

BELLICUM PHARMACEUTICALS, INC  
Form 10-K  
March 13, 2018

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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 001-36783

Bellicum Pharmaceuticals, Inc.  
(Exact name of registrant as specified in its charter)

Delaware 20-1450200  
(State or other jurisdiction of incorporation or organization) (I.R.S. Employer Identification No.)

2130 W. Holcombe Blvd., Ste. 800, Houston, TX 77030  
(Address of principal executive offices) (Zip Code)  
(832) 384-1100  
(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, par value \$0.01 per share	The NASDAQ Global Market

Securities registered pursuant to Section 12(g) of the Act: None

Indicate by check mark if the registrant is a well-known seasoned issuer, as defined in Rule 405 of the Securities Act. Yes  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 registrant (1) has filed all reports required to be filed by Section 13 or 15(d) of the Securities Exchange Act of 1934 during the preceding 12 months (or for such shorter period that the registrant was required to file such reports), and (2) has been subject to 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 (§229.405 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 is not contained herein, and will not be contained, to the best of registrant's knowledge, in definitive proxy or information statements

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incorporated by reference in Part III of this Form 10-K or any amendment to this Form 10-K.  x  
Indicate by check mark whether the registrant is a large accelerated filer, an accelerated filer, a non-accelerated filer, or a smaller reporting company. See the definitions of "large accelerated filer," "accelerated filer" and "smaller reporting company" in Rule 12b-2 of the Exchange Act.

Large accelerated filer  " Accelerated filer  x  
Non-accelerated filer  " (Do not check if a smaller reporting company) Smaller reporting company  "  
Emerging growth company  x

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.  x

Indicate by check mark whether the registrant is a shell company (as defined in Rule 12b-2 of the Act). Yes  No  x

The approximate aggregate market value of the voting and non-voting common equity held by non-affiliates of the Registrant, based upon the last sale price of the common stock reported on The NASDAQ Global Market as of June 30, 2017 was \$249,930,906 \*

As of February 28, 2018, there were 33,571,884 shares of the Registrant's common stock, par value \$0.01 per share, outstanding.

**DOCUMENTS INCORPORATED BY REFERENCE**

Portions of the Registrant's definitive Proxy Statement relating to its 2017 Annual Meeting of Stockholders are incorporated by reference into Part III of this Annual Report on Form 10-K. Such Proxy Statement will be filed with the U.S. Securities and Exchange Commission within 120 days following the Registrant's fiscal year ended December 31, 2017.

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\*Excludes 11,795,035 shares of common stock held by directors and officers and by stockholders that the registrant concluded were affiliates of the Registrant as of June 30, 2017. Exclusion of such shares should not be construed to indicate that any such holder possesses the power, direct or indirect, to direct or cause the direction of the management or policies of the Registrant, or that such person is controlled by or under common control with the Registrant.

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SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS

This Annual Report on Form 10-K, including the sections entitled “Business,” “Risk Factors” and “Management’s Discussion and Analysis of Financial Condition and Results of Operations,” may contain “forward-looking statements.” We may, in some cases, use words such as “anticipate,” “believe,” “could,” “estimate,” “expect,” “intend,” “may,” “plan,” “project,” “predict,” “should,” “will,” “would” or the negative of those terms, and similar expressions that convey uncertainty of future events or outcomes to identify these forward-looking statements. Any statements contained herein that are not statements of historical facts may be deemed to be forward-looking statements. Forward-looking statements in this Annual Report include, but are not limited to, statements about:

