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

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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;

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- 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.

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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 pr