promotion activities under the VIBERZI Co-Promotion Agreement through December 31, 2017. In connection with these co-promotion activities, the net profit share adjustments payable to Allergan under the linaclotide collaboration agreement for North America were reduced by approximately $5.3 million during the year ended December 31, 2016 and approximately $2.9 million during the year ended December 31, 2015. During the three months ended September 30, 2016, the Company also met the requirement for the minimum number of VIBERZI calls on physicians for 2016, which resulted in the Company's reversal of an approximately $2.4 million unfavorable adjustment previously recorded to collaborative arrangements revenue related to the linaclotide collaboration agreement with Allergan for North America. This approximately $2.4 million adjustment was originally recorded as an unfavorable adjustment to collaborative arrangements revenue during the six months ended June 30, 2015. During the years ended December 31, 2016 and 2015, the Company also recognized approximately $1.8 million and approximately $0.2 million in revenue related to the VIBERZI Co-Promotion Agreement for the performance of medical education services.

Other Collaboration and License Agreements

The Company has other collaboration and license agreements that are not individually significant to its business. Pursuant to the terms of one agreement, the Company may be required to pay $7.5 million for development milestones, of which, approximately $2.5 million had been paid as of December 31, 2016, and $18.0 million for regulatory milestones, none of which had been paid as of December 31, 2016. In addition, pursuant to the terms of another agreement, the contingent milestones could total up to $114.5 million per product to one of the Company's collaboration partners, including $21.5 million for development milestones, $58.0 million for regulatory milestones and $35.0 million for sales based milestones. Further, under such agreements, the Company is also required to fund certain research activities and, if any product related to these collaborations is approved for marketing, to pay significant royalties on future sales. The Company did not record any research and development expense associated with the Company's other collaboration and license agreements during the year ended December 31, 2016. During the year ended December 31, 2015, the Company incurred an insignificant amount in research and development expense

associated with the Company's other collaboration and license agreements. During the year ended December 31, 2014, the Company incurred approximately $1.0 million in research and development expense associated with the Company's other collaboration and license agreements.

Product Revenue

In October 2016, ZURAMPIC became commercially available in the U.S. During the year ended December 31, 2016, the Company recognized an insignificant amount of revenue related to product sales of ZURAMPIC in the U.S.

Table of Contents

This revenue is included as part of collaborative arrangements revenue on the Company's consolidated statements of operations.

6. Fair Value of Financial Instruments

The tables below present information about the Company's assets that are measured at fair value on a recurring basis as of December 31, 2016 and 2015 and indicate the fair value hierarchy of the valuation techniques the Company utilized to determine such fair value. In general, fair values determined by Level 1 inputs utilize observable inputs such as quoted prices in active markets for identical assets or liabilities. Fair values determined by Level 2 inputs utilize data points that are either directly or indirectly observable, such as quoted prices for similar instruments in active markets, interest rates and yield curves. Fair values determined by Level 3 inputs utilize unobservable data points in which there is little or no market data, which require the Company to develop its own assumptions for the asset or liability.

The Company's investment portfolio includes mainly fixed income securities that do not always trade on a daily basis. As a result, the pricing services used by the Company apply other available information as applicable through processes such as benchmark yields, benchmarking of like securities, sector groupings and matrix pricing to prepare valuations. In addition, model processes are used to assess interest rate impact and develop prepayment scenarios. These models take into consideration relevant credit information, perceived market movements, sector news and economic events. The inputs into these models may include benchmark yields, reported trades, broker-dealer quotes, issuer spreads and other relevant data. The Company validates the prices provided by its third party pricing services by obtaining market values from other pricing sources and analyzing pricing data in certain instances.

The following tables present the assets and liabilities the Company has measured at fair value on a recurring basis (in thousands):

| | | Fair Value Measurements at Reporting Date Using | | |
|---|---|---|---|---|
| | December 31, 2016 | Quoted Prices in Active Markets for Identical Assets (Level 1) | Significant Other Observable Inputs (Level 2) | Significant Unobservable Inputs (Level 3) |
| Assets: | | | | |
| Cash and cash equivalents: | | | | |
| Money market funds | $ 32,486 | $ 32,486 | $ — | $ — |
| Available-for-sale securities: | | | | |
| U.S. Treasury securities | 115,021 | 115,021 | — | — |
| U.S. government-sponsored securities | 136,191 | — | 136,191 | — |
| Convertible Note Hedges | 132,521 | — | — | 132,521 |
| Total assets measured at fair value | $ 416,219 | $ 147,507 | $ 136,191 | $ 132,521 |
| Liabilities: | | | | |
| Note Hedge Warrants | $ 113,237 | $ — | $ — | $ 113,237 |
| Contingent Consideration | 77,660 | — | — | 77,660 |
| Total liabilities measured at fair value | $ 190,897 | $ — | $ — | $ 190,897 |

Table of Contents

| | | Fair Value Measurements at Reporting Date Using | | |
|---|---|---|---|---|
| | December 31, 2015 | Quoted Prices in Active Markets for Identical Assets (Level 1) | Significant Other Observable Inputs (Level 2) | Significant Unobservable Inputs (Level 3) |
| Assets: | | | | |
| Cash and cash equivalents: | | | | |
| Money market funds | $ 254,903 | $ 254,903 | $ — | $ — |
| U.S. government-sponsored securities | 3,340 | — | 3,340 | — |
| Available-for-sale securities: | | | | |
| U.S. Treasury securities | 50,091 | 50,091 | — | — |
| U.S. government-sponsored securities | 128,016 | — | 128,016 | — |
| Convertible Note Hedges | 86,466 | — | — | 86,466 |
| Total assets measured at fair value | $ 522,816 | $ 304,994 | $ 131,356 | $ 86,466 |
| Liabilities: | | | | |
| Note Hedge Warrants | $ 75,328 | $ — | $ — | $ 75,328 |
| Total liabilities measured at fair value | $ 75,328 | $ — | $ — | $ 75,328 |

There were no transfers between fair value measurement levels during the years ended December 31, 2016 or 2015.

Cash equivalents, accounts receivable, related party accounts receivable, prepaid expenses and other current assets, accounts payable, related party accounts payable, accrued expenses and the current portion of capital lease obligations at December 31, 2016 and 2015 are carried at amounts that approximate fair value due to their short-term maturities.

The non current portion of the capital lease obligations at December 31, 2016 and 2015 approximates fair value as it bears interest at a rate approximating a market interest rate.

Convertible Note Hedges and Note Hedge Warrants

The Company’s Convertible Note Hedges and the Note Hedge Warrants are recorded as derivative assets and liabilities, and are classified as Level 3 under the fair value hierarchy. These derivatives are not actively traded and are valued using the Black-Scholes option-pricing model which requires the use of subjective assumptions. Significant inputs used to determine the fair value as of December 31, 2016 included the price per share of the Company’s Class A common stock, time to maturity of the derivative instruments, the strike prices of the derivative instruments, the risk-free interest rate, and the volatility of the Company’s Class A common stock. The Company has not paid and does not anticipate paying cash dividends on its shares of common stock in the foreseeable future; therefore, the expected dividend yield is assumed to be zero. Changes to these inputs could materially affect the valuation of the Convertible Note Hedges and Note Hedge Warrants.

The following inputs were used in the fair market valuation of the Convertible Note Hedges and Note Hedge Warrants as of December 31, 2016 and 2015:

| | 2016 Convertible Note Hedge | 2015 Convertible Note Hedge |
|---|---|---|

| | Note Hedges | Warrants | Note Hedges | Warrants |
|---|---|---|---|---|
| Risk-free interest rate (1) | 2.0 % | 2.1 % | 2.0 % | 2.1 % |
| Time to maturity | 5.5 | 6.0 | 6.5 | 7.0 |
| Stock price (2) | $ 15.29 | $ 15.29 | $ 11.59 | $ 11.59 |
| Strike price (3) | $ 16.58 | $ 21.50 | $ 16.58 | $ 21.50 |
| Common stock volatility (4) | 47.4 % | 45.8 % | 45.0 % | 45.0 % |
| Dividend yield | — % | — % | — % | — % |

(1) Based on U.S. Treasury yield curve, with terms commensurate with the terms of the Convertible Note Hedges and the Note Hedge Warrants

Table of Contents

(2) The closing price of the Company's Class A common stock on the last trading day of the year ended December 31, 2016 and December 31, 2015, respectively.
(3) As per the respective agreements for the Convertible Note Hedges and Note Hedge Warrants.
(4) Selected volatility based on historical volatility and implied volatility of the Company's Class A common stock.

The Convertible Note Hedges and the Note Hedge Warrants are recorded at fair value at each reporting period and changes in fair value are recorded in other expense, net within the Company's consolidated statements of operations. Gains and losses for these derivative financial instruments are presented separately in the Company's consolidated statements of cash flows.

The following table reflects the change in the Company's Level 3 convertible note derivatives from their initial value at issuance through December 31, 2016 (in thousands):

| | Convertible Note Hedges | Note Hedge Warrants |
|---|---|---|
| Balance at December 31, 2014 | $ — | $ — |
| Issuance of Note Hedge Warrants | — | (70,849) |
| Purchase of Convertible Note Hedges | 91,915 | — |
| Change in fair value, recorded as a component of gain (loss) on derivatives | (5,449) | (4,479) |
| Balance at December 31, 2015 | $ 86,466 | $ (75,328) |
| Change in fair value, recorded as a component of gain (loss) on derivatives | 46,055 | (37,909) |
| Balance at December 31, 2016 | $ 132,521 | $ (113,237) |

Contingent Consideration

In connection with the Lesinurad Transaction, the Company recorded a liability of $87.6 million as of the Acquisition Date, representing the initial fair value of the contingent consideration. Subsequently, the Company recorded a decrease of approximately $19.8 million as part of a measurement period adjustment to the Acquisition Date fair value. This valuation was based on a Monte-Carlo simulation, which includes significant estimates related to probability weighted net cash outflow projections, discounted using a yield curve equivalent to the Company's credit risk, which was the estimated cost of debt financing for market participants. This estimate represents the probability weighted analysis of expected future milestone and royalty payments based on net sales to be made to AstraZeneca. Changes to these inputs are re-evaluated each reporting period and could materially affect the valuation of the contingent consideration. The estimated fair value of contingent consideration was approximately $77.7 million as of December 31, 2016.

The following table reflects the change in the Company's Level 3 contingent consideration payable from December 31, 2015 through December 31, 2016 (in thousands):

| | Contingent Consideration |
|---|---|
| Fair value at December 31, 2015 | $ — |
| Additions (1) | 67,885 |
| Changes in fair value | 9,831 |
| Payments/transfers to accrued expenses and other current liabilities | (56) |
| Fair value at December 31, 2016 | $ 77,660 |

(1) Includes approximately $19.8 million in measurement period adjustments to the Acquisition Date fair value recorded during the year ended December 31, 2016.

11% PhaRMA Notes

In January 2013, the Company closed a private placement of $175.0 million in aggregate principal amount of the PhaRMA Notes due on or before June 15, 2024. The estimated fair value of the PhaRMA Notes was approximately $134.9 million and approximately $166.8 million as of December 31, 2016 and 2015, respectively, and was determined using Level 3 inputs, including a quoted rate.

Table of Contents

2.25% Convertible Senior Notes

In June 2015, the Company issued approximately $335.7 million of its 2022 Notes. The Company separately accounted for the liability and equity components of the 2022 Notes by allocating the proceeds between the liability component and equity component (Note 11). The fair value of the 2022 Notes, which differs from their carrying value, is influenced by interest rates, the price of the Company's Class A common stock and the volatility thereof, and the prices for the 2022 Notes observed in market trading, which are Level 2 inputs. The estimated fair value of the 2022 Notes as of December 31, 2016 and 2015 was approximately $384.2 million and approximately $311.6 million, respectively.