- the success, cost and timing of our product development activities and clinical trials;
- our ability to advance Chemical Induction of Dimerization, or CID, CID-based technologies, including CaspaCIDE and GoCAR-T;
- our ability to obtain and maintain regulatory approval of BPX-501 and any other product candidates, and any related restrictions, limitations and/or warnings in the label of an approved product candidate;
- our ability to obtain funding for our operations, including funding necessary to complete further development and commercialization of our product candidates;
- the commercialization of our product candidates, if approved;
  - our plans to research, develop and commercialize our product candidates;
- our ability to attract collaborators with development, regulatory and commercialization expertise and the success of any such collaborations;
- future agreements with third parties in connection with the commercialization of our product candidates and any other approved product;
- the size and growth potential of the markets for our product candidates, and our ability to serve those markets;
- the rate and degree of market acceptance of our product candidates;
- regulatory developments in the United States, or U.S., and foreign countries;
- our ability to contract with third-party suppliers and manufacturers and their ability to perform adequately;
- the success of competing therapies that are or may become available;
- our ability to attract and retain key scientific or management personnel;
- our ability to grow our organization and increase the size of our facilities to meet our anticipated growth;
- the accuracy of our estimates regarding expenses, future revenue, capital requirements and needs for additional financing;
- our expectations regarding the period during which we qualify as an emerging growth company under the Jumpstart Our Business Startups Act of 2012, or the JOBS Act;
- our use of cash and other resources; and
- our expectations regarding our ability to obtain and maintain intellectual property protection for our product candidates.

These forward-looking statements reflect our management’s beliefs and views with respect to future events and are based on estimates and assumptions as of the filing date of this Annual Report and are subject to risks and uncertainties. We discuss many of these risks in greater detail under the heading “Risk Factors.” Moreover, we operate in a very competitive and rapidly changing environment. New risks emerge from time to time. It is not possible for our management to predict all risks, nor can we assess the impact of all factors on our business or the extent to which any factor, or combination of factors, may cause actual results to differ materially from those contained in any forward-looking statements we may make. Given these uncertainties, you should not place undue reliance on these forward-looking statements.

You should carefully read this Annual Report and the documents that we reference in this Annual Report completely and with the understanding that our actual future results may be materially different from what we expect. We qualify all of the forward-looking statements in this Annual Report by these cautionary statements.

Except as required by law, we undertake no obligation to update these forward-looking statements publicly, or to update the reasons that actual results could differ materially from those anticipated in any forward-looking statements, whether as a result of new information, future events or otherwise.

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### ITEM 1. Business

#### Overview

We are a clinical stage biopharmaceutical company focused on discovering and developing novel cellular immunotherapies for various forms of cancer, including both hematological cancers and solid tumors, as well as orphan inherited blood disorders. We are using our proprietary Chemical Induction of Dimerization, or CID, technology platform to engineer our product candidates with switch technologies that are designed to control components of the immune system in real time. By incorporating our CID platform, our product candidates may offer better safety and efficacy outcomes than are seen with current cellular immunotherapies.

We are developing next-generation product candidates in some of the most important areas of cellular immunotherapy, including chimeric antigen receptor T cell therapy, or CAR T, T cell receptors, or TCRs and hematopoietic stem cell transplantation, or HSCT. CAR T and TCR cell therapies are an innovative approach in which a patient's T cells are genetically modified to carry chimeric antigen receptors, or CARs, or TCRs which redirect the T cells against cancer cells. While high objective response rates have been reported in some hematological malignancies, serious and sometimes fatal toxicities have arisen in patients treated with CAR T cell therapies. These toxicities include instances in which the CAR T cells have caused high levels of cytokines due to over-activation, referred to as "cytokine release syndrome," or CRS, neurologic toxicities and cases in which they have attacked healthy organs. In each case, these toxicities have sometimes resulted in death. In solid tumors, where the behavior of CAR T cells is particularly unpredictable and results have been inconsistent, researchers are developing enhanced CAR T cell approaches that raise even greater safety concerns. HSCT, also known as bone marrow transplantation, has for decades been curative for many patients with hematological cancers or orphan inherited blood disorders. However, adoption of HSCT to date has been limited by the risks of transplant-related morbidity and mortality from graft-versus-host-disease, or GvHD, and the potential for serious infections due to the lack of an effective immune system following a transplant.

