CytomX Therapeutics, Inc.
Form 10-K
March 07, 2018

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, 2017

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, a smaller reporting company or an emerging growth company. See the definitions of "large accelerated filer," "accelerated filer," "smaller reporting company" and "emerging growth 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
Emerging growth company		

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act.

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, 2017, 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 $360.5 million, based on the closing price of the registrant's common stock on NASDAQ Global Select Market on June 30, 2017 of $15.50 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 March 5, 2018, 38,611,158 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 2018 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:

- our expectations regarding the potential benefits, activity, effectiveness and safety of our product candidates and therapeutics developed utilizing our Probody platform technology;

- the initiation, timing, progress and results of our ongoing clinical trials, research and development programs, preclinical studies, and Investigational New Drug application ("IND"), Clinical Trial Application, New Drug Application ("NDA"), Biologics License Application ("BLA") and other regulatory submissions;

- the timing of the completion of our ongoing clinical trials and the timing and availability of clinical data from such clinical trials;

- our ability to identify and develop additional product candidates;

- our dependence on collaborators for developing, obtaining regulatory approval for and commercializing product candidates in the collaboration;

- our or a collaborator's ability to obtain and maintain regulatory approval of any of our product candidates;

- our receipt and timing of any milestone payments or royalties under any research collaboration and license agreements or arrangements;

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our expectations and beliefs regarding the evolution of the market for cancer therapies and development of the immuno-oncology industry;

- 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 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 ability to secure and maintain licenses of intellectual property to protect our technologies and product candidates;

- 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

Overview

We are a clinical-stage, oncology-focused biopharmaceutical company with a vision of transforming lives with safer, more effective therapeutics. We are pioneering a novel class of investigational antibody therapeutics, based on our Probody™ technology platform, for the treatment of cancer. The Probody therapeutic approach is designed to more specifically target antibody therapeutics to the tumor microenvironment and reduce drug activity in healthy tissue and in circulation. We believe this approach has the potential to make meaningful enhancements to the combined efficacy and safety profile of antibody therapeutics known as the therapeutic window. We believe that Probody therapeutics have the potential to create or widen the therapeutic window for certain antibody therapeutics, allowing for the development of new approaches to the treatment of cancer. We are utilizing our Probody Platform to develop potential best-in-class immunotherapies against clinically-validated targets and potential first-in-class therapeutics against novel, difficult to drug targets. Furthermore, we believe the Probody therapeutic approach has the potential to enable safer, more effective combination therapy for cancer. CytomX is building a clinical stage pipeline, composed entirely of Probody therapeutics, as shown below:

CytomX pipeline of Probody Therapeutics

Our most advanced product candidate is CX-072, a wholly owned Probody therapeutic targeting programmed cell death ligand 1 (“PD-L1”), a clinically and commercially validated anti-cancer target. In normal physiology, PD-L1 plays a role in suppressing the immune system in healthy tissue, preventing autoimmunity. Tumors can co-opt this inhibitory function by upregulating PD-L1 expression and evading anti-cancer immune surveillance. Inhibitors of the PD-L1 pathway have therefore been designed and developed that restore anti-cancer immune surveillance and such inhibitors have demonstrated anti-cancer activity in a wide variety of cancer types. Regulatory approval has been granted for PD-L1 inhibitors and/or programmed cell death 1 (“PD-1”) inhibitors in advanced melanoma, renal cell cancers, non-small cell lung cancer, urothelial cancers, gastric cancer, merkel cell carcinoma, Hodgkins disease and microsatellite instability-high cancers.

While PD-L1 inhibitors have been shown to enhance anti-cancer immunity, systemic administration of inhibitors of the PD-L1 pathway can result in impairment of normal immune tolerance of healthy tissues, and severe immune-related toxicities can emerge. These toxicities can be particularly serious when PD-L1 inhibitors are combined with other anti-cancer agents. Our PD-L1 Probody therapeutic, CX-072, is designed to uncouple the anti-cancer immunity enhancing properties of PD-L1 inhibitors from the associated autoimmune toxicities by inhibiting PD-L1 primarily in the tumor microenvironment. We are currently evaluating CX-072 in a Phase 1/2 study that we call PROCLAIM-CX-072. This study is designed to assess the safety, activity, and translational biology of CX-072 as a single agent and in combination with other anticancer therapies. We expect to disclose initial clinical data regarding CX-072 in mid-2018.

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Our second most advanced product candidate is CX-2009, a wholly owned Probody Drug Conjugate ("PDC") against CD166, a novel tumor antigen that has historically been considered difficult to drug. We believe CD166 is an attractive target because it is highly and homogenously expressed on many solid tumors. However, it has not been considered appropriate for traditional antibody drug conjugate ("ADC") technology because it is also expressed abundantly on many healthy tissues, which would ordinarily be expected to lead to unacceptable toxicity. Our Probody Platform is designed to focus the activity of antibody therapeutics to the tumor microenvironment, which we believe could enable the development of a therapeutic against targets such as CD166. CX-2009 is currently in the dose escalation portion of a Phase 1/2 study that we call PROCLAIM-CX-2009. We expect to disclose initial clinical data regarding CX-2009 in the second half of 2018.

In addition to our wholly owned programs, we have entered into several strategic collaborations with leading oncology-focused pharmaceutical companies, such as AbbVie Inc., through its subsidiary AbbVie Ireland Unlimited Company ("AbbVie"), Amgen, Inc. ("Amgen") and Bristol-Myers Squibb Company ("BMS"). The most advanced program from our partnerships is a CTLA-4 Probody therapeutic which BMS is currently advancing through the dose escalation phase of a Phase 1/2 clinical trial. We also plan to file an investigational new drug ("IND") application for CX-2029, a PDC targeting CD71 that we have partnered with AbbVie, in the first half of 2018 and initiate a clinical trial shortly thereafter.

Finally, we are also advancing CX-188, a wholly owned Probody therapeutic targeting PD-1, a clinically and commercially validated anti-cancer target. CX-188 is currently in IND enabling studies. We anticipate filing an IND on CX-188 in the second half of 2018 and initiating clinical studies shortly thereafter. We have also extended our Probody platform to the T-cell engaging bispecific modality. Our most advanced program in that modality is an EGFR-CD3 T-cell bispecific, which is currently in lead optimization stage, and partnered with Amgen.

Our broad Probody therapeutic technology platform and lead product candidates are supported by more than a decade of thorough scientific research and strong intellectual property. We are a leader in the emerging field of localizing antibody therapeutics to the tumor microenvironment, as evidenced by our patent estate of 60 issued patents (8 of which are co-owned with a third party) and 233 pending patent applications (13 of which are co-owned with a third party) as of February 15, 2018. We also have an exclusive license from University of California, Santa Barbara ("UCSB") to three patent families (22 issued patents and 7 pending patent applications) covering screening tools to identify masks and substrates.