7. Available for Sale Securities

The following tables summarize the available for sale securities held at December 31, 2016 and 2015 (in thousands):

| | Amortized Cost | Gross Unrealized Gains | Gross Unrealized Losses | Fair Value |
|---|---|---|---|---|
| December 31, 2016 | | | | |
| U.S. Treasury securities | $ 115,026 | $ 6 | $ (11) | $ 115,021 |
| U.S. government-sponsored securities | 136,193 | 10 | (12) | 136,191 |
| Total | $ 251,219 | $ 16 | $ (23) | $ 251,212 |

| | Amortized Cost | Gross Unrealized Gains | Gross Unrealized Losses | Fair Value |
|---|---|---|---|---|
| December 31, 2015 | | | | |
| U.S. Treasury securities | $ 50,124 | $ — | $ (33) | $ 50,091 |
| U.S. government-sponsored securities | 128,069 | 2 | (55) | 128,016 |
| Total | $ 178,193 | $ 2 | $ (88) | $ 178,107 |

The contractual maturities of all securities held at December 31, 2016 are one year or less. There were 34 and 32 available for sale securities in an unrealized loss position at December 31, 2016 and 2015, respectively, none of which had been in an unrealized loss position for more than twelve months. The aggregate fair value of these securities at December 31, 2016 and 2015 was approximately $111.3 million and approximately $167.6 million, respectively. The Company reviews its investments for other-than-temporary impairment whenever the fair value of an investment is less than amortized cost and evidence indicates that an investment's carrying amount is not recoverable within a reasonable period of time. To determine whether an impairment is other-than-temporary, the Company considers whether it has the ability and intent to hold the investment until a market price recovery and considers whether evidence indicating the cost of the investment is recoverable outweighs evidence to the contrary. The Company does not intend to sell the investments and it is not more likely than not that the Company will be required to sell the investments before recovery of their amortized cost bases, which may be maturity. The Company did not hold any securities with other-than-temporary impairment at December 31, 2016.

There were no sales of available-for-sale securities during the years ended December 31, 2016, 2015 and 2014. Net unrealized holding gains or losses for the period that have been included in accumulated other comprehensive income were not material to the Company's consolidated results of operations.

Table of Contents

8. Inventory

Inventory consisted of the following (in thousands):

| | December 31, | |
|---|---|---|
| | 2016 | 2015 |
| Raw Materials | $ 1,010 | $ — |
| Work in Progress | 71 | — |
| | $ 1,081 | $ — |

The Company’s inventory represents linaclotide API and drug product that is available for commercial sale. The Company evaluates inventory levels quarterly and any inventory that has a cost basis in excess of its expected net realizable value, inventory that becomes obsolete, inventory in excess of expected sales requirements, inventory that fails to meet commercial sale specifications or is otherwise impaired is written down with a corresponding charge to the statement of operations in the period that the impairment is first identified.

The Company has entered into multiple commercial supply agreements for the purchase of linaclotide API. Two of the Company’s linaclotide API supply agreements for supplying API to its collaboration partners outside of North America contain minimum purchase commitments (Note 12). Prior to October 2015, the Company was also responsible for the manufacturing of linaclotide API for Europe. As part of the Company's net realizable value assessment of its inventory, the Company assesses whether it has any excess non-cancelable purchase commitments resulting from its minimum supply agreements with its suppliers of linaclotide API.

The determination of the net realizable value of inventory and non-cancelable purchase commitments is based on demand forecasts from the Company's partners, that are received quarterly, to project the next 24 months of demand and the Company’s internal forecast for projected demand in subsequent years. During the three months ended June 30, 2015, Almirall, the Company’s former European partner, reduced its forecasted purchases of linaclotide API for its territory for the subsequent 18 months. In addition, regulatory changes made by the CFDA to the marketing approval process in China resulted in a potentially lengthened approval timeline for the commercialization of linaclotide. The reduced demand from Almirall and the potential extended timeline for commercialization of linaclotide in China resulted in lower projected sales of linaclotide API to the Company’s partners in Europe and China. As a result, during the three months ended June 30, 2015, the Company wrote-down the balance of its inventory of approximately $5.0 million to zero and accrued approximately $3.2 million for excess non-cancelable inventory purchase commitments.

In October 2015, Almirall transferred its exclusive license to develop and commercialize linaclotide in Europe to Allergan, and the Company separately entered into an amendment to the license agreement with Allergan relating to the development and commercialization of linaclotide in Europe. Pursuant to the terms of the amendment, Allergan assumed responsibility for the manufacturing of linaclotide API for Europe, as well as the associated costs (Note 5). Upon the execution of the amendment to the license agreement, the Company recorded an incremental loss on non-cancelable API purchase commitments of approximately $6.9 million related to one of the Company’s API supply agreements covering the commercial supply of linaclotide API for the European market. During the three months ended September 30, 2015, the Company also recorded an incremental loss on non-cancelable API purchase commitments related to in-process API batches. As of December 31, 2016, the Company has evaluated all remaining minimum purchase commitments under its linaclotide API supply agreements through 2023 (Note 12) and concluded that the approximately $20.1 million of purchase commitments from the second API supply agreement covering the Japan, China, Hong Kong and Macau markets are realizable based on the current forecasts received from the Company’s partners in these territories and the Company’s internal forecasts.

During the year ended December 31, 2014, the Company wrote-down approximately $20.3 million in inventory to an estimated net realizable value of approximately $5.0 million. This write-down was primarily attributable to Almirall's reduced inventory demand forecasts for the European territory, mainly due to the suspension of commercialization of CONSTELLA in Germany and a challenging commercial environment throughout Europe.

The write-downs of inventory to net realizable value and the loss on non-cancelable inventory purchase commitments are recorded as a separate line item in the Company's consolidated statement of operations. As of December 31, 2016, the accrual for excess purchase commitments is recorded as approximately $2.5 million in accrued

Table of Contents

expenses and other current liabilities and approximately $7.6 million in other liabilities in the Company's consolidated balance sheet.

9. Property and Equipment

Property and equipment, net consisted of the following (in thousands):

| | December 31, | |
|---|---|---|
| | 2016 | 2015 |
| Manufacturing equipment | $ 3,748 | $ 3,748 |
| Laboratory equipment | 15,021 | 13,681 |
| Computer and office equipment | 2,553 | 3,596 |
| Furniture and fixtures | 2,078 | 2,062 |
| Software | 12,945 | 12,715 |
| Construction in process | 814 | 375 |
| Leased vehicles | 7,058 | 3,039 |
| Leasehold improvements | 38,513 | 38,465 |
| | 82,730 | 77,681 |
| Less accumulated depreciation and amortization | (62,218) | (56,606) |
| | $ 20,512 | $ 21,075 |

As of December 31, 2016 and 2015, substantially all of the Company’s manufacturing equipment was located in the United Kingdom at one of the Company’s contract manufacturers. All other property and equipment were located in the U.S. for the periods presented.

The Company has entered into capital leases for certain computers, vehicles and office equipment (Note 12). As of December 31, 2016 and 2015, the Company had approximately $7.8 million and approximately $3.8 million of assets under capital leases with accumulated amortization balances of approximately $1.6 million and approximately $1.3 million, respectively.

Depreciation and amortization expense of property and equipment, including amounts recorded under capital leases, was approximately $10.3 million, approximately $11.6 million, and approximately $12.3 million for the years ended December 31, 2016, 2015 and 2014, respectively. In addition, the Company wrote-down approximately $0.5 million of leasehold improvement assets not utilized by the Company under the terms of its subleases during the year ended December 31, 2014.

10. Accrued Expenses

Accrued expenses consisted of the following (in thousands):

| | December 31, | |
|---|---|---|
| | 2016 | 2015 |
| Salaries and benefits | $ 25,884 | $ 19,582 |
| Professional fees | 1,213 | 507 |
| Accrued interest | 971 | 1,103 |
| Repurchasable Stock | 882 | — |
| Other | 9,351 | 2,109 |
| | $ 38,301 | $ 23,301 |

As of December 31, 2016, other accrued expenses of approximately $9.4 million includes approximately $2.8 million related to expenses incurred under the Lesinurad TSA.

Table of Contents

11. Notes Payable

8.375% Notes due 2026

On September 23, 2016, the Company closed a direct private placement, pursuant to which the Company subsequently issued $150.0 million in aggregate principal amount of 8.375% notes due 2026 on the Funding Date, January 5, 2017. The proceeds from the issuance of the 2026 Notes were used to redeem the outstanding principal balance of the PhaRMA Notes on the Funding Date. As of December 31, 2016, the Company capitalized approximately $0.5 million of debt issuance costs, which are included in other assets on the Company's consolidated balance sheet. Upon funding, the issuance costs were netted against the outstanding 2026 Notes.

The 2026 Notes bear an annual interest rate of 8.375%, with interest payable March 15, June 15, September 15 and December 15 of each year (each "8.375% Payment Date") commencing on June 15, 2017. Principal of the 2026 Notes will be payable on the 8.375% Payment Dates beginning March 15, 2019. From March 15, 2019, the Company will make quarterly payments on the 2026 Notes equal to the greater of (i) 7.5% of net sales of linaclotide in the U.S. for the preceding quarter (the "8.375% Synthetic Royalty Amount") and (ii) accrued and unpaid interest on the 2026 Notes (the "8.375% Required Interest Amount"). Principal on the 2026 Notes will be repaid in an amount equal to the 8.375% Synthetic Royalty Amount minus the 8.375% Required Interest Amount, when this is a positive number, until the principal has been paid in full. Given the principal payments on the 2026 Notes are based on the 8.375% Synthetic Royalty Amount, which will vary from quarter to quarter, the 2026 Notes may be repaid prior to September 15, 2026, the final legal maturity date.

The 2026 Notes are secured by a security interest in a segregated bank account established to receive the required quarterly payments as well as certain limited accounts receivables, payment intangibles or other rights to payment or proceeds, in each case, up to the 8.375% Synthetic Royalty Amount or estimated equivalent thereto, as applicable. Up to the amount of the required quarterly payments under the 2026 Notes, Allergan will deposit its quarterly profit (loss) sharing payments due to the Company related to net sales of linaclotide in the U.S. pursuant to the collaboration agreement for North America, if any, into the segregated bank account. If the funds deposited by Allergan into the segregated bank account are insufficient to make a required payment of interest or principal on a particular 8.375% Payment Date, the Company is obligated to deposit such shortfall out of the Company's general funds into the segregated bank account.

The 2026 Notes may be redeemed at any time prior to maturity, in whole or in part, at the option of the Company. If the applicable redemption of the 2026 Notes occurs prior to March 15, 2018, the Company will pay a redemption price equal to the outstanding principal balance of the 2026 Notes being redeemed, plus (i) the difference between (A) the required interest amount that would have otherwise been payable from the date of redemption through March 15, 2018 on the outstanding principal balance of the 2026 Notes being redeemed, minus (B) the aggregate amount of interest the purchasers would earn if the outstanding principal balance of the 2026 Notes being redeemed were reinvested for the period from the date of redemption through March 15, 2018 at a rate per annum equal to the yield expressed as a rate listed in The Wall Street Journal for United States Treasury securities having a term of not greater than 12 months on the date three business days prior to the date of redemption, plus (ii) an amount equal to the

redemption premium that would otherwise be payable as if such redemption had occurred at March 15, 2018. If the applicable redemption of the 2026 Notes occurs on or after March 15, 2018, the Company will pay a redemption price equal to the percentage of outstanding principal balance of the 2026 Notes being redeemed specified below for the period in which the redemption occurs (plus the accrued and unpaid interest to the redemption date on the 2026 Notes being redeemed):

| Payment Dates | Redemption Percentage | |
|---|---|---|
| From and including March 15, 2018 to and including March 14, 2019 | 108.00 | % |
| From and including March 15, 2019 to and including March 14, 2020 | 105.50 | % |
| From and including March 15, 2020 to and including March 14, 2021 | 102.75 | % |
| From and including March 15, 2021 and thereafter | 100.00 | % |

The 2026 Notes contain certain covenants related to the Company's obligations with respect to the commercialization of linaclotide and the related collaboration agreement with Allergan for North America, as well as certain customary covenants, including covenants that limit or restrict the Company's ability to incur certain liens, merge or consolidate or make dispositions of assets. The 2026 Notes also specify a number of events of default (some of which

Table of Contents

are subject to applicable cure periods), including, among other things, covenant defaults, other non-payment defaults, and bankruptcy and insolvency defaults. Upon the occurrence of an event of default, subject to cure periods in certain circumstances, all amounts outstanding may become immediately due and payable.

The accounting for the 2026 Notes will require the Company to make certain estimates and assumptions about the future net sales of linaclotide in the U.S. Linaclotide has been marketed as LINZESS in the U.S. since December 2012 and the estimates of the magnitude and timing of linaclotide net sales are subject to significant variability and uncertainty. These estimates and assumptions are likely to change, which may result in future adjustments to the portion of the 2026 Notes that will be classified as a current liability, the amortization of debt issuance costs and discounts as well as the accretion of the interest expense. Any such adjustments could be material to the Company's consolidated financial statements.