Our proprietary CID platform is designed to address these challenges. Events inside a cell are controlled by cascades of specialized signaling proteins. CID consists of molecular switches, modified forms of these signaling proteins, which are triggered inside the patient by infusion of a small molecule, rimiducid, instead of by natural upstream signals. We include these molecular switches in the appropriate immune cells and deliver the cells to the patient in the manner of conventional cellular immunotherapy. We have developed two such switches: a "safety switch," designed to initiate programmed cell death, or apoptosis, of the immunotherapy cells, and an "activation switch," designed to stimulate activation and in some cases proliferation and/or persistence of the immunotherapy cells. Each of our product candidates incorporates one of these switches, for enhanced, real time control of safety and efficacy:

CaspaCIDE (also known as inducible Caspase-9, or iC9) is our safety switch, incorporated into our HSCT and TCR product candidates, and into academic CAR T collaborations, where it is inactive unless the patient experiences a serious side effect. In that event, rimiducid is administered to induce Caspase-9 and eliminate a majority of the cells, with the goal of attenuating the therapy and resolving the serious side effect.

Our activation switch incorporated into our GoCAR-T product candidates (also known as inducible MyD88/CD40, or iMC), is designed to enable control of the activation and proliferation of the T cells through the scheduled administration of a course of rimiducid infusions that may continue until the desired patient outcome is achieved. In the event of emergence of side effects, the level of activation of the GoCAR-T cells is designed to be attenuated by extending the interval between rimiducid doses, reducing the dosage per infusion, or suspending further rimiducid administration.

In addition, we have an active research effort to develop other advanced molecular switch approaches, including a "dual-switch" that is designed to provide a user-controlled system for managing proliferation and/or persistence and

safety of tumor antigen-specific CAR T cells.

By incorporating our novel switch technologies, we are developing product candidates with the potential to elicit positive clinical outcomes and ultimately change the treatment paradigm in various areas of cellular immunotherapy. Our clinical product candidates are described below.

BPX-501 is a CaspaCIDE product candidate designed as an adjunct T cell therapy administered after allogeneic HSCT. BPX-501 is designed to improve transplant outcomes by enhancing the recovery of the immune system following an HSCT procedure. BPX-501 addresses the risk of infusing donor T cells by enabling the elimination of donor T cells through the activation of the CaspaCIDE safety switch if there is an emergence of uncontrolled GvHD.

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The European Commission has granted orphan drug designations to BPX-501 for treatment in HSCT, and for activator agent rimiducid for the treatment of GvHD. Additionally, BPX-501 and rimiducid have received orphan drug status from the U.S. Food and Drug Administration, or the FDA, as a combination replacement T-cell therapy for the treatment of immunodeficiency and GvHD after allogeneic HSCT.

Based on interactions with European Medicines Agency, or the EMA, we believe that data from the European arm of our BP-004 trial could form the basis of MAAs for BPX-501 and rimiducid for pediatric patients with certain orphan inherited blood disorders or treatment-refractory hematological cancers. In addition, the EMA's Committee for Medicinal Products for Human Use, or the CHMP, has agreed that review and approval under "exceptional circumstances" may be suitable, recognizing that a randomized trial may not be feasible in the pediatric haploidentical hematopoietic stem cell transplant setting. In place of a randomized trial, we are collecting data from a concurrent observational study in the pediatric matched unrelated donor hematopoietic stem cell transplant setting, which will include both retrospective patients and prospective patients. We expect to report updated results from the European BP-004 clinical trial in the fourth quarter of 2018 and to file MAAs for European marketing approvals in 2019.

We are currently planning additional clinical trials for BPX-501. In the adult malignant patient setting, we are designing a randomized, controlled trial in adults with acute myeloid leukemia, and potentially other hematological cancers, to compare outcomes in patients receiving a haplo-transplant with and without BPX-501. For the U.S. pediatric patient setting, we are designing a clinical trial, that we believe could be registrational, to evaluate BPX-501 in a distinct orphan disease population. We expect to initiate both of these clinical trials in the second half of 2018.