We believe the market opportunity for Probody therapeutics could be large. 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 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 2016. 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 suppressive mechanisms like the PD-L1 pathway that cancer cells have developed to evade the immune system. In addition, new classes of monoclonal antibody-based therapeutics have also

reached the market. These new classes include ADCs, bispecific antibodies, and Chimeric Antigen Receptor ("CAR") based cellular therapies. We have demonstrated that our Probody therapeutic technology can be applied to many antibody modalities, including antibodies against immuno-oncology targets, ADCs, and bispecific antibodies, and therefore we believe that significant opportunities exist for CytomX to develop and capture market share with innovative anti-cancer treatments.

Our Corporate Strategy

We are utilizing our proprietary and differentiated Probody Platform to develop a leading pipeline of innovative anti-cancer therapies to improve the lives of people with cancer and to build a long-term, multi-product, integrated biotechnology company. We aim to achieve this goal by:

- Applying the Probody Platform to discover and develop potentially best-in-class therapies for which we believe we can make meaningful enhancements to the therapeutic window, of monoclonal antibody-based cancer therapeutics. Our wholly owned PD-L1 Probody therapeutic (CX-072), partnered CTLA-4 Probody therapeutic (BMS 986249), and wholly owned PD-1 Probody therapeutic (CX-188) are our most advanced programs in this class of targets.

- Applying the Probody Platform to discover and develop potentially first-in-class therapies against targets we believe could have therapeutic benefits within oncology, but have not yet been drugged because of broad expression in healthy tissue. Our wholly owned CD-166 Probody Drug Conjugate (CX-2009) and partnered CD-71 Probody Drug Conjugate (CX-2029) are our most advanced programs in this class of targets.

- Applying our Probody Platform to develop novel and improved combination therapies with the potential to improve outcomes for cancer patients. For example, we are studying CX-072, our PD-L1 Probody therapeutic, in multiple combinations in our ongoing Phase 1/2 clinical trial.

- Applying our Probody Platform to enable new potent therapeutic antibody and cell therapy formats, thereby positioning ourselves at the cutting edge of anti-cancer therapeutic research and development. For example, we are collaborating on a Probody therapeutic version of an Epidermal Growth Factor Receptor-CD3 ("EGFR-CD3") T-cell engaging bispecific with Amgen.

- Partnering with leading biopharmaceutical companies to access capital, additional resources and expertise, as well as increase the number of Probody therapeutic candidates being advanced into clinic trials. To date, we have formed several strategic collaborations, including with AbbVie, Amgen, BMS, ImmunoGen Inc. ("ImmunoGen") and others.

- Accessing technologies or programs that can complement our Probody platform and our pipeline through licenses or acquisitions.

- Fostering a unique culture of execution, alignment and accountability centered around our vision, mission and values

Our Probody Platform

Localization of therapeutic antibody activity within disease tissue is of increasing interest in the biopharmaceutical industry. We believe this is due to the desire to maximize the activity of antibody-based drugs whilst reducing their toxicities. At CytomX, we call our approach to therapeutic antibody localization our Probody Platform. A Probody therapeutic consists of three components: an active anti-cancer antibody, a mask for the antibody, and a protease-cleavable linker which tethers the mask to the antibody. Probody therapeutics are produced as a single protein by standard antibody production methodology. The mask is a peptide designed to disguise the active binding site of the antibody to prevent the therapeutic from binding to the target present on healthy tissue. The following graphic depicts the three components of a Probody therapeutic, interacting with a protease:

Depiction of the structure of a Probody therapeutic and a protease that may cleave the linker and activate the molecule

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 bind to the target when it is expressed on the tumor. The following graphic depicts the activation of a Probody therapeutic by proteases:

Depiction of how a Probody therapeutic is designed to enter the tumor microenvironment (left), be activated by protease cleavage to remove the mask (middle), thereby enabling the released antibody to bind to the tumor target (right)

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 only small amounts of extracellular protease activity being 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:

Probody therapeutics are designed to remain masked and inactive in healthy tissue (right) but be unmasked and activated in diseased tissue, such as in tumors (left)

Probody therapeutics are 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 and our partners have demonstrated the applicability of our Probody Platform across more than 10 targets in multiple monoclonal antibody modalities, including cancer immunotherapy, ADCs, and T-cell-recruiting bispecifics. We are also investigating the application of our Probody Platform technology to CAR-based cellular therapies.

We have designed 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 across a large number of tumor types. We have generated in vivo efficacy data in dozens of human tumor models in mice and ex-vivo data from hundreds of human tumor explants to suggest that our Probody therapeutics can be activated across a broad set of tumors. We are now assessing our first Probody therapeutics in clinical trials.

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.

Our Development Programs

We are leveraging our Probody Platform to build a leading pipeline of innovative anti-cancer therapies. We currently retain worldwide development and commercialization rights to our two most advanced Probody therapeutics in the clinic, CX-072 and CX-2009. In addition, we have multiple partnered development programs including BMS 986249, an anti-CTLA-4 Probody program with BMS, and CX-2029, an anti-CD71 PDC program in collaboration with AbbVie.

The successful development of our product candidates involves a lengthy and expensive process with an uncertain outcome, and results of earlier studies and trials may not be predictive of future trial results. This is due to the numerous risks and uncertainties associated with the development of product candidates. If one or more of our product candidates or our Probody therapeutic technology generally prove to be ineffective, unsafe or commercially unviable, our entire platform and pipeline would have little, if any, value, which would have a material and adverse effect on our business, financial condition, results of operations and prospects. See “Risk Factors” for a discussion of the risks and uncertainties associated with our product candidates and our research and development projects.

CX-072 (PD-L1 Probody therapeutic) Program

Overview and Limitations of Existing Therapies

Our most advanced product candidate is CX-072, a wholly owned Probody therapeutic targeting PD-L1, a clinically and commercially validated cancer target. The PD pathway consists principally of two targets: PD-1, which is typically expressed on T-cells, and PD-L1, which is typically expressed on the tumor cells as well as on healthy tissue.

In healthy tissue, PD-1 and PD-L1 work together to negatively regulate immune response and maintain tolerance between the immune system and healthy tissue. Tumors, however, upregulate PD-L1 to evade immune surveillance by the host's immune system. Therefore, development of antibodies against PD-1 and PD-L1 have become a key focal point in cancer drug development, with two PD-1 antibodies nivolumab (Opdivo™) and pembrolizumab (Keytruda™), and three PD-L1 antibodies atezolizumab (Tecentriq™), durvalumab (Imfinzi™), and avelumab (Bavencio™) approved as of February 2018. In addition to assessment as single agents, PD-1 and PD-L1 antibodies have been studied extensively as the centerpiece of oncology combination therapies. According to the Cancer Research Institute, as of November 2017, there were 1,105 combination studies ongoing with a PD-1 or PD-L1 therapeutic.

While inhibitors of the PD-L1 and/or PD-1 pathway offer the potential for clinical benefit in patients with a wide-variety of cancer types, there are a number of risks imposed by administration of these agents. According to U.S. Labels for Opdivo, Keytruda, Tecentriq, Bavencio, and Imfinzi, the most common side effects (defined as either >15% or >20%, depending upon the agent) that were observed with commercially available anti-PD-L1 and anti-PD-1 agents include: fatigue, decreased appetite, nausea, vomiting, diarrhea, dyspnea, constipation, cough, musculoskeletal pain, back pain, abdominal pain, arthralgia, urinary tract infection, upper respiratory tract infection, urinary tract infection, peripheral edema, infusion-related reaction, rash, asthenia, pruritus, headache, and pyrexia.