2.25% Convertible Senior Notes due 2022

In June 2015, the Company issued approximately $335.7 million aggregate principal amount of the 2022 Notes. The Company received net proceeds of approximately $324.0 million from the sale of the 2022 Notes, after deducting fees and expenses of approximately $11.7 million. The Company used approximately $21.1 million of the net proceeds from the sale of the 2022 Notes to pay the net cost of the Convertible Note Hedges (after such cost was partially offset by the proceeds to the Company from the sale of the Note Hedge Warrants), as described below.

The 2022 Notes are governed by an indenture (the "Indenture") between the Company and U.S. Bank National Association, as the trustee. The 2022 Notes are senior unsecured obligations and bear cash interest at the annual rate of 2.25%, payable on June 15 and December 15 of each year, which began on December 15, 2015. The 2022 Notes will mature on June 15, 2022, unless earlier converted or repurchased. The Company may settle conversions of the 2022 Notes through payment or delivery, as the case may be, of cash, shares of Class A common stock of the Company or a combination of cash and shares of Class A common stock, at the Company's option (subject to, and in accordance with, the settlement provisions of the Indenture). The initial conversion rate for the 2022 Notes is 60.3209 shares of Class A common stock (subject to adjustment as provided for in the Indenture) per $1,000 principal amount of the 2022 Notes, which is equal to an initial conversion price of approximately $16.58 per share and 20,249,665 shares. Holders of the 2022 Notes may convert their 2022 Notes at their option at any time prior to the close of business on the business day immediately preceding December 15, 2021 in multiples of $1,000 principal amount, only under the following circumstances:

- during any calendar quarter commencing after the calendar quarter ending on September 30, 2015 (and only during such calendar quarter), if the last reported sale price of the Company's Class A common stock for at least 20 trading days (whether or not consecutive) during a period of 30 consecutive trading days ending on the last trading day of the immediately preceding calendar quarter is greater than or equal to 130% of the conversion price for the 2022 Notes on each applicable trading day;
- during the five business day period after any five consecutive trading day period (the "measurement period") in which the "trading price" (as defined in the Indenture) per $1,000 principal amount of the 2022 Notes for each trading day of the measurement period was less than 98% of the product of the last reported sale price of the Company's Class A common stock and the conversion rate for the 2022 Notes on each such trading day; or
- upon the occurrence of specified corporate events described in the Indenture.

On or after December 15, 2021, until the close of business on the second scheduled trading day immediately preceding June 15, 2022, holders may convert their 2022 Notes, in multiples of $1,000 principal amount, at the option

of the holder regardless of the foregoing circumstances.

If a make-whole fundamental change, as described in the Indenture, occurs and a holder elects to convert its 2022 Notes in connection with such make-whole fundamental change, such holder may be entitled to an increase in the conversion rate as described in the Indenture. The Company may not redeem the 2022 Notes prior to the maturity date and no "sinking fund" is provided for by the 2022 Notes, which means that the Company is not required to periodically redeem or retire the 2022 Notes. Upon the occurrence of certain fundamental changes involving the Company, holders of

Table of Contents

the 2022 Notes may require the Company to repurchase for cash all or part of their 2022 Notes at a repurchase price equal to 100% of the principal amount of the 2022 Notes to be repurchased, plus accrued and unpaid interest.

The Indenture does not contain any financial covenants or restrict the Company's ability to repurchase the Company's securities, pay dividends or make restricted payments in the event of a transaction that substantially increases the Company's level of indebtedness. The Indenture provides for customary events of default. In the case of an event of default with respect to the 2022 Notes arising from specified events of bankruptcy or insolvency, all outstanding 2022 Notes will become due and payable immediately without further action or notice. If any other event of default with respect to the 2022 Notes under the Indenture occurs or is continuing, the trustee or holders of at least 25% in aggregate principal amount of the then outstanding 2022 Notes may declare the principal amount of the 2022 Notes to be immediately due and payable. Notwithstanding the foregoing, the Indenture provides that, upon the Company's election, and for up to 180 days, the sole remedy for an event of default relating to certain failures by the Company to comply with certain reporting covenants in the Indenture consists exclusively of the right to receive additional interest on the 2022 Notes.

In accordance with accounting guidance for debt with conversion and other options, the Company separately accounted for the liability and equity components of the 2022 Notes by allocating the proceeds between the liability component and the embedded conversion option, or equity component, due to the Company's ability to settle the 2022 Notes in cash, its Class A common stock, or a combination of cash and Class A common stock at the option of the Company. The carrying amount of the liability component was calculated by measuring the fair value of a similar liability that does not have an associated convertible feature. The allocation was performed in a manner that reflected the Company's non-convertible debt borrowing rate for similar debt. The equity component of the 2022 Notes was recognized as a debt discount and represents the difference between the gross proceeds from the issuance of the 2022 Notes and the fair value of the liability of the 2022 Notes on their respective dates of issuance. The excess of the principal amount of the liability component over its carrying amount, or debt discount, is amortized to interest expense using the effective interest method over seven years, or the life of the 2022 Notes. The equity component is not remeasured as long as it continues to meet the conditions for equity classification.

The Company's outstanding Convertible Note balances as of December 31, 2016 and 2015 consisted of the following (in thousands):

| | December 31, | |
|---|---|---|
| Liability component: | 2016 | 2015 |
| Principal | $ 335,699 | $ 335,699 |
| Less: unamortized debt discount | (94,675) | (107,636) |
| Less: unamortized debt issuance costs | (6,781) | (7,443) |
| Net carrying amount | $ 234,243 | $ 220,620 |
| Equity component | $ 114,199 | $ 114,199 |

In connection with the issuance of the 2022 Notes, the Company incurred approximately $11.7 million of debt issuance costs, which primarily consisted of initial purchasers’ discounts and legal and other professional fees. The Company allocated these costs to the liability and equity components based on the allocation of the proceeds. The portion of these costs allocated to the equity components totaling approximately $4.0 million were recorded as a reduction to additional paid-in capital. The portion of these costs allocated to the liability components totaling approximately $7.7 million were recorded as a reduction in the carrying value of the debt on the balance sheet and are amortized to interest expense using the effective interest method over the expected life of the 2022 Notes.

The Company determined the expected life of the 2022 Notes was equal to their seven-year term. The effective interest rate on the liability components of the 2022 Notes for the period from the date of issuance through December

31,

Table of Contents

2016 was 9.34%. The following table sets forth total interest expense recognized related to the 2022 Notes during the years ended December 31, 2016 and 2015 (in thousands):

| | Year Ended December 31, | |
|---|---|---|
| | 2016 | 2015 |
| Contractual interest expense | $ 7,553 | $ 4,069 |
| Amortization of debt issuance costs | 661 | 305 |
| Amortization of debt discount | 12,961 | 6,563 |
| Total interest expense | $ 21,175 | $ 10,937 |

Future minimum payments under the 2022 Notes as of December 31, 2016, are as follows (in thousands):

| | |
|---|---|
| 2017 | $ 7,553 |
| 2018 | 7,553 |
| 2019 | 7,553 |
| 2020 | 7,553 |
| 2021 | 7,553 |
| Thereafter | 339,477 |
| Total future minimum payments under the 2022 Notes | 377,242 |
| Less: amounts representing interest | (41,543) |
| Less: unamortized debt discount | (94,675) |
| Less: unamortized debt issuance costs | (6,781) |
| Convertible senior notes balance | $ 234,243 |

Convertible Note Hedge and Warrant Transactions with Respect to 2022 Notes

To minimize the impact of potential dilution to the Company's Class A common stockholders upon conversion of the 2022 Notes, the Company entered into the Convertible Note Hedges covering 20,249,665 shares of the Company's Class A common stock in connection with the issuance of the 2022 Notes. The Convertible Note Hedges have an exercise price of approximately $16.58 per share and are exercisable when and if the 2022 Notes are converted. If upon conversion of the 2022 Notes, the price of the Company's Class A common stock is above the exercise price of the Convertible Note Hedges, the counterparties are obligated to deliver shares of the Company's Class A common stock and/or cash with an aggregate value approximately equal to the difference between the price of the Company's Class A common stock at the conversion date and the exercise price, multiplied by the number of shares of the Company's Class A common stock related to the Convertible Note Hedge being exercised.

Concurrently with entering into the Convertible Note Hedges, the Company also sold Note Hedge Warrants to the Convertible Note Hedge counterparties to acquire 20,249,665 shares of the Company's Class A common stock, subject to customary anti-dilution adjustments. The strike price of the Note Hedge Warrants is initially $21.50 per share, subject to adjustment, and such warrants are exercisable over the 150 trading day period beginning on September 15, 2022. The Note Hedge Warrants could have a dilutive effect on the Class A common stock to the extent that the market price per share of the Company's Class A common stock exceeds the applicable strike price of such warrants.

The Convertible Note Hedges and the Note Hedge Warrants are separate transactions entered into by the Company and are not part of the terms of the 2022 Notes. Holders of the 2022 Notes and the Note Hedge Warrants do not have any rights with respect to the Convertible Note Hedges. The Company paid approximately $91.9 million for the Convertible Note Hedges and recorded this amount as a long-term asset on the consolidated balance sheet. The Company received approximately $70.8 million for the Note Hedge Warrants and recorded this amount as a long-term liability, resulting in a net cost to the Company of approximately $21.1 million. The Convertible Note Hedges and Note Hedge Warrants are accounted for as derivative assets and liabilities, respectively, in accordance with ASC 815 (Note 6).

11% PhaRMA Notes due 2024

In January 2013, the Company closed a private placement of $175.0 million in aggregate principal amount of notes due on or before June 15, 2024. The PhaRMA Notes were redeemed on the 2026 Notes' Funding Date, January 5, 2017. The redemption is more fully described in Note 20, Subsequent Events. The PhaRMA Notes bore an annual

Table of Contents

interest rate of 11%, with interest payable March 15, June 15, September 15 and December 15 of each year (each "11% Payment Date") which began on June 15, 2013. On March 15, 2014, the Company began making quarterly payments on the PhaRMA Notes equal to the greater of (i) 7.5% of net sales of LINZESS in the U.S. for the preceding quarter (the "11% Synthetic Royalty Amount") and (ii) accrued and unpaid interest on the PhaRMA Notes (the "11% Required Interest Amount"). Principal on the PhaRMA Notes was repaid in an amount equal to the 11% Synthetic Royalty Amount minus the 11% Required Interest Amount, when this was a positive number, until the notes were fully redeemed. The Company made principal payments of approximately $40.7 million through December 31, 2016.

As of December 31, 2016, the PhaRMA Notes were secured solely by a security interest in a segregated bank account established to receive the required quarterly payments. Up to the amount of the required quarterly payments under the PhaRMA Notes, Allergan deposited its quarterly profit (loss) sharing payments due to the Company under the collaboration agreement for North America, if any, into the segregated bank account. If the funds deposited by Allergan into the segregated bank account were insufficient to make a required payment of interest or principal on a particular 11% Payment Date, the Company was obligated to deposit such shortfall out of the Company's general funds into the segregated bank account.

The PhaRMA Notes could be redeemed at any time prior to maturity, in whole or in part, at the option of the Company. The Company was required to pay a redemption price equal to the percentage of outstanding principal balance of the PhaRMA Notes being redeemed specified below for the period in which the redemption was to occur (plus the accrued and unpaid interest to the redemption date on the PhaRMA Notes being redeemed):

| Payment Dates | Redemption Percentage | |
|---|---|---|
| From and including January 1, 2016 to and including December 31, 2016 | 102.75 | % |
| From and including January 1, 2017 and thereafter | 100.00 | % |

The PhaRMA Notes contained certain covenants related to the Company's obligations with respect to the commercialization of LINZESS and the related collaboration agreement with Allergan for North America, as well as certain customary covenants, including covenants that limited or restricted the Company's ability to incur certain liens, merge or consolidate or make dispositions of assets. The PhaRMA Notes also specified a number of events of default (some of which are subject to applicable cure periods), including, among other things, covenant defaults, other non-payment defaults, and bankruptcy and insolvency defaults.