BPX-601 is a GoCAR-T product candidate containing our proprietary inducible MyD88/CD40, or iMC, activation switch, designed to treat solid tumors expressing prostate stem cell antigen, or PSCA. Preclinical data shows enhanced T cell proliferation, persistence and in vivo anti-tumor activity compared to traditional CAR T therapies. A Phase 1 clinical trial in patients with non-resectable pancreatic cancer is ongoing and we expect to report initial data from this clinical trial in the second half of 2018. In addition to pancreatic cancer, PSCA is expressed in several other solid tumor indications, including: gastric, esophageal, cholangiocarcinoma, glioblastoma, prostate and bladder cancers. In 2018 we are planning to expand the clinical development of BPX-601 to include additional PSCA expressing cancer types.

BPX-701 is a CaspaCIDE-enabled natural high affinity TCR product candidate designed to target malignant cells expressing the preferentially-expressed antigen in melanoma, or PRAME. The ongoing Phase 1 clinical trial for BPX-701 is in adult patients with refractory or relapsed acute myeloid leukemia, or AML, and myelodysplastic syndromes, or MDS. We expect to report initial data from this clinical trial in the second half of 2018.

CD19 CAR T Program - We are working with academic collaborators to establish clinical proof of concept for CaspaCIDE® in the CD19-expressing B cell malignancies setting. We believe that this strategy allows a cost-effective approach for clinical evaluation of CaspaCIDE in attenuating the acute toxicities of CD19-targeted therapies. As part of this strategy, in November 2016 we announced an expanded collaboration with Ospedale Pediatrico Bambino Gesù, or OPBG, a leading European pediatric research center and hospital. Clinical development of a CaspaCIDE-enabled CD19 CAR T cell therapy is ongoing at OPBG.

We have developed efficient and scalable processes to manufacture genetically modified T cells of high quality, which are currently being used to produce BPX-501, BPX-601 and BPX-701 for our clinical trials. We are leveraging this know how in combination with our proprietary cellular control technologies, resources, capabilities and expertise for the manufacture of CAR T and TCR product candidates to create and develop first and best-in-class product candidates.



We have established in-house cell manufacturing and vector production capabilities at our headquarters facility in Houston, Texas. In the first quarter of 2017, the initial phase of the build-out was completed and we began manufacturing clinical trial material from this site. We completed the facility build-out in early 2018, and we expect that our facilities will meet our U.S. clinical trial and early commercialization requirements. For the European market, we plan to continue working with established contract manufacturers, with our U.S. manufacturing facility as a potential backup supply source.

#### Pipeline

The following table summarizes our product candidate pipeline:

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Cellular Immunotherapy

Cellular immunotherapy harnesses a patient's own immune cells to attack and eliminate harmful diseased cells in the body. The immune system is the body's defense network. It consists of a number of cells (leukocyte) and organs that, working together, recognize and respond to threats in the form of pathogens-modified or transformed cells. T cells are a type of white blood cell that recognize pathogens and can target and eliminate them upon full activation through the addition of appropriate co-stimulatory signals.

The following therapeutic applications of cellular immunotherapy have been primary areas of research and development by research institutes and biopharmaceutical companies, given their promise of effectively treating patients suffering from severe and life-threatening diseases.

Genetically Modified T-cell Therapy (CAR T and TCR). This approach entails collecting a patient's T cells, genetically modifying them *ex vivo*, or outside of the body, to incorporate specific receptors which target cancer cells and then re-infusing the modified T cells back into the patient. Two types of cancer-specific receptors are typically used, CARs that recognize whole antigens on the surface of cancer cells, and TCRs that bind to cancer-associated peptides, or fragments of proteins, from either inside or on the surface of the cancer cells. In early human clinical trials, CAR T cell therapy has demonstrated an unprecedented ability to achieve durable complete responses in some leukemias and lymphomas, even in patients who have suffered multiple relapses.