Based on our analysis of publicly available data, we believe that while in general, the addition of second or third combination partners to PD-L1 or PD-1 inhibitors can result in increased anti-cancer activity, there is often a corresponding increase in the toxicity of these combinations. For example, according to the New England Journal of Medicine, the most common adverse reactions (greater than or equal to 20%) in patients with melanoma receiving nivolumab with ipilimumab were fatigue, rash, diarrhea, nausea, and pruritus. In some cases, administration of an inhibitor of the PD-L1 pathway with another type of anti-cancer agent in combination have resulted in severe toxicities that have prevented further development of the combination. In these cases, the toxicity levels caused by the multiple agents in the periphery creates an unacceptable risk to patients, despite the potential for synergy of efficacy in the tumor. Examples include concomitant administration of inhibitors of the PD-L1 pathway with EGFR inhibitors or Vascular Endothelial Growth Factor (“VEGF”) inhibitors.

We believe that a locally activated Probody therapeutic targeting PD-L1 has the potential to maintain the anti-tumor activity of the PD pathway blockade whilst reducing the autoimmunity that results from blocking such pathway systemically. As such, we believe that CX-072 has the potential to enable combination therapies that cannot be appropriately dosed because of synergistic toxicity, and ultimately that CX-072 may have the potential to be a center point of combination PD therapy.

Our near-term value creation strategy for CX-072 has four primary elements:

- Evaluate initial safety and efficacy profile in cancer patients
- Determine clinical and commercial potential as a monotherapy in one or more cancer indications
- Broadly evaluate clinical and commercial potential in combination with a range of anti-cancer agents/mechanisms
- Evaluate a partnering strategy to maximize clinical and commercial potential as a differentiated centerpiece of anti-cancer treatment across multiple indications

CX-072 pre-clinical data

CX-072 is derived from a CytomX discovered, phage-derived, fully human PD-L1 antibody that has high affinity binding to PD-L1 according to a standard binding assay. Using our proprietary technology, we have developed a Probody therapeutic that is effectively masked when active proteases are absent but can be specifically activated by one of several tumor-associated proteases. The figure below shows binding (A450, y-axis) of the parental antibody and Probody therapeutic as a function of concentration (x-axis). The unmasked underlying parental antibody of CX-072 (inverted triangles) is a potent binder to PD-L1. The masked Probody therapeutic, CX-072 (circles), has significantly reduced binding which can be restored to levels comparable to the parental antibody once proteolytically activated with uPA or MMP14, two proteases known to be active in the tumor microenvironment (squares and upright triangles, respectively).

Binding of CX-072 and its parental antibody to PD-L1 in vitro

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We have completed extensive preclinical testing comparing either CX-072 or a surrogate PD-L1 Probody therapeutic to its antibody parent, the results of which are reflected in in the figure below:

Comparison of PD-L1 Probody therapeutic versus antibody parent

In this experiment, MC-38 tumor bearing mice were treated with a single dose of either the Probody therapeutic or the underlying antibody. In this study, CX-072 (shown in blue) demonstrated similar anti-tumor activity as its underlying antibody parent in traditional mouse syngeneic tumor models (as illustrated in Figure A). In addition, CX-072 concentrated in the tumor similarly to the parental antibody (as illustrated in Figure B). Figure C demonstrates the potential advantage that a CX-072 as a PD-L1 Probody therapeutic has in avoiding systemic autoimmunity, in the non-obese diabetic ("NOD") mouse model. NOD mice are bred to develop spontaneous autoimmune diabetes, which is exacerbated by systemic inhibition of the PD-1 pathway. As expected, a single dose of the PD-L1 antibody (shown in green) resulted in more than half of the treated mice developing diabetes, while mice treated with the same dose of the Probody therapeutic (shown in blue) remained diabetes free. Binding of each test article on peripheral T-cells was measured. As Figure D shows, the antibody saturated circulating, peripheral T-cells at a low concentration, while binding of the Probody therapeutic was significantly reduced. The differentiated profile that we observed in these preclinical data, along with the results of our GLP toxicity study, supported our decision to advance CX-072 into clinical trials. We treated our first patient with CX-072 in January 2017 as part of our PROCLAIM umbrella clinical trial program.

The PROCLAIM Clinical Trial Design

PROCLAIM (Probody Clinical Assessment In Man) is an international umbrella clinical program for Phase 1/2 evaluation of all Probody therapeutics whose development is sponsored by CytomX. PROCLAIM centers around a core protocol that includes all of the common elements of a typical Phase 1/2 design without reference to an experimental drug. Each PROCLAIM module supplements the core and focuses exclusively on Probody-specific elements (e.g. background, guidance on patient selection and care). We refer to the CX-072 module as PROCLAIM-CX-072.

As of February 2018, we had 38 PROCLAIM sites active worldwide.

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PROCLAIM-CX-072

PROCLAIM-CX-072 is evaluating tolerability and preliminary antitumor activity of multiple doses of CX-072 as a monotherapy or as a combination therapy with ipilimumab (BMS' Yervoy) or vemurafenib (Roche's Zelboraf) in patients with advanced, unresectable solid tumors or lymphoma. The figure below describes the design and status, as of March 2018, for PROCLAIM-CX-072.

Design of CX-072 Phase 1/2 clinical trial

Enrollment of Part A1 of the clinical trial, the initial dose escalation stage, was completed in December 2017. This arm enrolled patients who were PD agent naïve and were either ineligible to receive or did not have access to PD-1 or PD-L1 agents for their disease. We did not pre-select patients based on their PD-L1 status in this arm. As such, we enrolled a broad mix of tumor types in Part A1, including patients with tumors that were not expected to respond to PD-L1 therapy. Our primary goals for Part A1 are to:

- demonstrate safety of CX-072, the first Probody therapeutic to be evaluated in patients;
- further our understanding of the pharmacokinetic ("PK") properties of CX-072, including assessing whether the Probody therapeutic remains stable and masked in circulation; and
- demonstrate initial evidence of anti-cancer activity.

We expect to present initial clinical data from Part A1 in mid-2018.

In the second half of 2017, we initiated Part A2 of the clinical trial. We are still enrolling patients with a broad range of cancer types in this portion of the study and restricting enrollment to those patients whose tumors are PD-L1 positive by the commercially available DAKO assay. In addition, we are requiring mandatory biopsies in this arm of the study. Such tumor biopsies will serve as the basis of our translational program, in which we will be assessing protease activity in the tumor, whether CX-072 is activated in the tumor, whether activated CX-072 engages target in the tumor, and whether engagement of the target activates downstream signaling. We expect to present initial clinical data from Part A2 in the second half of 2018.

Finally, with regards to the monotherapy program, we initiated Part D, our first monotherapy expansion cohort arm, in late 2017. In this arm, we are assessing CX-072 in an undisclosed indication. Previous clinical trial data, generated with other PD-pathway inhibitors, suggests that this undisclosed indication is responsive to PD-pathway inhibitors.