The up-front cash proceeds of $175.0 million, less a discount of approximately $0.4 million for payment of legal fees incurred on behalf of the noteholders, were recorded as notes payable at issuance. The Company also capitalized approximately $7.3 million of debt issuance costs in connection with the PhaRMA Notes. The PhaRMA Notes issuance costs and discount were amortized over the estimated term of the obligation using the effective interest method. The repayment provisions represent embedded derivatives that are clearly and closely related to the PhaRMA Notes and as such did not require separate accounting treatment.

The accounting for the PhaRMA Notes required the Company to make certain estimates and assumptions about the future net sales of LINZESS in the U.S. prior to December 31, 2016. As of December 31, 2016, the Company did not make estimates and assumptions about the future net sales of LINZESS in the U.S. to record the classification of the PhaRMA Notes on the consolidated balance sheets. In accordance with ASC Topic 470, Debt, the Company recorded the outstanding PhaRMA Notes balance as a long-term obligation, as the balance was subsequently redeemed on the Funding Date, January 5, 2017, with proceeds from the 2026 Notes. Principal of the 2026 Notes will be payable on the 8.375% Payment Dates beginning March 15, 2019.

12. Commitments and Contingencies

Lease Commitments

The Company leases its facility, offsite data storage location, vehicles and various equipment under leases that expire at varying dates through 2018. Certain of these leases contain renewal options, and require the Company to pay operating costs, including property taxes, insurance, maintenance and other operating expenses.

Table of Contents

As of December 31, 2016, the Company rents office and laboratory space at its corporate headquarters in Cambridge, Massachusetts under a non cancelable operating lease, entered into in January 2007, as amended ("2007 Lease Agreement"). The 2007 Lease Agreement contains various provisions for renewal at the Company's option and, in certain cases, free rent periods and rent escalation tied to the Consumer Price Index and fair market rent. The rent expense, inclusive of the escalating rent payments and free rent periods, is recognized on a straight line basis over the lease term through January 2018. The Company maintains a letter of credit securing its obligations under the lease agreement of approximately $7.6 million, which is recorded as restricted cash. In addition to rents due under this lease, the Company is obligated to pay facilities charges, including utilities and taxes. In connection with the 2007 Lease Agreement, the Company was provided allowances totaling approximately $22.9 million as reimbursement for financing capital improvements to the facility. The reimbursement amount is recorded as deferred rent on the consolidated balance sheets and is being amortized as a reduction to rent expense over the lease term, as applicable.

In 2014, the Company entered into arrangements, with the landlord's consent, to sublease a portion of its Cambridge, Massachusetts corporate headquarters as it did not intend to use the space for its operations. Under the first sublease, the Company's operating lease obligations through 2018 are partially offset by future sublease payments to it of approximately $16.1 million (of which approximately $9.9 million has been received through December 31, 2016) and under the second sublease, the Company's operating lease obligations through 2016 were partially offset by sublease payments to it of approximately $1.9 million received through December 31, 2016. During the year ended December 31, 2014, the Company recorded aggregate charges of approximately $2.6 million, which represent its obligations to the landlord associated with the sublet space, net of sublease income due to the Company under the subleases, and a partial write-down of leasehold improvement assets not utilized by the Company under the terms of the subleases.

Effective in February 2016, the Company's obligations due to the landlord of its corporate headquarters increased in connection with a rent escalation tied to the Consumer Price Index and fair market rent, pursuant to the terms of the 2007 Lease Agreement, which resulted in a change in the accounting estimate of rent expense. This change in accounting estimate is recognized on a prospective, straight-line basis. Rent expenses related to the 2007 Lease Agreement, net of sublease income, recorded during the years ended December 31, 2016, 2015 and 2014 were approximately $11.6 million, approximately $6.3 million and approximately $10.2 million, respectively. Sublease income was approximately $5.2 million, approximately $5.3 million and approximately $2.6 million under the operating leases for the years ended December 31, 2016, 2015 and 2014, respectively. In accordance with ASC Topic 420, Exit or Disposal Cost Obligations, the Company recorded all obligations to the landlord associated with sublet space, net of sublease income due to the Company under the subleases in the period in which the change occurred. As a result, the rent expense associated with the 2007 Lease Agreement for the year ended December 31, 2016 includes charges of approximately $3.5 million of estimated obligations to the landlord associated with the sublet space, net of sublease income due to the Company under the subleases.

In 2013, the Company entered into 36 month capital leases (the "2013 Vehicle Leases") for the vehicle fleet for its field-based sales force and medical science liaisons. The 2013 Vehicle Leases expired at various times through September 2016.

In November 2015, the Company entered into 12-month capital leases (the "2015 Vehicle Leases") for certain vehicles within its vehicle fleet for its field-based sales force and medical science liaisons. The 2015 Vehicle Leases expire at varying times through December 2017. In accordance with the terms of the 2015 Vehicle Leases, the Company maintains a letter of credit securing its obligations under the lease agreements of $0.6 million, which is recorded as restricted cash. In connection with entering into the 2015 Vehicle Leases, all of the 2013 Vehicle Leases were terminated as of December 31, 2016. At December 31, 2016, the weighted average interest rate on the outstanding

2015 Vehicle Lease obligations was approximately 3.3%.

The Company has also entered into capital leases for certain computer and office equipment. These capital leases expire in April 2018. At December 31, 2016, the weighted average interest rate on the outstanding capital lease obligations was approximately 14.5%.

Table of Contents

At December 31, 2016, future minimum lease payments under all non cancelable lease arrangements were as follows (in thousands):

| | Operating Lease Payments | Lease Payments to be Received from Subleases | Net Operating Lease Payments | Capital Lease Payments |
|---|---|---|---|---|
| 2017 | 20,498 | $ (5,649) | $ 14,849 | $ 6,370 |
| 2018 | 831 | $ (475) | $ 356 | $ 85 |
| Total future minimum lease payments | $ 21,329 | $ (6,124) | $ 15,205 | $ 6,455 |
| Less: amounts representing interest | | | | (146) |
| Capital lease obligations at December 31, 2016 | | | | 6,309 |
| Less: current portion of capital lease obligations | | | | (6,227) |
| Capital lease obligations, net of current portion | | | | $ 82 |

Commercial Supply Commitments

The Company has entered into multiple commercial supply agreements for the purchase of linaclotide finished drug product and API. Two of the Company’s API supply agreements for supplying API to its collaboration partners outside of North America contain minimum purchase commitments. In July 2015 and August 2015, the Company entered into amendments to its agreements with two of its suppliers of linaclotide API. One amendment reduced the Company's non-cancelable purchase commitments and the other increased the Company's non-cancelable purchase commitments, but extended the timeframe over which the Company must purchase the API. The amended contracts include remaining total non-cancelable commercial supply purchase obligations of approximately $30.2 million through 2023.

During the year ended December 31, 2015, the Company recognized approximately $10.1 million as an accrual for excess purchases commitments (Note 8). The first payment of approximately $2.5 million related to these accrued excess purchase commitments is in 2017, and is reflected as an other current liability in the Company’s consolidated balance sheet. The remaining payments under these accrued excess purchase commitments begin in 2018, and are approximately $2.5 million in each of the years 2018, 2019 and 2020. Such payments are recorded as other liabilities in the Company’s consolidated balance sheet. As of December 31, 2016, the Company's unrecognized minimum purchase requirements and other firm commitments related to the supply contracts associated with the territories not covered by the partnerships with Allergan for North America were as follows (in thousands):

| | |
|---|---|
| 2017 | $ 2,259 |
| 2018 | 2,322 |
| 2019 | 3,096 |
| 2020 | 3,096 |
| 2021 | 3,096 |
| Thereafter | 6,192 |
| Total unrecognized minimum purchase requirements | $ 20,061 |

In addition, the Company and Allergan are jointly obligated to make minimum purchases of linaclotide API for the territories covered by the Company's collaboration with Allergan for North America. Currently, Allergan fulfills all such minimum purchase commitments and, as a result, they are excluded from the amounts above. As of December

31, 2016, the Company has evaluated all remaining minimum purchase commitments under its linaclotide API supply agreements and has concluded that the remaining purchase commitments are realizable based on the current forecasts received from certain of the Company's partners and the Company's internal forecasts.

The Lesinurad CSA with AstraZeneca provides for commercial supply and samples of ZURAMPIC, and, if approved by the FDA, DUZALLO. The Lesinurad CSA includes certain purchase obligations based on the Company's forecasted demand for commercial product and samples. As of December 31, 2016, the Company had approximately $6.6 million of such commitments related to lesinurad commercial supply and samples for 2017 and none thereafter. During the TSA period, the Company records purchases of ZURAMPIC commercial supply and samples in prepaid assets as title does not pass to the Company. During the year ended December 31, 2016, the Company wrote-down approximately $0.4 million of prepaid ZURAMPIC commercial supply as result of revised demand forecasts. This

Table of Contents

write-down was recorded in write-downs of inventory to net realizable value and the loss on non-cancelable inventory purchase commitments in the Company's consolidated statement of operations.

As of December 31, 2016, the Company has evaluated all remaining non-cancelable purchase commitments under the Lesinurad CSA and concluded that its non-cancelable purchase commitments are realizable based on the Company's forecasted demand.

Commitments Related to the Collaboration and License Agreements

Under the collaborative agreements with Allergan for North America and AstraZeneca for China, Hong Kong and Macau, respectively, the Company shares with Allergan and AstraZeneca all development and commercialization costs related to linaclotide in the U.S. and for China, Hong Kong and Macau, respectively. The actual amounts that the Company pays its partners or that partners pay to the Company will depend on numerous factors outside of the Company's control, including the success of certain clinical development efforts with respect to linaclotide, the content and timing of decisions made by the regulators, the reimbursement and competitive landscape around linaclotide and the Company's other product candidates, and other factors.

Under the Lesinurad License, the Company is undertaking the development and commercialization of lesinurad in the U.S. Pursuant to the terms of the Lesinurad License, the Company will pay a tiered royalty to AstraZeneca in the single-digits as a percentage of net sales of ZURAMPIC, and if approved DUZALLO, in the U.S., as well as commercial and other milestones of up to $165.0 million over the duration of the agreement. Additionally, AstraZeneca is obligated to conduct certain development activities on the Company's behalf for (i) ZURAMPIC, including the post-marketing requirement activities currently required by the FDA, for which the Company is obligated to reimburse AstraZeneca up to $100.0 million over up to ten years, and (ii) DUZALLO, for which the Company will also reimburse AstraZeneca.

In addition, the Company has commitments to make potential future milestone payments to third parties under certain of its license and collaboration arrangements. These milestones primarily include the commencement and results of clinical trials, obtaining regulatory approval in various jurisdictions and the future commercial success of development programs, the outcome and timing of which are difficult to predict and subject to significant uncertainty. In addition to the milestones discussed above, the Company is obligated to pay royalties on future sales, which are contingent on generating levels of sales of future products that have not been achieved and may never be achieved.

These agreements are more fully described in Note 4, Business Combinations and Note 5, Collaboration, License, Co-promotion and Other Commercial Agreements, to these consolidated financial statements.

Other Funding Commitments

As of December 31, 2016, the Company has several on going studies in various clinical trial stages. The Company's most significant clinical trial expenditures are to contract research organizations ("CRO"). The contracts with CROs generally are cancellable, with notice, at the Company's option and do not have any significant cancellation penalties.

Guarantees

As permitted under Delaware law, the Company indemnifies its officers and directors for certain events or occurrences while the officer or director is, or was, serving at the Company's request in such capacity. The maximum potential amount of future payments the Company could be required to make is unlimited; however, the Company has directors' and officers' insurance coverage that is intended to limit its exposure and enable it to recover a portion of any future amounts paid.

The Company enters into certain agreements with other parties in the ordinary course of business that contain indemnification provisions. These typically include agreements with directors and officers, business partners, contractors, landlords, clinical sites and customers. Under these provisions, the Company generally indemnifies and holds harmless the indemnified party for losses suffered or incurred by the indemnified party as a result of the Company's activities. These indemnification provisions generally survive termination of the underlying agreements. The maximum potential amount of future payments the Company could be required to make under these indemnification provisions is unlimited. However, to date the Company has not incurred material costs to defend lawsuits or settle claims

Table of Contents

related to these indemnification provisions. As a result, the estimated fair value of these obligations is minimal. Accordingly, the Company had no liabilities recorded for these obligations as of December 31, 2016 and 2015.