In addition to these monotherapy arms, we are testing CX-072 in combination with either ipilumumab, a CTLA-4 antibody commercialized by BMS as Yervoy (Part B in the graphic above) and vemurafenib, a small molecule BRAF inhibitor commercialized by Roche as Zelboraf (Part C in the graphic above). According to the New England Journal of Medicine and the Society for Melanoma Research, previously reported data suggests that a combination of a PD-pathway inhibitor with either ipilumumab or vemurafenib resulted in improved efficacy but also significantly increased toxicity and drug discontinuation, as shown in the tables below:

Objective response rates ("ORR") and adverse event ("AE") rates in published clinical studies of PD-(L)1 in combination with ipilimumab and vemurafenib in melanoma

In Part B of PROCLAIM-CX-072, we are assessing CX-072 in combination with ipilumumab. This study began enrolling patients in the second half of 2017. In this arm, we are combining CX-072 with the approved, labeled dose of ipilumumab (3 mg/kg every three weeks) with the potential to increase the dose of ipilumumab to 10 mg/kg every three weeks. This is in contrast to other studies combining PD-pathway inhibitors and ipilumumab, for example,

BMS's Checkmate 227 study, where the dose and dosing frequency of ipilumumab has been reduced to 1 mg/kg every 6 weeks. We expect to present initial clinical data from Part B in mid-2018.

Finally, in Part C of PROCLAIM-CX-072, we are assessing CX-072 in combination with vemurafenib in PD-naïve V600E BRAF mutated melanoma patients. This study began enrolling in the second half of 2017. In this arm, we are combining CX-072 with the labeled dose of vemurafenib (960 mg twice daily). Standard of care for patients with V600E mutated melanoma in the United States has shifted to a BRAF inhibitor in combination with a MEK inhibitor. Our study does not include a MEK inhibitor, and therefore, we are expecting to enroll this study outside of the United States, and primarily in Eastern Europe. We expect to present initial clinical data from Part C in 2019.

CX-2009 (CD166 Probody Drug Conjugate) Program

Our second most advanced product candidate is CX-2009, a wholly owned PDC directed against CD166, a novel, difficult to drug target. CX-2009 is similar to ADCs, which are antibodies that have been conjugated to a small molecule cytotoxic agent via a labile chemical linker. Several ADCs have been approved in the United States, including Kadcyla™, which targets HER2 for HER2 positive metastatic breast cancer, and Adcetris™, which targets CD30 for Classical Hodgkin Lymphoma. To avoid target-related toxicity, traditional ADCs have historically been limited to targeting proteins that are expressed highly in tumors, but that are also absent or poorly expressed in healthy tissues. Very few cancer-associated proteins have this profile. Because our Probody therapeutics are designed to minimize delivery of potent anti-cancer therapy to normal tissues, we believe such therapeutics could potentially enable us to generate ADCs for a new class of targets with attractive features that were previously unsuitable because of expression on normal tissues. CD166 is an example of this kind of target, and CX-2009 is our Probody therapeutic directed to CD166 and conjugated to a cytotoxic agent. The graphic below describes CD166 expression across multiple tumor types and healthy tissue.

Expression of CD166 in human tumors and normal tissues

(Human Protein Atlas: Uhlen et al (2015). Tissue-based map of the human proteome. Science. DOI: 10.1126/science.1260419)

In the figure above, the highest expression of CD166 is denoted in deep blue. As reflected in the figure, CD166 is highly expressed in a variety of different cancers. CD166 is also expressed in moderate to high levels on certain normal tissues, as denoted by the figure above. The high and homogenous expression of CD166 in multiple different tumors makes it an attractive target for a Probody drug conjugate therapeutic; however, the high expression on normal tissues makes CD166 a difficult target to drug with a traditional ADC.

CX-2009 Target Validation and Pre-clinical data

CX-2009 is derived from a CytomX discovered humanized CD166 antibody that has exhibited high affinity binding to CD166 according to a standard binding assay. Using our proprietary technology, we have developed a Probody therapeutic that is designed to be masked when active proteases are absent but can be specifically activated by any one of several different tumor-associated proteases. Through our license with ImmunoGen, we have gained access to ImmunoGen's potent microtubule inhibiting payload DM4. Therefore, CX-2009 is a Probody therapeutic conjugated to DM4 and designed to bind to CD166 specifically in the tumor microenvironment, as shown in the figure below:

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CX-2009 is a Probody drug conjugate directed to CD166

We have completed multiple preclinical efficacy studies for CX-2009 and demonstrated tumor regressions at doses that we believe may be achievable in clinical trials. Preclinical efficacy data along with IHC staining that demonstrates high expression of CD166 in these tumors, is shown in the figures below. In these figures, tumor growth curves are shown in mice-bearing HCC1806 xenograft tumors, H292 xenograft tumors, or an Ovarian patient derived tumor model. Mice treated with CX-2009 (squares) are compared to either a control without treatment (circles) or an ADC to CD166 (triangles). The figures indicate that CX-2009 led to greater tumor growth regression than control, and similar tumor growth regression as the ADC

Examples of pre-clinical anti-tumor activity of a CD166-directed ADC (red) and CX-2009 (blue) in mouse models

Doses of CX-2009 up to 15 mg/kg were tested in GLP non-human primate toxicology studies. The findings were consistent with the off-target, non-specific toxicity typically seen with other DM4-based ADCs that target other proteins. CX-2009 was advanced into human clinical trials on the basis of the anti-tumor activity and safety and tolerability observed in these preclinical studies. We treated our first patient with CX-2009 in June 2017 as part of our PROCLAIM umbrella clinical trial program.

PROCLAIM-CX-2009

Our second module in our PROCLAIM umbrella is our CX-2009 Phase 1/2 clinical trial. PROCLAIM-CX-2009 is evaluating tolerability and preliminary antitumor activity of CX-2009 as a monotherapy. We are focusing this study in seven tumor types that have high CD166 expression: breast carcinoma, castration-resistant prostate carcinoma, cholangiocarcinoma, endometrial carcinoma, epithelial ovarian carcinoma, head and neck squamous cell carcinoma, and non-small cell lung carcinoma. The figure below describes the design and status of PROCLAIM-CX-2009.

Design of PROCLAIM-CX-2009 Phase 1/2 clinical trial

We initiated enrollment of Part A of the clinical trial in June 2017. This arm is enrolling patients across the seven tumor types without pre-determination of CD166 expression levels. Our primary goals for Part A are to:

- demonstrate safety of CX-2009, which we believe is particularly relevant because CD166 is so broadly expressed on healthy tissue;
- further our understanding of the pharmacokinetic ("PK") properties of CX-2009; and
- assess whether our Probody therapeutic remains stable and masked in circulation.

We expect to disclose initial clinical data regarding Part A of CX-2009 in the second half of 2018.

In the first quarter of 2018, we initiated Part A2 of the clinical trial. In this arm, we plan to enroll only those patients who have high CD166 expression, as determined by an immunohistochemistry assay we have developed. In addition, we are requiring mandatory biopsies in this arm of the study to inform our translational science program. In this translational program, we expect to assess protease activity in the tumor, whether CX-2009 is activated in the tumor, whether activated CX-2009 engages target in the tumor, and whether engagement of the target activates downstream signaling.

Initiation of Part B of the clinical trial is planned for late 2018. This arm is designed to be a cohort expansion study where we would dose patients from one or more of the seven tumor types at a single dose level of CX-2009.

Other Selected Product Candidates in Development

We are actively pursuing the application of our Probody Platform technology to multiple other product candidates. These include other product candidates directed against other immunotherapy targets, additional first-in-class PDC product candidates, and T-Cell Engaging bispecific product candidates. Below are selected examples of product candidates that we are pursuing.

BMS-986249, a CTLA-4 Probody Therapeutic in Collaboration with BMS

As part of our strategic oncology collaboration, BMS has advanced BMS-986249, a CTLA-4 Probody therapeutic, into a Phase 1/2 clinical trial. 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 the treatment of unresectable or metastatic melanoma. CTLA-4 antibodies have been shown to lead to T-cell activation towards tumor antigens, which is the basis for its anti-tumor effect, and towards self-antigens, which may be the basis for the autoimmune toxicities associated with CTLA-4 antibodies therapies. The U.S. Food and Drug Administration ("FDA") approval for ipilimumab has a black box warning about potential severe and fatal immune-related adverse events. We believe that our CTLA-4 Probody therapeutic may be able to effectively localize the CTLA-4 antibody activity to the tumor microenvironment, 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.

At various scientific congresses in 2017 and 2018, BMS presented pre-clinical efficacy and safety data on the CTLA-4 Probody therapeutic. For example, at the 2018 Keystone Drugs as Antibodies Conference, BMS scientists presented preclinical efficacy data that showed that an CTLA-4 Probody therapeutic demonstrates comparable anti-tumor activity to ipilumumab in preclinical models. At the Society of Immunotherapy of Cancer meeting in 2017, BMS scientists presented preclinical data that showed that cynomologous monkeys treated with a CTLA-4 Probody therapeutic demonstrated reduced peripheral T-cell activation compared to ipilumumab.

Finally, BMS scientists presented data on the toxicity profile of the CTLA-4 Probody Therapeutic and ipilumumab at the AACR-EORTC-NCI meeting in 2017. BMS scientists concluded that the highest non-severely toxic dose ("HNSTD") of the CTLA-4 Probody therapeutic was 50 mg/kg, while the HNSTD of ipilumumab was determined to be 10 mg/kg. The efficacy data, along with the peripheral T-cell activation data and the widened safety window suggests that BMS-986249 has the potential to widen therapeutic window compared to ipilumumab. BMS-986249 is currently in a Phase 1/2 clinical study that is being conducted by BMS.

CX-2029, a CD71 Probody Drug Conjugate 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 CD71 a difficult target for conventional ADCs, but potentially a good candidate for development of PDCs.

In preclinical efficacy models, we have demonstrated that CX-2029 is highly efficacious in many cell line and patient-derived xenograft models that represent many different cancer types. In the figure below, an example is shown on the left of tumor growth curves in OV-90 tumor bearing mice treated with CX-2029 (triangles) compared to a control without treatment (circles), indicating that CX-2029 led to greater tumor growth regression. A summary of additional studies of 42 different tumor models tested with anti-CD71 PDCs at varying doses and schedules is presented in the table on the right. This data shows that anti-CD71 PDCs had efficacy across nearly all preclinical models tested.

Preclinical anti-tumor activity of anti-CD71 PDCs

We have also compared the toxicity profile of a CD71 Antibody Drug Conjugate ("CD71-ADC") to a CD71 Probody Drug Conjugate ("CD71-PDC"). As the figure below shows, a single dose of the CD71-ADC results in significant decrease in the number of neutrophils, a type of infection-fighting cell, in the blood in cynomologus monkeys (squares), while the CD71-PDC at the same dose does not (triangles).

Neutrophil counts in monkeys treated with CD71 ADC or PDC

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Taken together, we believe that CX-2029 has the potential to create a therapeutic window for a CD71 targeting therapeutic. We are planning to file an IND on CX-2029 in the first half of 2018 and initiate a clinical trial shortly thereafter. This program is partnered with AbbVie as part of our global co-development collaboration, and we are responsible for filing the IND and conducting the Phase 1/2 clinical trial.

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 (Opdivo) and pembrolizumab (Keytruda). As with PD-L1, inhibiting PD-1 elicits T-cell anti-tumor responses in a variety of different cancers, and also induces systemic autoimmunity and toxicity. Given the size of the market and the breadth of opportunities for differentiated PD-pathway inhibitors, we are developing CX-188, a PD-1 Probody therapeutic in addition to our clinical stage CX-072 program. CX-188 is a wholly owned program and we expect to file an IND on the program in the second half of 2018 and initiate a clinical trial shortly thereafter.

We have compared an anti-mouse PD-1 Probody therapeutic ("PD-1 Pb-Tx") to the parenteral anti-mouse PD-1 antibody ("PD-1 Ab") in efficacy and toxicity studies in a mouse MC38 tumor model, both as single agents (left) and in combination with anti-CTLA4 antibody (right). In the figure below, tumor growth curves are shown for animals treated with control (black circles), the PD-1 Ab (blue triangles), and PD-1 Pb-Tx (red triangles). The Probody therapeutic demonstrated similar anti-tumor activity to the antibody, both as a single agent (Figure A) and also when combined with an anti-mouse CTLA-4 antibody (Figure B). Treatment with the CTLA-4 antibody with a 10 mg/kg bi-weekly dosing for three weeks as a single agent is also shown (grey triangles).

Comparison of pre-clinical anti-tumor activity of an anti-PD-1 Probody therapeutic in mouse MC38 tumor model, both as single agents (left) and in combination with anti-CTLA4 antibody (right)

However, the Probody therapeutic showed a differentiated safety profile when compared with the antibody in the NOD mouse model. As Figure A below shows, most animals treated with a low dose (1 mg/kg) of PD-1 Ab (blue) develop autoimmune diabetes, while a minority of animals treated with a 10-fold higher dose (10 mg/kg) of PD-1 Pb-Tx (red) do so. Control animals (black lines) do not develop diabetes in these experiments. As Figure B below shows, treatment with the combination of a CTLA-4 antibody and a PD-1 antibody also induced autoimmune diabetes in most mice, while the combination of a CTLA-4 antibody administered in combination with the PD-1 Probody therapeutic induced no diabetes.

Comparison of induction of autoimmune diabetes in the NOD mouse by a single dose of a PD-1 antibody (1 mg/kg), Probody therapeutic (10 mg/kg) or control either as monotherapy (left) or in combination with a CTLA-4 antibody with agents dosed at 10 mg/kg on days 0, 4 and 7 (right)

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EGFR T-Cell Bispecific

We believe that our Probody Platform can be applied to T-cell engaging bispecific antibodies ("TCBs"). TCBs are a highly potent therapeutic modality, designed to direct the activity of cytotoxic T-cells to tumors. TCBs such as Blincyto, a CD19-directed TCB commercialized by Amgen, have shown clinical activity in hematologic malignancies, but development of TCBs for solid tumor indications is proving challenging. Due to their high potency, TCBs can target normal tissues with low antigen expression, resulting in significant on-target, off-tumor toxicity that can limit dosing to low levels. As a result, it has been difficult to reach the level of drug exposure required for efficacy without excessive toxicity. Therefore, novel methods are needed to enable the potent anti-tumor activity of TCBs while limiting toxicity due to cytokine release and the resulting damage to healthy tissues.