Litigation

From time to time, the Company is involved in various legal proceedings and claims, either asserted or unasserted, which arise in the ordinary course of business. While the outcome of these other claims cannot be predicted with certainty, management does not believe that the outcome of any of these ongoing legal matters, individually and in aggregate, will have a material adverse effect on the Company's consolidated financial statements.

In 2016, the Company and Allergan received Paragraph IV certification notice letters ("Notice Letters") regarding abbreviated new drug applications ("ANDAs") submitted to the FDA by generic drug manufacturers requesting approval to engage in commercial manufacture, use, sale and offer for sale of linaclotide capsules (145 mcg and 290 mcg), proposed generic versions of our FDA-approved drug LINZESS. In response to the four ANDAs received in 2016, the Company and Allergan filed a lawsuit against these generic drug manufacturers in Delaware District Court in November 2016. In accordance with the Hatch-Waxman Act, the timely filing of the lawsuit against the generic drug manufacturers triggered an automatic stay of the FDA's approval of the four ANDAs until February 29, 2020, unless there is a final court decision sooner and absent any adjustments by the court adverse to the Company and Allergan. The Company is unable to estimate the outcome of this lawsuit at this time.

13. Stockholders' Equity

Preferred Stock

The Company's preferred stock may be issued from time to time in one or more series, with each such series to consist of such number of shares and to have such terms as adopted by the board of directors. Authority is given to the board of directors to determine and fix such voting powers, full or limited, or no voting powers, and such designations, preferences and relative participating, optional or other special rights, and qualifications, limitation or restrictions thereof, including without limitation, dividend rights, conversion rights, redemption privileges and liquidation preferences.

Common Stock

The Company has designated two series of common stock, Series A common stock ("Class A Common Stock") and Series B common stock ("Class B Common Stock"). All shares of common stock that were outstanding immediately prior to August 2008 were converted into shares of Class B Common Stock. The holders of Class A Common Stock and Class B Common Stock vote together as a single class. Class A Common Stock is entitled to one vote per share. Class B Common Stock is also entitled to one vote per share with the following exceptions: (1) after the completion of an initial public offering ("IPO") of the Company's stock, the holders of the Class B Common Stock are entitled to ten votes per share if the matter is an adoption of an agreement of merger or consolidation, an adoption of a resolution with respect to the sale, lease, or exchange of the Company's assets or an adoption of dissolution or liquidation of the Company, and (2) Class B common stockholders are entitled to ten votes per share on any matter if any individual, entity, or group seeks to obtain or has obtained beneficial ownership of 30% or more of the Company's outstanding shares of common stock. Class B Common Stock can be sold at any time and irrevocably converts to Class A Common Stock, on a one for one basis, upon sale or transfer. The Class B Common Stock is also entitled to a separate class vote for the issuance of additional shares of Class B Common Stock (except pursuant to dividends, splits or convertible securities), or any amendment, alteration or repeal of any provision of the Company's charter. All Class B Common Stock will automatically convert into Class A Common Stock upon the earliest of:

- the later of (1) the first date on which the number of shares of Class B Common Stock then outstanding is less than 19,561,556 which represents 25% of the number of shares of Class B Common Stock outstanding immediately following the completion of the Company's IPO or (2) December 31, 2018;
- December 31, 2038; or
- a date agreed to in writing by a majority of the holders of the Class B Common Stock.

Table of Contents

The Company has reserved such number of shares of Class A Common Stock as there are outstanding shares of Class B Common Stock solely for the purpose of effecting the conversion of the Class B Common Stock.

The holders of shares of Class A Common Stock and Class B Common Stock are entitled to dividends if and when declared by the board of directors. In the event that dividends are paid in the form of common stock or rights to acquire common stock, the holders of shares of Class A Common Stock shall receive Class A Common Stock or rights to acquire Class A Common Stock and the holders of shares of Class B Common Stock shall receive Class B Common Stock or rights to acquire Class B Common Stock, as applicable.

In the event of a voluntary or involuntary liquidation, dissolution, distribution of assets, or winding up of the Company, the holders of shares of Class A Common Stock and the holders of shares of Class B Common Stock are entitled to share equally, on a per share basis, in all assets of the Company of whatever kind available for distribution to the holders of common stock.

The Company has reserved, out of its authorized but unissued shares of Class A Common Stock, sufficient shares to affect the conversion of the 2022 Notes and the Note Hedge Warrants, pursuant to the terms thereof (Note 11).

In the first quarter of 2014, the Company sold 15,784,325 shares of its Class A Common Stock through a firm commitment, underwritten public offering at a price to the public of $12.75 per share. As a result of this offering, the Company received aggregate net proceeds, after underwriting discounts and commissions and other offering expenses, of approximately $190.4 million.

14. Stock Benefit Plans

The following table summarizes the expense recognized for share based compensation arrangements in the consolidated statements of operations (in thousands):

| | Year Ended December 31, | | |
|---|---|---|---|
| | 2016 | 2015 | 2014 |
| Employee stock options | $ 21,412 | $ 20,668 | $ 19,373 |
| Restricted stock units | 4,023 | 1,536 | — |
| Restricted stock awards | 2,325 | 2,408 | 2,671 |
| Non-employee stock options | 529 | — | 2,618 |
| Employee stock purchase plan | 910 | 833 | 941 |
| Workforce reduction | — | — | 551 |
| Stock award | 20 | 24 | 30 |
| | $ 29,219 | $ 25,469 | $ 26,184 |

Share based compensation is reflected in the consolidated statements of operations as follows for the years ended December 31, 2016, 2015 and 2014 (in thousands):

| | Years Ended December 31, | | |
|---|---|---|---|
| | 2016 | 2015 | 2014 |
| Research and development | $ 11,344 | $ 10,065 | $ 9,482 |
| Selling, general and administrative | 17,875 | 15,404 | 16,702 |
| | $ 29,219 | $ 25,469 | $ 26,184 |

On November 4, 2014, the Company agreed to accelerate the vesting of a former executive officer’s outstanding unvested stock options on the executive officer’s departure date of December 31, 2014, and to allow the exercise of

vested stock options for up to two years subsequent to the departure date, or until their expiration, whichever is earlier. These equity modifications resulted in an incremental charge of approximately $2.3 million, which was recorded within selling, general and administrative expenses during the year ended December 31, 2014.

Stock Benefit Plans

The Company has two share based compensation plans pursuant to which awards are currently being made: the Amended and Restated 2010 Employee, Director and Consultant Equity Incentive Plan (“2010 Equity Plan”) and the

Table of Contents

Amended and Restated 2010 Employee Stock Purchase Plan ("2010 Purchase Plan"). The Company also has two share based compensation plans under which there are outstanding awards, but from which no further awards will be made: the Amended and Restated 2005 Stock Incentive Plan ("2005 Equity Plan") and the Amended and Restated 2002 Stock Incentive Plan ("2002 Equity Plan"). At December 31, 2016, there were 15,751,858 shares available for future grant under all such plans.

2010 Equity Plan

During 2010, the Company's stockholders approved the 2010 Equity Plan under which stock options, restricted stock awards, RSUs, and other stock-based awards may be granted to employees, officers, directors, or consultants of the Company. There were 6,000,000 shares of common stock initially reserved for issuance under the 2010 Equity Plan. The number of shares available for future grant may be increased on the first day of each fiscal year by an amount equal to the lesser of: (i) 6,600,000; (ii) 4% of the number of outstanding shares of common stock on the first day of each fiscal year; and (iii) an amount determined by the board of directors. Awards that are returned to the Company's other equity plans as a result of their expiration, cancellation, termination or repurchase are automatically made available for issuance under the 2010 Equity Plan. At December 31, 2016, there were 12,959,613 shares available for future grant under the 2010 Equity Plan.

2010 Purchase Plan

During 2010, the Company's stockholders approved the 2010 Purchase Plan, which gives eligible employees the right to purchase shares of common stock at the lower of 85% of the fair market value on the first or last day of an offering period. Each offering period is six months. There were 400,000 shares of common stock initially reserved for issuance pursuant to the 2010 Purchase Plan. The number of shares available for future grant under the 2010 Purchase Plan may be increased on the first day of each fiscal year by an amount equal to the lesser of: (i) 1,000,000 shares, (ii) 1% of the Class A shares of common stock outstanding on the last day of the immediately preceding fiscal year, or (iii) such lesser number of shares as is determined by the board of directors. At December 31, 2016, there were 2,792,245 shares available for future grant under the 2010 Purchase Plan.

2005 Equity Plan and 2002 Equity Plan

The 2005 Equity Plan and 2002 Equity Plan provided for the granting of stock options, restricted stock awards, RSUs, and other share based awards to employees, officers, directors, consultants, or advisors of the Company. At December 31, 2016, there were no shares available for future grant under the 2005 Equity Plan or the 2002 Equity Plan.

Restricted Stock Awards

In 2016, the Company granted an aggregate of 191,977 shares of Class A Common Stock to independent members of the board of directors under restricted stock agreements in accordance with the terms of the 2010 Equity Plan and the Company's director compensation plan, effective in January 2014. These shares of restricted stock vest ratably over the period of service from the Company's 2016 annual meeting of stockholders through the Company's 2017 annual meeting of stockholders, provided the individual continues to serve on the Company's board of directors through each vest date.

In 2015, the Company granted an aggregate of 151,604 shares of Class A Common Stock to independent members of the board of directors under restricted stock agreements in accordance with the terms of the 2010 Equity Plan and the Company's director compensation plan, effective in January 2014. These shares of restricted stock vested ratably over the period of service from the Company's 2015 annual meeting of stockholders through the Company's 2016 annual

meeting of stockholders, provided the individual continued to serve on the Company’s board of directors through each vest date. The fair value of all RSAs is based on the market value of the Company's Class A Common Stock on the date of grant. Compensation expense, including the effect of estimated forfeitures, is recognized over the applicable service period.

Table of Contents

A summary of the unvested shares of restricted stock as of December 31, 2016 is presented below:

| | Number of Shares | Weighted-Average Grant Date Fair Value |
|---|---|---|
| Unvested as of December 31, 2015 | 74,502 | $ 14.14 |
| Granted | 191,977 | $ 12.68 |
| Vested | (171,783) | $ 13.30 |
| Forfeited | — | $ — |
| Unvested as of December 31, 2016 | 94,696 | $ 12.69 |

Restricted Stock Units

In 2015, the Company began utilizing RSUs, in addition to stock options as part of the equity compensation it provides to its employees, each RSU representing the right to receive one share of the Company’s Class A Common Stock pursuant to the terms of the applicable award agreement and granted pursuant to the terms of the Company’s 2010 Equity Plan. The RSUs generally vest 25% per year on the approximate anniversary of the date of grant until fully vested, provided the employee remains continuously employed with the Company through each vesting date. Shares of the Company's Class A Common Stock are delivered to the employee upon vesting, subject to payment of applicable withholding taxes. The fair value of all RSUs is based on the market value of the Company's Class A Common Stock on the date of grant. Compensation expense, including the effect of estimated forfeitures, is recognized over the applicable service period.

A summary of RSU activity for the year ended December 31, 2016 is as follows:

| | Number of Shares | Weighted-Average Grant Date Fair Value |
|---|---|---|
| Unvested as of December 31, 2015 | 900,051 | $ 13.36 |
| Granted | 716,357 | $ 11.74 |
| Vested | (230,065) | $ 13.34 |
| Forfeited | (86,886) | $ 12.42 |
| Unvested as of December 31, 2016 | 1,299,457 | $ 12.53 |

Stock Options

Stock options granted under the Company’s equity plans generally have a ten-year term and vest over a period of four years, provided the individual continues to serve at the Company through the vesting dates. Options granted under all equity plans are exercisable at a price per share not less than the fair market value of the underlying common stock on the date of grant. The estimated fair value of options, including the effect of estimated forfeitures, is recognized over the requisite service period, which is typically the vesting period of each option.

The weighted average assumptions used to estimate the fair value of the stock options using the Black Scholes option-pricing model were as follows for the years ended December 31, 2016, 2015 and 2014:

Year Ended

| | December 31, | | |
|---|---|---|---|
| | 2016 | 2015 | 2014 |
| Expected volatility | 45.9 % | 46.1 % | 46.8 % |
| Expected term (in years) | 6.06 | 6.04 | 6.10 |
| Risk-free interest rate | 1.5 % | 1.7 % | 1.8 % |
| Expected dividend yield | — % | — % | — % |

Expected volatility is based on the historic volatility of the Company's Class A common stock. The Company estimates the expected term using historical data. The risk-free interest rate used for each grant is based on a zero-coupon U.S. Treasury instrument with a remaining term similar to the expected term of the share-based award. The

Table of Contents

Company has not paid and does not anticipate paying cash dividends on its shares of common stock in the foreseeable future; therefore, the expected dividend yield is assumed to be zero.