Our most advanced asset in this modality is a T cell-engaging Bispecific Probody therapeutic ("Pb-TCB") targeting EGFR and CD3. In in vitro preclinical studies, we have demonstrated that the unmasked EGFR-CD3 TCB (diamonds) can exhibit potent dose-dependent tumor cell killing, while the masked EGFR-CD3 Pb-TCB (filled squares) reduced cytotoxicity by more than 100,000-fold, as shown in the figure below. A TCB which does not bind EGFR (open squares) does not kill tumor cells, demonstrating that the activity of the TCB is target dependent.

Cytotoxicity of HT-29 tumor cells induced by unmasked, active EGFR-CD3 bispecific antibody (red) and by masked EGFR-CD3 bispecific Probody therapeutic (blue). An inactive control is shown in blue squares

However, in established tumor models, we have demonstrated that Pb-TCBs potently can induce tumor regressions. As the figure below shows, in the HT29 xenograft model, the Pb-TCB at 0.5 mg/kg (open squares) demonstrated significant anti-tumor activity, and at 1.5 mg/kg (closed squares) was able to induce complete tumor regression. A control treated with inactive PBS buffer ("PBS") is also shown (circles).

Example of pre-clinical anti-tumor activity of a Probody TCB at 2 different doses (microgram/kg) in a mouse model, compared to vehicle control (PBS, black). Asterisks indicate statistical significance compared to control.

In nonhuman primates, the EGFR-CD3 Pb-TCB has a significantly higher maximum tolerated dose than the unmasked TCB. Cynomologus monkeys were able to tolerate a dose of 4,000 microgram/kg of the Pb-TCB, while the maximum tolerated dose of the unmasked TCB was 60 microgram/kg. Furthermore, as shown in the figure below, the tolerated exposure of the Pb-TCB (blue symbols) was greater than 10,000-fold higher than that of the unmasked TCB (red symbols).

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Concentration in plasma over time of 60 or 180 micrograms/kg single dose of an unmasked, active EGFR-CD3 TCB (red) and of 2000 micrograms/kg as a single dose of a masked EGFR-CD3 Probody therapeutic TCB (blue).

Taken together, we believe our Probody Platform has the potential to enable the development of T-cell engaging bispecific therapeutics against broadly expressed targets such as EGFR. Our EGFR-CD3 Pb-TCB program is partnered with Amgen, and as of March 2018, is in the pre-clinical lead optimization stage.

Our Collaborations

We believe that the Probody platform has broad applicability across a number of targets and antibody formats. We have leveraged strategic partnering to (a) extend the reach of our therapeutic opportunity and (b) bring in significant non-dilutive capital into the Company. Since 2013, we have entered into collaborations with AbbVie, Amgen, BMS and ImmunoGen, among others, 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, broaden the number of Probody therapeutics that ultimately reach the clinic, and to retain significant milestones, royalties, and in some cases product rights, for long term upside. Details of our existing collaborations are described below.

AbbVie Ireland Unlimited Company

In April 2016, CytomX and AbbVie Ireland Unlimited Company ("AbbVie") entered into two agreements, a CD71 Co-Development and Licensing Agreement (the "CD71 Agreement") and a Discovery Collaboration and Licensing Agreement (the "Discovery Agreement" and together with the CD71 Agreement the "AbbVie Agreements"). Under the terms of the CD71 Agreement, CytomX and AbbVie will co-develop a Probody Drug Conjugate ("PDC") against CD71, and 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. We will assume 35% of the net profits or net losses related to later development unless we opt-out. If we opt-out from participation of co-development of the CD71 PDC, AbbVie will have sole right and responsibility for the further development, manufacturing and commercialization of such CD71 PDC. AbbVie, at its sole discretion, may stop development of any CD71 PDC and terminate the CD71 Agreement if we do not meet certain preclinical research criteria by the applicable deadline. In such case, CytomX and AbbVie may evaluate and approve an alternate CD71 PDC. If such alternate CD71 PDC is approved, then CytomX and AbbVie will, in good faith, negotiate amendments to the timelines and, if necessary, the content in the research and development plan and budget and extensions to the deadlines to achieve defined success criteria.

Under the CD71 Agreement, we received an upfront payment of $20.0 million in April 2016, and we are eligible to receive up to $470.0 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 we opt-out from the co-development of the CD71 PDC. Our share of later stage co-development costs for each CD71 PDC is capped, provided that AbbVie may offset our co-development cost above the capped amounts from future payments such as milestone payments and royalties. In July 2017, we received a milestone payment of $14.0 million (net of the associated sublicense fee) from AbbVie for achieving certain milestones required to be met to begin GLP toxicology studies under the CD71 Agreement.

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Under the terms of the Discovery Agreement, AbbVie receives exclusive worldwide rights to develop and commercialize PDC against up to two targets, one of which was selected in March 2017. We shall perform research services to discover the Probody therapeutics and create PDCs for the nominated collaboration targets. From that point, AbbVie shall have sole right and responsibility for development and commercialization of products comprising or containing such PDCs ("Discovery Licensed Products").

Under the Discovery Agreement, we received an upfront payment of $10.0 million in April 2016 and may receive an additional payment upon the selection by AbbVie of the second target and the satisfaction of certain performance conditions under the CD71 Agreement. AbbVie has not selected the second target, but the performance conditions under the CD71 Agreement were met in September 2016. We are also eligible to receive up to $275.0 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.

Amgen, Inc.

On September 29, 2017, CytomX and Amgen, Inc. ("Amgen") entered into a Collaboration and License Agreement (the "Amgen Agreement"). Pursuant to the Amgen Agreement, we received an upfront payment of $40.0 million in October 2017. Concurrent with the entry into the Amgen Agreement, CytomX and Amgen entered into a Share Purchase Agreement (the "Purchase Agreement") pursuant to which Amgen agreed to purchase 1,156,069 shares of our common stock, par value $0.00001 per share, at a price of $17.30 per share (calculated based on a 20-day volume-weighted average price), for total proceeds of $20.0 million, which we received on October 6, 2017, the closing date of the transaction.

Under the terms of the Amgen Agreement, CytomX and Amgen will co-develop a Probody T-cell engaging bi-specific therapeutic targeting EGFR ("EGFR Products"). We will be responsible for early-stage development of EGFR Products and all related costs (up to certain pre-set costs and certain limits based on clinical study size). Amgen will be responsible for late-stage development, commercialization, and all related costs of EGFR Products. Following early-stage development, we will have the right to elect to participate financially in the global co-development of EGFR Products with Amgen, during which we would bear certain of the worldwide development costs for EGFR Products and Amgen would bear the rest of such costs (the "EGFR Co-Development Option"). If we exercise our EGFR Co-Development Option, we will share in somewhat less than 50% of the profit and losses from sales of such EGFR Products in the U.S., subject to certain caps, offsets, and deferrals. If we choose not to exercise our EGFR Co-Development Option, we will not bear any costs of later stage development. We are eligible to receive up to $455.0 million in development, regulatory, and commercial milestone payments for EGFR Products, and royalties in the low-double digit to mid-teen percentage of worldwide commercial sales, provided that if we exercise our EGFR Co-Development option, we shall only receive royalties in the low-double digit to mid-teen percentage of commercial sales outside of the United States.

Amgen also has the right to select a total of up to three targets, including the two additional targets discussed below. CytomX and Amgen will collaborate in the research and development of Probody T-cell engaging bi-specifics products directed against such targets. Amgen has selected one such target (the "Amgen Other Product"). If Amgen exercises its option within a specified period of time, it can select two such additional targets (the "Amgen Option Products" and, together with the Amgen Other Product, the "Amgen Products"). Except with respect to preclinical

activities to be conducted by CytomX, Amgen will be responsible, at its expense, for the development, manufacture, and commercialization of all Amgen Products. If Amgen exercises all of its options and advances all three of the Amgen Products, CytomX is eligible to receive up to $950.0 million in upfront, development, regulatory, and commercial milestones and tiered high single-digit to low-teen percentage royalties.

CytomX has the option to select, from programs specified in the Amgen Agreement, an existing pre-clinical stage T-cell engaging bispecific product from the Amgen pre-clinical pipeline. CytomX will be responsible, at its expense, for converting this program to a Probody T-cell engaging bispecific product, and thereafter, be responsible for development, manufacturing, and commercialization of the product ("CytomX Product"). Amgen is eligible to receive up to $203.0 million in development, regulatory, and commercial milestone payments for the CytomX Product, and tiered mid-single digit to low double-digit percentage royalties.

Bristol-Myers Squibb Company

On May 23, 2014, CytomX and Bristol-Myers Squibb Company ("BMS") entered into a Collaboration and License Agreement (the "BMS Agreement") to discover and develop compounds for use in human therapeutics aimed at multiple immuno-oncology targets using our Probody therapeutic technology. The effective date of the BMS Agreement was July 7, 2014.

Under the terms of the BMS Agreement, we granted BMS exclusive worldwide rights to develop and commercialize Probody therapeutics for up to four oncology targets, two of which were selected upon the execution of the BMS Agreement. In January 2016, BMS selected the third target pursuant to the BMS Agreement. Under the terms of the BMS Agreement, BMS paid us a $10.0 million payment. In December 2016, BMS selected the fourth and its final target pursuant to the BMS Agreement. Under the terms of the BMS Agreement, BMS paid us a $15.0 million payment.

Pursuant to the BMS Agreement, the financial consideration from BMS was comprised of an upfront payment of $50.0 million and were initially entitled to receive contingent payments of up to an aggregate of $1,217.0 million as follows: (i) up to $25.0 million for additional targets; (ii) up to $114.0 million in development milestone payments per research target program or up to $456.0 million if the maximum of four research targets are selected; (iii) up to $124.0 million in milestone payments for the first commercial sale in various territories for up to three indications per research target program or up to $496.0 million if the maximum of four research targets are selected, and (iv) up to $60.0 million in sales milestones payments per research target program or up to $240.0 million if maximum of four research targets are selected. We are entitled to royalty payments in the mid-single digit to low double digits from potential future sales. We will also receive research and development service fees based on a prescribed full-time employee ("FTE") rate that is capped.

Upon selection of the third target, we received a $10.0 million payment from BMS. Upon selection of the fourth target, we received a $15.0 million payment from BMS. In December 2016, BMS selected a clinical candidate pursuant to the BMS Agreement, which triggered a $2.0 million pre-clinical milestone payment to CytomX. In November 2017, BMS received acceptance of the IND from the FDA for a CTLA-4-directed Probody therapeutic, which triggered a $10.0 million milestone payment to CytomX.

On March 17, 2017, CytomX and BMS entered into Amendment Number 1 to Extend Collaboration and License Agreement (the "Amendment"). The Amendment grants BMS exclusive worldwide rights to develop and commercialize Probody therapeutics for up to six additional oncology targets and two non-oncology targets. The effective date of the Amendment was April 25, 2017 ("Amendment Effective Date").

Under the terms of the Amendment, we will continue to collaborate with BMS to discover and conduct preclinical development of Probody therapeutics against targets selected by BMS under the terms of the Amendment.

Pursuant to the Amendment, the financial consideration from BMS was comprised of an upfront payment of $200.0 million and we will be eligible to receive up to an aggregate of $3,586.0 million as follows: (i) up to $116.0 million in development milestone payments per target or up to $928.0 million if the maximum of eight targets are selected for the first product modality; (ii) up to $124.0 million in milestone payments for the first commercial sale in various territories for up to three indications per target program or up to $992.0 million if the maximum of eight targets are selected for the first product modality; (iii) up to $60.0 million in sales milestone payments per target or up to $480.0 million if maximum of eight targets are selected for the first product modality; and (iv) up to $56.3 million in development milestone payments or up to $450.0 million if the maximum of eight targets are selected for the second product modality; (v) up to $62.0 million in milestone payments for the first commercial sale in various territories for up to three indications per target program or up to $496.0 million if the maximum of eight targets are selected for the second product modality; (iii) up to $30.0 million in sales milestone payments per target or up to $240.0 million if maximum of eight targets are selected for the second product modality. We are also entitled to tiered mid-single to low double-digit percentage royalties from potential future sales.

ImmunoGen, Inc.

In January 2014, CytomX and ImmunoGen, Inc. ("ImmunoGen") entered into the Research Collaboration Agreement (the "ImmunoGen Agreement"). The ImmunoGen Agreement provides us with the right to use ImmunoGen's Antibody Drug Conjugate ("ADC") technology in combination with our Probody therapeutic technology to create a PDC directed at one specified target under a research license, and to subsequently obtain an exclusive, worldwide development and commercialization license to use ImmunoGen's ADC technology to develop and commercialize such PDCs. We made no upfront cash payment in connection with the execution of the agreement. Instead, we provided ImmunoGen with the rights to CytomX's Probody therapeutic technology to create PDCs directed at two targets under the research license and to subsequently obtain exclusive, worldwide development and commercialization licenses to develop and

commercialize such PDCs. In February 2017, ImmunoGen exercised its option to obtain a development and commercialization license for the first of its two targets. ImmunoGen discontinued this program in July 2017 and substitution rights for this program terminated in February 2017.

Under the terms of the agreement, both CytomX and ImmunoGen are required to perform research activities on behalf of the other party for no monetary consideration. Each party is solely responsible for the development, manufacturing and commercialization of any products resulting from the exclusive development and commercialization license obtained by such party under the agreement. Each party may be liable to pay annual maintenance fees to the other party if the licensed product candidate covered under each development and commercialization license has not progressed to the clinical stage of development within six years of the exercise of the development and commercialization license.