The weighted-average grant date fair value per share of options granted during the years ended December 31, 2016, 2015 and 2014 was $5.08, $6.73 and $6.47, respectively.

The Company's Class B Common Stock is issuable upon exercise of options granted prior to the closing of the Company's IPO under the 2002 Equity Plan and the 2005 Equity Plan, and its Class A Common Stock is issuable upon exercise of all options granted after the closing of the Company's IPO under the Company's equity plans. At December 31, 2016, options exercisable into 2,318,017 shares of Class B Common Stock and 18,136,642 shares of Class A Common Stock were outstanding.

Subject to approval by the board of directors, option grantees under the 2002 Equity Plan and the 2005 Equity Plan may have the right to exercise an option prior to vesting. The exercise of these shares is not substantive and as a result, the cash paid for the exercise prices is considered a deposit or prepayment of the exercise price and is recorded as a liability. The Company recorded a liability of approximately $0.9 million as of December 31, 2016 for cash received related to the exercise of such options. Amounts received upon the exercise of these shares were not material to the consolidated financial statements as of December 31, 2015.

The Company, from time to time, issues certain time accelerated stock options to certain employees. The vesting of these options accelerates upon the achievement of certain performance based milestones. If these criteria are not met, such options will vest between six and ten years after the date of grant. During the year ended December 31, 2016, 100,000 shares vested as a result of milestone or service period achievements. At December 31, 2016 and 2015, there were 300,000 shares and 400,000 shares issuable under unvested time accelerated options, respectively. When achievement of the milestone is not deemed probable, the Company recognizes compensation expense associated with time-accelerated stock options initially over the vesting period of the respective stock option. When deemed probable of achievement, the Company expenses the remaining unrecognized compensation over the implicit service period. The Company recorded an insignificant amount in share based compensation related to these time-accelerated options during each of the years ended December 31, 2016 and 2015. The Company recorded approximately $1.2 million in share-based compensation related to these time-accelerated options during the year ended December 31, 2014.

The Company also grants to certain employees performance based options to purchase shares of common stock. These options are subject to performance based milestone vesting. During the year ended December 31, 2016, 35,000 shares vested as a result of performance milestone achievements. The Company recorded share based compensation related to these performance based options of approximately $1.4 million, approximately $0.2 million and approximately $0.5 million, respectively, during the years ended December 31, 2016, 2015 and 2014.

The following table summarizes stock option activity under the Company's share based compensation plans, including performance based options:

| | Shares of Common Stock Attributable to Options | Weighted-Average Exercise Price | Weighted-Average Contractual Life (in years) | Aggregate Intrinsic Value (in thousands) |
|---|---|---|---|---|
| Outstanding at December 31, 2015 | 20,566,860 | $ 11.18 | 5.90 | $ 38,279 |
| Granted | 4,484,086 | $ 11.22 | | |

| | | | | |
|---|---|---|---|---|
| Exercised | (3,467,252) | $ 6.36 | | |
| Cancelled | (1,129,035) | $ 12.75 | | |
| Outstanding at December 31, 2016 | 20,454,659 | $ 11.92 | 6.35 | $ 70,247 |
| Vested or expected to vest at December 31, 2016 | 19,048,936 | $ 11.94 | 6.23 | $ 64,923 |
| Exercisable at December 31, 2016 (1) | 13,116,064 | $ 11.82 | 5.38 | $ 46,007 |

(1) All stock options granted under the 2002 Equity Plan and the 2005 Equity Plan contain provisions allowing for the early exercise of such options into restricted stock. The exercisable shares disclosed above represent those that were vested as of December 31, 2016.

Table of Contents

The total intrinsic value of options exercised during the years ended December 31, 2016, 2015 and 2014 was approximately $23.9 million, approximately $17.7 million and approximately $26.9 million, respectively. The intrinsic value was calculated as the difference between the fair value of the Company's common stock and the exercise price of the option issued.

The following table sets forth the Company's unrecognized share based compensation expense, net of estimated forfeitures, as of December 31, 2016, by type of award and the weighted-average period over which that expense is expected to be recognized:

| | Unrecognized Expense, Net of Estimated Forfeitures (in thousands) | Weighted-Average Remaining Recognition Period (in years) |
|---|---|---|
| Type of award: | | |
| Stock options with time-based vesting | $ 30,066 | 2.67 |
| Restricted stock awards | 1,001 | 0.42 |
| Restricted stock units | 10,300 | 2.91 |
| Time-accelerated stock options (1) | 3 | — |
| Performance-based options (1) | 1,670 | — |

(1) The weighted-average remaining recognition period cannot be determined for performance-based or time-accelerated options due to the nature of such awards, as detailed above.

The total unrecognized share based compensation cost will be adjusted for future changes in estimated forfeitures.

15. Income Taxes

In general, the Company has not recorded a provision for federal or state income taxes as it has had cumulative net operating losses since inception.

A reconciliation of income taxes computed using the U.S. federal statutory rate to that reflected in operations follows (in thousands):

| | Year Ended December 31, | | |
|---|---|---|---|
| | 2016 | 2015 | 2014 |
| Income tax benefit using U.S. federal statutory rate | $ (27,780) | $ (48,507) | $ (64,470) |
| Permanent differences | 1,140 | 688 | 1,916 |
| State income taxes, net of federal benefit | (4,606) | (4,826) | (5,632) |
| Non-deductible share-based compensation | 3,528 | 3,824 | 3,584 |
| Excess tax benefits | (5,453) | — | — |
| Fair market valuation of Note Hedge Warrants and Convertible Note Hedges | (3,160) | 3,711 | — |
| Tax credits | (3,014) | (1,987) | (2,652) |
| Expiring net operating losses and tax credits | 39 | 194 | 3,590 |
| Effect of change in state tax rate on deferred tax assets and deferred tax liabilities | (3,564) | (627) | 5,490 |
| Change in the valuation allowance | 42,975 | 47,587 | 58,185 |

| | | | |
|---|---|---|---|
| Other | (105) | (57) | (11) |
| | $ — | $ — | $ — |

Table of Contents

Components of the Company's deferred tax assets and liabilities are as follows (in thousands):

| | Year Ended December 31, | |
|---|---|---|
| | 2016 | 2015 |
| Deferred tax assets: | | |
| Net operating loss carryforwards | $ 333,442 | $ 280,191 |
| Tax credit carryforwards | 36,963 | 33,996 |
| Capitalized research and development | 25,030 | 30,064 |
| Contingent consideration | 30,131 | — |
| Deferred revenue | — | 3,360 |
| Share-based compensation | 19,364 | 15,275 |
| Basis difference on North America collaboration agreement | 24,813 | 16,830 |
| Accruals and reserves | 17,144 | 19,034 |
| Other | 15,867 | 15,311 |
| Total deferred tax assets | 502,754 | 414,061 |
| Deferred tax liabilities: | | |
| Basis difference on 2022 Notes | (1,071) | (5,877) |
| Intangibles | (27,162) | — |
| Total deferred tax liabilities | (28,233) | (5,877) |
| Net deferred tax asset | 474,521 | 408,184 |
| Valuation allowance | (474,521) | (408,184) |
| Net deferred tax asset | $ — | $ — |

Management of the Company has evaluated the positive and negative evidence bearing upon the realizability of its deferred tax assets. Management has considered the Company's history of operating losses and concluded, in accordance with the applicable accounting standards, that it is more likely than not that the Company will not realize the benefit of its deferred tax assets. Accordingly, the deferred tax assets have been fully reserved at December 31, 2016 and 2015. Management reevaluates the positive and negative evidence on a quarterly basis.

The valuation allowance increased approximately $66.3 million during the year ended December 31, 2016, primarily due to an increase in net operating losses, tax credit carryforwards, basis difference on the North America collaboration agreement and share-based compensation expense. During the year ended December 31, 2016, the Company closed the Lesinurad Transaction which resulted in an approximately $0.3 million deferred tax impact. Additionally, the 2016 change in valuation allowance noted in the table above reflects the impact of the Company's early adoption of ASC 2016-09 of an approximately $23.1 million increase in net operating losses recorded through retained earnings. The valuation allowance increased approximately $40.7 million during the year ended December 31, 2015, due primarily to an increase in the Company's tax credit carryforwards, capitalized research and development expenses and share-based compensation expense.

Subject to the limitations described below, at December 31, 2016 and 2015, the Company has net operating loss carryforwards of approximately $952.7 million and approximately $857.9 million, respectively, to offset future federal taxable income, which expire beginning in 2018 continuing through 2036. As of December 31, 2016 and 2015, the Company had state net operating loss carryforwards of approximately $686.2 million and approximately $566.7 million, respectively, to offset future state taxable income, which will begin to expire in 2027 and will continue to expire through 2036. The Company also had tax credit carryforwards of approximately $40.4 million and approximately $37.1 million as of December 31, 2016 and 2015, respectively, to offset future federal and state income taxes, which expire at various times through 2036.

Utilization of net operating loss carryforwards and research and development credit carryforwards may be subject to a substantial annual limitation due to ownership change limitations that could occur in the future in accordance with Section 382 of the Internal Revenue Code of 1986 (“IRC Section 382”) and with Section 383 of the Internal Revenue Code of 1986, as well as similar state provisions. These ownership changes may limit the amount of net operating loss carryforwards and research and development credit carryforwards that can be utilized annually to offset future taxable income and taxes, respectively. In general, an ownership change, as defined by IRC Section 382, results from transactions increasing the ownership of certain stockholders or public groups in the stock of a corporation by more than 50 percentage points over a three-year period. The Company has completed several financings since its inception

Table of Contents

which may result in a change in control as defined by IRC Section 382, or could result in a change in control in the future.

The following table summarizes the changes in the Company's unrecognized income tax benefits for the years ended December 31, 2016 and 2015 (in thousands):

| | Year Ended December 31, | |
|---|---|---|
| | 2016 | 2015 |
| Balance at the beginning of the period | $ 17,614 | $ — |
| Increases based on tax positions related to the current period | 26,393 | 17,614 |
| Increases for tax positions related to prior periods | — | 10,174 |
| Decreases for tax positions in prior periods | (17,614) | (10,174) |
| Decreases for statute of limitation expiration | — | — |
| Decreases for settlement of tax audits | — | — |
| Balance at the end of the period | $ 26,393 | $ 17,614 |

The Company had gross unrecognized tax benefits of approximately $26.4 million and approximately $17.6 million as of December 31, 2016 and 2015, respectively. The Company did not have any unrecognized tax benefits as of December 31, 2014. Of the approximately $26.4 million of total unrecognized tax benefits at December 31, 2016, none of the unrecognized tax positions would, if recognized, affect the Company's effective tax rate, as this item only impacts the Company's deferred tax accounting.

The Company will recognize interest and penalties, if any, related to uncertain tax positions in income tax expense. As of December 31, 2016, 2015 and 2014, the Company had no accrued interest or penalties related to uncertain tax positions and no amounts have been recognized in the Company's consolidated statements of operations.

The statute of limitations for assessment by the Internal Revenue Service ("IRS") and state tax authorities is open for tax years ended December 31, 2015, 2014, and 2013, although carryforward attributes that were generated prior to tax year 2013 may still be adjusted upon examination by the IRS or state tax authorities if they either have been, or will be, used in a future period. There are currently no federal or state income tax audits in progress.

16. Defined Contribution Plan

The Ironwood Pharmaceuticals, Inc. 401(k) Savings Plan is a defined contribution plan in the form of a qualified 401(k) plan in which substantially all employees are eligible to participate upon employment. Subject to certain IRS limits, eligible employees may elect to contribute from 1% to 100% of their compensation. Company contributions to the plan are at the sole discretion of the Company's board of directors. Currently, the Company provides a matching contribution of 75% of the employee's contributions, up to $6,000 annually. During the years ended December 31, 2016, 2015 and 2014, the Company recorded approximately $3.2 million, approximately $2.5 million and approximately $2.6 million of expense related to its 401(k) company match, respectively.