In consideration for the exclusive development and commercialization license that may be obtained by ImmunoGen, we are entitled to receive up to $30.0 million in development and regulatory milestone payments per the research program target, up to $50.0 million in sales milestone payments per target and royalties in the mid-single digits on the commercial sales of any resulting product. For the development and commercialization license that may be obtained by CytomX, ImmunoGen is entitled to receive up to $60.0 million in development and regulatory milestone payments, up to $100.0 million in sales milestone payments and royalties in the mid to high single digits on the commercial sales of any resulting product. In August 2017, we made a milestone payment of $1.0 million to ImmunoGen for the first patient dosing with CX-2009.

In December 2017, we entered into a license agreement with ImmunoGen (the "ImmunoGen Amendment") pursuant to ImmunoGen's exercise of its option to obtain a development and commercialization license for the second research program target under the ImmunoGen Agreement. The ImmunoGen Amendment extended our obligation to provide research services from January 8, 2018 to June 30, 2018.

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 CytomX in cancer immunotherapy. In October 2017, we extended the research term of the agreement. Under the research collaboration agreement, we have the right to exercise an option, during the option period expiring on October 23, 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 PDC Collaboration

In May 2013, we entered into a collaboration with Pfizer for up to four targets. CytomX received a letter, dated March 6, 2018, from Pfizer Inc. ("Pfizer") indicating that Pfizer was terminating our research collaboration, option and license agreement with Pfizer in its entirety. Such termination will become effective on the date that is 60 days after the date of the letter. Pfizer had previously declined its option to select a fourth target and had discontinued its epidermal growth factor receptor Probody Drug Conjugate. In the termination letter, Pfizer indicated that it was terminating the collaboration agreement because it had decided not to pursue the two targets it had previously selected for development, which were the last two remaining programs under the collaboration agreement. We will no longer be eligible to receive up to $263.5 million of contingent payments as follows: (i) up to $4.5 million upon exercise of the license options, (ii) up to $38.0 million from the achievement of development milestones for the research target programs, (iii) up to $101.0 million in milestone payments for the first commercial sale in various territories for up to three indications per research target program, and (iv) up to $120.0 million in sales milestones payments for the research target programs. We will also no longer be entitled to receive royalties in the mid-single digit royalties from potential future sales of product candidates or research and development service fees based on a prescribed FTE rate per year that was capped. No early termination penalties will be incurred by us as a result of the termination of the collaboration agreement.

Manufacturing

Our Probody therapeutic candidates are designed to be produced as fully recombinant antibody prodrugs. Our Probody therapeutic 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 a contract manufacturing organization ("CMO"). A CMO is 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 incorporate 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 biopharmaceutical products, particularly with respect to in immuno-oncology therapeutics, where competition is intense and rapidly evolving. These competitors generally fall within the following categories:

Masking and conditional activation: Several companies, including Akriveia, Amgen, Amunix, BioAtla, Halozyme, Maverick Therapeutics, Revitope, and Roche are exploring antibody masking and/or conditional activation strategies, which could compete with our Probody Platform.

Cancer immunotherapies: Cancer immunotherapy is one of the most competitive and fastest growing segments of the pharmaceutical industry. Almost every large pharmaceutical company is developing cancer immunotherapies, including Amgen, AstraZeneca PLC, BMS, Celgene, GlaxoSmithKline plc, Merck & Co., Inc., Novartis AG, Pfizer, Roche Holding Ltd and Sanofi SA. In addition, many large and mid-sized biotech companies such as BeiGene Incyte, TESARO, Inc., Nektar, and Alkermes have ongoing efforts in cancer immunotherapy. Finally, numerous small companies are also working in the space.

Antibody drug conjugates: Several large pharmaceutical companies, such as AbbVie, Pfizer, Roche, and Takeda are developing ADCs. Two mid-sized companies, ImmunoGen and Seattle Genetics, Inc., are also leaders in this space. Finally, numerous small companies have ongoing efforts in the space.

T-cell engaging bispecifics: Several large pharmaceutics companies, such as Amgen, Novartis, and Roche, have on-going efforts in the space of TCBs. In additional, several mid-sized biotech companies such as Macrogenics and Xencor have ongoing efforts in TCBs. Finally, numerous small companies have ongoing efforts in the space.

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 of 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 therapeutic technology, platform and product candidates. Our patent portfolio as of February 15, 2018 contains 60 issued patents (8 of which are co-owned with a third party) and 233 pending patent applications (13 of which are co-owned with a third party). We have exclusively licensed UCSB’s interest in the co-owned patent family (currently comprising 6 issued patents and 6 pending applications) covering Probody and other pro-protein technology in the fields of therapeutics, in vivo diagnostics and prophylactics.

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- and/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;
- Probody drug conjugates, e.g., CD-166, CD-71 (transferrin receptor), CD49c (integrin alpha 3), and CD147 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;
- Antibodies that bind key targets;
- Antibodies that bind the active site of uPA protease;
- Compositions and methods to discriminate between intact Probody therapeutics and activated versions thereof, as well as other translation assays;

- Methods to produce intact Probody therapeutics; and

- Methods to use any of the above-referenced compounds and compositions.

In addition, we have exclusively licensed a patent portfolio of three patent families from UCSB that includes 22 issued patents and seven pending patent applications that cover compositions and methods related to screening for 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, Europe, Hong Kong, India, Indonesia, Israel, Japan, Malaysia, Mexico, New Zealand, Russia or Eurasian Patent Organization, Singapore, 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 2039, 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 therapeutic 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 therapeutic 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 therapeutic 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 CYTOMX and IHZ marks as well as the CytomX Logo with the USPTO. Both the PROBODY and IHZ marks were allowed by the USPTO in 2016. The PROBODY mark was registered in class 5 by the USPTO in 2017.

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 UCSB, that grants us an exclusive license, with the right to sublicense, under the patent rights owned by UCSB covering mask and screening technologies relating to the identification and discovery of pro-protein biologics, including masks and substrates, for the identification of pro-proteins, for use in the fields of therapeutics, in vivo diagnostics, and prophylactics (the "UCSB Agreement"). The UCSB Agreement also grants us an exclusive license, with the right to sublicense, under UCSB's interest in certain patent rights we co-own with UCSB covering Probody antibodies and other pro-proteins in the fields of therapeutics, in vivo diagnostics and prophylactics.

We had no upfront payment obligations under the agreement. We are obligated to pay to UCSB royalties on net sales of licensed products in the low single digit percentages, subject to annual minimum amounts as well as certain reductions. We are required to make milestone payments to UCSB on the accomplishment of certain milestones totaling up to $1,075 million for each of the first two indications for each licensed product consisting of a molecule or

compound covered by the licensed patent rights. We were also obligated to make a payment to UCSB upon the first occurrence of an IPO or change of control. If the Company sublicenses its rights under the UCSB Agreement, it must pay UCSB a percentage of our total sublicense revenues ranging from the mid-single to mid-teen percentages, which total amount would be first reduced by the aggregate amount of certain research and development related expenses incurred by the Company and other permitted deductions.

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 "Our Collaborations—ImmunoGen PDC Collaboration" 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.

In addition, the orphan drug credit is available for qualifying costs incurred between the date the FDA designates a drug as an orphan drug and the date the FDA approves the drug. The recent tax reform legislation, which was signed into law on December 22, 2017, reduced the amount of the qualified clinical research costs for a designated orphan pro