17. Related Party Transactions

In September 2009, Allergan became a related party when the Company sold to Allergan 2,083,333 shares of the Company's convertible preferred stock. In November 2009, Almirall became a related party when the Company sold to Almirall 681,819 shares of the Company's convertible preferred stock (Note 5). These shares of preferred stock converted to the Company's Class B common stock on a 1:1 basis upon the completion of the Company's initial public offering in February 2010. At December 31, 2016, Almirall was no longer a related party because it converted and

sold all such shares during the three months ended September 30, 2016. Amounts due to and due from Allergan are reflected as related party accounts payable and related party accounts receivable, respectively. These balances are reported net of any balances due to or from the related party. As of December 31, 2016 and 2015, the Company had approximately $63.9 million and approximately $51.6 million, respectively, in related party accounts receivable, net of related party accounts payable, associated with Allergan.

The Company has and currently obtains health insurance services for its employees from an insurance provider whose President and Chief Executive Officer became a member of the Company's Board of Directors in April 2016. The Company paid approximately $8.5 million and approximately $7.0 million in insurance premiums to this insurance

Table of Contents

provider during the years ended December 31, 2016 and 2015, respectively. At December 31, 2016 and 2015, the Company had an insignificant amount and no accounts payable, respectively, due to this related party.

The Company entered into a research and collaboration agreement with a biotechnology company during 2016. The co-founder and Chief Executive Officer of this biotechnology company subsequently became a member of the Company's Board of Directors in January 2017. The Company paid an insignificant amount to this biotechnology company during the year ended December 31, 2016. At December 31, 2016, the Company had no accounts payable due to this related party.

18. Workforce Reduction

On January 8, 2014, the Company announced a headcount reduction of approximately 10% to align its workforce with its strategy. The field-based sales force and medical science liaison team were excluded from the workforce reduction.

During the three months ended March 31, 2014, the Company substantially completed the implementation of this reduction in workforce and, in accordance with ASC 420, Exit or Disposal Cost Obligations, recorded approximately $4.3 million of costs, including employee severance, benefits and related costs. These costs were reflected in the consolidated statement of operations as approximately $3.0 million in research and development expenses and approximately $1.2 million in selling, general and administrative expenses. The Company did not record any additional charges associated with this workforce reduction during the years ended December 31, 2016 and 2015. All payments related to this reduction in workforce were made by the end of 2014.

19. Selected Quarterly Financial Data (Unaudited)

The following table contains quarterly financial information for the years ended December 31, 2016 and 2015. The Company believes that the following information reflects all normal recurring adjustments necessary for a fair presentation of the information for the periods presented. The operating results for any quarter are not necessarily indicative of results for any future period.

| | First Quarter | Second Quarter | Third Quarter | Fourth Quarter | Total Year |
|---|---|---|---|---|---|
| | (in thousands, except per share data) | | | | |
| 2016 | | | | | |
| Collaborative arrangements revenue (1) | $ 66,042 | $ 54,350 | $ 66,106 | $ 87,459 | $ 273,957 |
| Total cost and expenses (2) | 68,010 | 69,665 | 94,393 | 93,759 | 325,827 |
| Other (expense) income, net (3) | (11,329) | (6,387) | (4,917) | (7,205) | (29,838) |
| Net loss | (13,297) | (21,702) | (33,204) | (13,505) | (81,708) |
| Net loss per share--basic and diluted | $ (0.09) | $ (0.15) | $ (0.23) | $ (0.09) | $ (0.56) |

| | First Quarter | Second Quarter | Third Quarter | Fourth Quarter | Total Year |
|---|---|---|---|---|---|
| | (in thousands, except per share data) | | | | |
| 2015 | | | | | |
| Collaborative arrangements revenue | $ 28,932 | $ 27,744 | $ 39,572 | $ 53,307 | $ 149,555 |

| | | | | | |
|---|---|---|---|---|---|
| Total cost and expenses (4) | 56,999 | 69,753 | 65,757 | 59,134 | 251,643 |
| Other (expense) income, net (5) | (5,155) | (6,011) | (21,205) | (8,210) | (40,581) |
| Net loss | (33,222) | (48,020) | (47,390) | (14,037) | (142,669) |
| Net loss per share--basic and diluted | $ (0.24) | $ (0.34) | $ (0.33) | $ (0.09) | $ (1.00) |

(1) Collaborative arrangements revenue includes the achievement of $30.0 million related to the receipt of milestone payments under the license agreement with Astellas, consisting of $15.0 million for the filing of an NDA for LINZESS with the Japanese Ministry of Health, Labor and Welfare during the first quarter of the year ended December 31, 2016, and $15.0 million for the subsequent approval of the NDA during the fourth quarter of the year ended December 31, 2016.

(2) Total costs and expenses for the third and fourth quarters of the year ended December 31, 2016 includes approximately $3.2 million and a subsequent reduction of approximately $3.3 million, respectively, related to the

Table of Contents

amortization of acquired intangible asset, as well as approximately $8.7 million and approximately $1.1 million during the third and fourth quarters, respectively, as a loss on fair value remeasurement of contingent consideration

(3) Other (expense) income, net for the year ended December 31, 2016 includes a loss of approximately $1.6 million for the first quarter, and gains of approximately $3.1 million, approximately $4.5 million, and approximately $2.1 million in the second, third and fourth quarters of 2016, respectively, related to gain on derivatives. The gain on derivatives for the year ended December 31, 2016 consists of the change in fair value of the Company's Convertible Note Hedges and Note Hedge Warrants, which are recorded as derivative assets and liabilities. The Convertible Note Hedges and the Note Hedge Warrants are recorded at fair value at each reporting period and changes in fair value are recorded in the Company's consolidated statements of operations (Note 6).

(4) Total costs and expenses for the second and third quarter of the year ended December 31, 2015 includes approximately $8.2 million and $9.4 million, respectively, related to a write down of inventory to net realizable value and accruals for excess non-cancelable inventory purchase commitments (Note 8).

(5) Other (expense) income, net for the second and third quarters of the year ended December 31, 2015 includes approximately $0.2 million and $11.4 million, respectively, as a loss on derivatives. Other (expense) income, net for the fourth quarter of the year ended December 31, 2015 includes approximately $1.6 million, as a gain on derivatives. The gain (loss) on derivatives consists of the change in fair value of the Company's Convertible Note Hedges and Note Hedge Warrants, which are recorded as derivative assets and liabilities. The Convertible Note Hedges and the Note Hedge Warrants are recorded at fair value at each reporting period and changes in fair value are recorded in the Company's consolidated statements of operations (Note 6).

20. Subsequent Events

On the Funding Date, January 5, 2017, the Company issued $150.0 million in aggregate principal amount for the 2026 Notes. The proceeds from the issuance of the 2026 Notes were primarily used to redeem the outstanding principal balance of the PhaRMA Notes.

In January 2017, the Company and Allergan entered into an amendment to the European License Agreement pursuant to which the license granted to Allergan was extended to a territory consisting of all countries worldwide not previously covered by the European License Agreement, other than China, Hong Kong, Macau, Japan, and the countries and territories of North America. On a country-by-country and product-by-product basis in such additional territory, Allergan will pay the Company an annual royalty as a percentage of net sales of products containing linaclotide as an active ingredient in the upper-single digits for five years following the first commercial sale of a linaclotide product in a country, and in the low-double digits thereafter. The royalty rate for products in expanded territory will decrease, on a country-by-country basis, to the lower-single digits, or cease entirely, following the occurrence of certain events. Allergan will also assume certain purchase commitments for quantities of linaclotide API under the Company's agreements with third-party API suppliers. Concurrently with entering into the amendment to the European License Agreement, the Company and Allergan entered into a commercial agreement under which the adjustments to the Company's or Allergan's share of the net profits under the share adjustment provision of the collaboration agreement for linaclotide in North America are eliminated, in full, in 2018 and all subsequent years. In addition, Allergan appointed the Company, on a non-exclusive basis, to promote CANASA, approved for the treatment of ulcerative proctitis, and DELZICOL, approved for the treatment of ulcerative colitis, in the U.S. for approximately two years. The Company will perform certain third position details and offer samples of such products to gastroenterology prescribers who are on the then-current call panel for LINZESS to which the Company provides first or second position details, and will purchase samples of CANASA and DELZICOL from Allergan at the actual

manufacturing cost. On a product-by-product basis, Allergan will pay the Company a royalty in the mid-teens on incremental sales of CANASA and DELZICOL above a mutually agreed upon sales baseline. The Company expects to commence these promotion activities on or about February 27, 2017 and, subject to the Company's or Allergan's rights of early termination, the commercial agreement will expire on February 26, 2019. The share adjustment relief will, in the case of Allergan's termination for convenience and certain other specified circumstances, survive termination of the commercial agreement.

Table of Contents

Exhibit Index

| | | Incorporated by reference herein | |
|---|---|---|---|
| Number | Description | Form | Date |
| 3.1 | Eleventh Amended and Restated Certificate of Incorporation | Annual Report on Form 10 K (File No. 001 34620) | March 30, 2010 |
| 3.2 | Fifth Amended and Restated Bylaws | Annual Report on Form 10 K (File No. 001 34620) | March 30, 2010 |
| 4.1 | Specimen Class A common stock certificate | Registration Statement on Form S 1, as amended (File No. 333 163275) | January 20, 2010 |
| 4.2 | Eighth Amended and Restated Investors' Rights Agreement, dated as of September 1, 2009, by and among Ironwood Pharmaceuticals, Inc., the Founders and the Investors named therein | Registration Statement on Form S 1, as amended (File No. 333 163275) | November 20, 2009 |
| 4.3 | Indenture, dated as of June 15, 2015, by and between Ironwood Pharmaceuticals, Inc. and U. S. Bank National Association (including the form of the 2.25% Convertible Senior Note due 2022) | Form 8 K (File No. 001 34620) | June 15, 2015 |
| 4.4 | Indenture, dated as of September 23, 2016, by and between Ironwood Pharmaceuticals, Inc. and U.S. Bank National Association (including the form of the 8.375% Notes due 2026) | Form 8 K (File No. 001 34620) | September 26, 2016 |
| 10.1# | Amended and Restated 2002 Stock Incentive Plan and form agreements thereunder | Registration Statement on Form S 1, as amended (File No. 333 163275) | December 23, 2009 |
| 10.2# | Amended and Restated 2005 Stock Incentive Plan and form agreements thereunder | Registration Statement on Form S 1, as amended (File No. 333 163275) | January 29, 2010 |
| 10.3# | Amended and Restated 2010 Employee, Director and Consultant Equity Incentive Plan | Registration Statement on Form S 8, as amended (File No. 333 184396) | October 12, 2012 |
| 10.3.1# | Form of Stock Option Agreement under the Amended and Restated 2010 Employee, Director and Consultant Equity Incentive Plan | Annual Report on Form 10 K (File No. 001 34620) | February 18, 2015 |
| 10.3.2# | Form of Non employee Director Restricted Stock Agreement under the Amended and Restated 2010 Employee, Director and Consultant Equity Incentive Plan | Annual Report on Form 10 K (File No. 001 34620) | February 18, 2015 |
| 10.3.3# | Form of Restricted Stock Unit Agreement under the Amended and Restated 2010 Employee, Director and Consultant Equity Incentive Plan | Annual Report on Form 10 K (File No. 001 34620) | February 18, 2015 |
| 10.4# | Amended and Restated 2010 Employee Stock Purchase Plan | Annual Report on Form 10 K (File No. 001 34620) | February 21, 2013 |

Table of Contents

| | | Incorporated by reference herein | |
|---|---|---|---|
| Number | Description | Form | Date |
| 10.5# | Change of Control Severance Benefit Plan, as amended and restated | Quarterly Report on Form 10 Q (File No. 001 34620) | April 29, 2014 |
| 10.6# | Form of Executive Severance Agreement | Annual Report on Form 10 K (File No. 001 34620) | February 18, 2015 |
| 10.7# | Director Compensation Plan effective January 1, 2014 | Annual Report on Form 10 K (File No. 001 34620) | February 7, 2014 |
| 10.8# | Form of Indemnification Agreement with Directors and Officers | Registration Statement on Form S 1, as amended (File No. 333 163275) | December 23, 2009 |
| 10.9# | Consulting Agreement, dated as of December 16, 2014, by and between Christopher Walsh and Ironwood Pharmaceuticals, Inc. | Annual Report on Form 10 K (File No. 001 34620) | February 18, 2015 |
| 10.10# | Consulting Agreement, dated December 3, 2014, by and between Lawrence S. Olanoff and Ironwood Pharmaceuticals, Inc. | Quarterly Report on Form 10 Q (File No. 001 34620) | May 6, 2015 |
| 10.11+ | Collaboration Agreement, dated as of September 12, 2007, as amended on November 3, 2009, by and between Forest Laboratories, Inc. and Ironwood Pharmaceuticals, Inc. | Registration Statement on Form S 1, as amended (File No. 333 163275) | February 2, 2010 |
| 10.11.1 | Amendment No. 2 to the Collaboration Agreement, dated as of January 8, 2013, by and between Forest Laboratories, Inc. and Ironwood Pharmaceuticals, Inc. | Annual Report on Form 10 K (File No. 001 34620) | February 21, 2013 |
| 10.12+ | License Agreement, dated as of April 30, 2009, by and between Allergan Pharmaceuticals International Ltd. (formerly with Almirall, S.A.) and Ironwood Pharmaceuticals, Inc. | Registration Statement on Form S 1, as amended (File No. 333 163275) | February 2, 2010 |
| 10.12.1+ | Amendment No. 1 to License Agreement, dated as of June 11, 2013, by and between Allergan Pharmaceuticals International Ltd. (formerly with Almirall, S.A.) and Ironwood Pharmaceuticals, Inc. | Quarterly Report on Form 10 Q (File No. 001 34620) | August 8, 2013 |
| 10.12.2+ | Amendment to the License Agreement, dated as of October 26, 2015, by and between Allergan Pharmaceuticals International Ltd. and Ironwood Pharmaceuticals, Inc. | Annual Report on Form 10 K (File No. 001 34620) | February 19, 2016 |
| 10.13+ | Novation Agreement, dated as of October 26, 2015, by and among Almirall, S.A., Allergan Pharmaceuticals International Ltd. and Ironwood Pharmaceuticals, Inc. | Annual Report on Form 10 K (File No. 001 34620) | February 19, 2016 |

Table of Contents

| | | Incorporated by reference herein | |
|---|---|---|---|
| Number | Description | Form | Date |
| 10.14+ | License Agreement, dated as of November 10, 2009, by and among Astellas Pharma Inc. and Ironwood Pharmaceuticals, Inc. | Registration Statement on Form S 1, as amended (File No. 333 163275) | February 2, 2010 |
| 10.15+ | Collaboration Agreement, dated as of October 23, 2012, by and between AstraZeneca AB and Ironwood Pharmaceuticals, Inc. | Annual Report on Form 10 K (File No. 001 34620) | February 21, 2013 |
| 10.16+ | License Agreement, dated as of April 26, 2016, by and between Ardea Biosciences, Inc. and Ironwood Pharmaceuticals, Inc. | Quarterly Report on Form 10 Q (File No. 001 34620) | August 8, 2016 |
| 10.17+ | Commercial Supply Agreement, dated as of June 23, 2010, by and among PolyPeptide Laboratories, Inc. and Polypeptide Laboratories (SWEDEN) AB, Forest Laboratories, Inc. and Ironwood Pharmaceuticals, Inc. | Quarterly Report on Form 10 Q (File No. 001 34620) | August 10, 2010 |
| 10.18+ | Commercial Supply Agreement, dated as of March 28, 2011, by and among Corden Pharma Colorado, Inc. (f/k/a Roche Colorado Corporation), Ironwood Pharmaceuticals, Inc. and Forest Laboratories, Inc. | Quarterly Report on Form 10 Q (File No. 001 34620) | May 13, 2011 |
| 10.18.1+ | Amendment No. 3 to Commercial Supply Agreement, dated as of November 26, 2013, by and between Corden Pharma Colorado, Inc. (f/k/a Roche Colorado Corporation), Ironwood Pharmaceuticals, Inc. and Forest Laboratories, Inc. | Annual Report on Form 10 K (File No. 001 34620) | February 7, 2014 |
| 10.19+ | Commercial Supply Agreement, dated as of April 26, 2016, by and between AstraZeneca Pharmaceuticals LP and Ironwood Pharmaceuticals, Inc. | Quarterly Report on Form 10 Q (File No. 001 34620) | August 8, 2016 |
| 10.20 | Lease for facilities at 301 Binney St., Cambridge, MA, dated as of January 12, 2007, as amended on April 9, 2009, by and between Ironwood Pharmaceuticals, Inc. and BMR Rogers Street LLC | Registration Statement on Form S 1, as amended (File No. 333 163275) | December 23, 2009 |
| 10.20.1 | Second Amendment to Lease for facilities at 301 Binney St., Cambridge, MA, dated as of February 9, 2010, by and between Ironwood Pharmaceuticals, Inc. and BMR-Rogers Street LLC | Annual Report on Form 10-K (File No. 001-34620) | March 30, 2010 |

Table of Contents

| | | Incorporated by reference herein | |
|---|---|---|---|
| Number | Description | Form | Date |
| 10.20.2 | Third Amendment to Lease for facilities at 301 Binney St., Cambridge, MA, dated as of July 1, 2010, by and between Ironwood Pharmaceuticals, Inc. and BMR Rogers Street LLC | Annual Report on Form 10 K (File No. 001 34620) | March 30, 2011 |
| 10.20.3 | Fourth Amendment to Lease for facilities at 301 Binney St., Cambridge, MA, dated as of February 3, 2011, by and between Ironwood Pharmaceuticals, Inc. and BMR Rogers Street LLC | Annual Report on Form 10 K (File No. 001 34620) | March 30, 2011 |
| 10.20.4 | Fifth Amendment to Lease for facilities at 301 Binney St., Cambridge, MA, dated as of October 18, 2011, by and between Ironwood Pharmaceuticals, Inc. and BMR Rogers Street LLC | Annual Report on Form 10 K (File No. 001 34620) | February 29, 2012 |
| 10.20.5 | Sixth Amendment to Lease for facilities at 301 Binney St., Cambridge, MA, dated as of July 19, 2012, by and between Ironwood Pharmaceuticals, Inc. and BMR Rogers Street LLC | Annual Report on Form 10 K (File No. 001 34620) | February 21, 2013 |
| 10.20.6 | Seventh Amendment to Lease for facilities at 301 Binney St., Cambridge, MA, dated as of October 30, 2012, by and between Ironwood Pharmaceuticals, Inc. and BMR Rogers Street LLC | Annual Report on Form 10 K (File No. 001 34620) | February 21, 2013 |
| 10.20.7 | Eighth Amendment to Lease for facilities at 301 Binney St., Cambridge, MA, dated as of July 8, 2014, by and between Ironwood Pharmaceuticals, Inc. and BMR Rogers Street LLC | Annual Report on Form 10 K (File No. 001 34620) | February 18, 2015 |
| 10.20.8 | Ninth Amendment to Lease for facilities at 301 Binney St., Cambridge, MA, dated as of October 27, 2014, by and between Ironwood Pharmaceuticals, Inc. and BMR Rogers Street LLC | Annual Report on Form 10 K (File No. 001 34620) | February 18, 2015 |
| 10.20.9 | Tenth Amendment to Lease for facilities at 301 Binney St., Cambridge, MA, dated as of January 21, 2015, by and between Ironwood Pharmaceuticals, Inc. and BMR Rogers Street LLC | Annual Report on Form 10 K (File No. 001 34620) | February 18, 2015 |
| 10.20.10* | Eleventh Amendment to Lease for facilities at 301 Binney St., Cambridge, MA, dated as of June 30, 2016, by and between Ironwood Pharmaceuticals, Inc. and BMR Rogers Street LLC | | |

Table of Contents

| | | Incorporated by reference herein | |
|---|---|---|---|
| Number | Description | Form | Date |
| 10.20.11 | Sublease, dated as of July 1, 2014, by and between Biogen Idec MA Inc. and Ironwood Pharmaceuticals, Inc. to Lease for facilities at 301 Binney St., Cambridge, MA, as amended, by and between Ironwood Pharmaceuticals, Inc. and BMR Rogers Street LLC | Annual Report on Form 10 K (File No. 001 34620) | February 18, 2015 |
| 10.21 | Base Call Option Transaction Confirmation, dated as of June 10, 2015, between Ironwood Pharmaceuticals, Inc. and JPMorgan Chase Bank, National Association, London Branch | Quarterly Report on Form 10 Q (File No. 001 34620) | August 7, 2015 |
| 10.22 | Base Call Option Transaction Confirmation, dated as of June 10, 2015, between Ironwood Pharmaceuticals, Inc. and Credit Suisse Capital LLC, through its agent Credit Suisse Securities (USA) LLC | Quarterly Report on Form 10 Q (File No. 001 34620) | August 7, 2015 |
| 10.23 | Base Warrants Confirmation, dated as of June 10, 2015, between Ironwood Pharmaceuticals, Inc. and JPMorgan Chase Bank, National Association, London Branch | Quarterly Report on Form 10 Q (File No. 001 34620) | August 7, 2015 |
| 10.24 | Base Warrants Confirmation, dated as of June 10, 2015, between Ironwood Pharmaceuticals, Inc. and Credit Suisse Capital LLC, through its agent Credit Suisse Securities (USA) LLC | Quarterly Report on Form 10 Q (File No. 001 34620) | August 7, 2015 |
| 10.25 | Additional Call Option Transaction Confirmation, dated as of June 22, 2015, between Ironwood Pharmaceuticals, Inc. and JPMorgan Chase Bank, National Association, London Branch | Quarterly Report on Form 10 Q (File No. 001 34620) | August 7, 2015 |
| 10.26 | Additional Call Option Transaction Confirmation, dated as of June 22, 2015, between Ironwood Pharmaceuticals, Inc. and Credit Suisse Capital LLC, through its agent Credit Suisse Securities (USA) LLC | Quarterly Report on Form 10 Q (File No. 001 34620) | August 7, 2015 |
| 10.27 | Additional Warrants Confirmation, dated as of June 22, 2015, between Ironwood Pharmaceuticals, Inc. and JPMorgan Chase Bank, National Association, London Branch | Quarterly Report on Form 10 Q (File No. 001 34620) | August 7, 2015 |

Table of Contents

| | | Incorporated by reference herein | |
|---|---|---|---|
| Number | Description | Form | Date |
| 10.28 | Additional Warrants Confirmation, dated as of June 22, 2015, between Ironwood Pharmaceuticals, Inc. and Credit Suisse Capital LLC, through its agent Credit Suisse Securities (USA) LLC | Quarterly Report on Form 10 Q (File No. 001 34620) | August 7, 2015 |
| 21.1* | Subsidiaries of Ironwood Pharmaceuticals, Inc. | | |
| 23.1* | Consent of Independent Registered Public Accounting Firm | | |
| 31.1* | Certification of Chief Executive Officer pursuant to Rules 13a 14 or 15d 14 of the Exchange Act | | |
| 31.2* | Certification of Chief Financial Officer pursuant to Rules 13a 14 or 15d 14 of the Exchange Act | | |
| 32.1‡ | Certification of Chief Executive Officer pursuant to Rules 13a 14(b) or 15d 14(b) of the Exchange Act and 18 U.S.C. Section 1350 | | |
| 32.2‡ | Certification of Chief Financial Officer pursuant to Rules 13a 14(b) or 15d 14(b) of the Exchange Act and 18 U.S.C. Section 1350 | | |
| 101.INS* | XBRL Instance Document | | |
| 101.SCH* | XBRL Taxonomy Extension Schema Document | | |
| 101.CAL* | XBRL Taxonomy Extension Calculation Linkbase Document | | |
| 101.LAB* | XBRL Taxonomy Extension Label Linkbase Database | | |
| 101.PRE* | XBRL Taxonomy Extension Presentation Linkbase Document | | |
| 101.DEF* | XBRL Taxonomy Extension Definition Linkbase Document | | |

*Filed herewith.

‡Furnished herewith.

+Confidential treatment granted under 17 C.F.R. §§200.80(b)(4) and 230.406. The confidential portions of this exhibit have been omitted and are marked accordingly. The confidential portions have been provided separately to the SEC pursuant to the confidential treatment request.

#Management contract or compensatory plan, contract, or arrangement.

Item 16. 10-K Summary

None.