HSCT. HSCT is the transplantation of stem cells and other immune cells derived from bone marrow, peripheral blood or umbilical cord blood. The transplantation may be autologous, using the patient's own cells, or allogeneic, using a donor's cells. HSCT is often the only curative option for a wide range of treatment-refractory hematological cancers, such as chronic myeloid leukemia. HSCT is also used as a high-risk treatment for orphan inherited blood disorders, such as sickle cell disease, beta-thalassemia and certain immune disorders.

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Limitations of Current Cellular Immunotherapy Approaches.

Despite rapid advances in various approaches to cellular immunotherapy and the biopharmaceutical industry’s considerable investment in research and development, certain challenges have prevented these therapies from realizing their maximum potential. Some of these obstacles and issues are highlighted below:

Cellular

Immunotherapy Approach	Safety Challenges	Efficacy Challenges
CAR T	<p>Serious immune toxicity (CRS) or neurotoxicity and chance for on target/off tumor autoimmune responses</p> <p>Standard-of-care corticosteroids and/or cytokine receptor antagonists, such as tocilizumab, can be ineffective; requirement for hospitalization and intensive care management; relapse of underlying disease; infections; death</p> <p>Other safety approaches* have slow onset of action or have safety issues of their own</p>	<p>CARs have not demonstrated the same high response rates to solid tumor antigens as had been seen against CD19-positive or BCMA-positive hematological malignancies</p> <p>Small number of validated tumor-specific antigens that can be targeted</p>
TCR	<p>High risk of off-target or off-tumor toxicities, especially if affinity is enhanced</p>	<p>MHC-restricted to a subset of patient’s human clinical data still early</p> <p>Attempts to control GvHD (steroids, T Cell depletion, etc.) increase likelihood of non-engraftment, relapse of underlying disease and/or viral infection</p>
Allogeneic HSCT	<p>GvHD and viral infections are frequent and are potentially fatal side effects</p>	

\* See discussion of other approaches below under "Our Proprietary Switch Technologies - CaspaCIDE"

Our Proprietary CID Technology Platform

Our proprietary CID technology platform is designed to address the challenges of current cellular immunotherapies. Cellular activities and functions, such as growth, activation, proliferation and cell death, are controlled by cascades of specialized signaling proteins. Our CID platform consists of molecular switches, modified forms of these signaling proteins, which are triggered inside the patient by infusion of a small molecule, rimiducid, instead of by natural upstream signals. Our current product candidates are based on either a “safety switch,” or an “activation switch.” After rimiducid is administered, the “safety switch” is designed to lead to apoptosis, and the “activation switch” is designed to lead to proliferation and/or activation and/or persistence of immune cells.

We incorporate the molecular switches in the appropriate immune cells and administer them to the patient. After the modified immune cells are inside the patient’s body, specific functions of these cells may be controlled by administering rimiducid by intravenous infusion. Rimiducid has been designed to bind to a specifically designed domain of CID switch proteins. Once introduced, rimiducid couples, or aggregates, CID switch proteins together to create a cluster that triggers the signaling cascade. Aside from its impact on CID-modified immune cells bearing switch proteins, rimiducid has no other known effect on the body.

Our proprietary CID-based product candidates depend on the following signaling molecules to trigger signaling cascades, resulting in different cell activities:

**Caspase-9: Signaling Molecule for Apoptosis.** Caspase-9 is the initiating enzyme in the apoptosis pathway. When activated, the caspase starts a signaling cascade, including the activation of caspase-3, which ultimately leads to apoptosis, a non-inflammatory process of cell elimination.

**IMC: Signaling Molecules for Activation and Proliferation.** Myeloid differentiation primary response gene, or MyD88, is a protein that has functions in cellular responses to stimuli such as stress, cytokines and bacteria or viruses. CD40 is a co-stimulatory protein found on antigen-presenting cells, such as dendritic cells and B cells and is required for their activation. Although the effects of MyD88 and CD40 have been studied previously in dendritic cell therapies,

our novel approach applies them to T cell based immunotherapies.

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## Our Proprietary Switch Technologies

With the CID platform as the foundation, we have created different molecular switch technologies customized for specific cellular immunotherapy approaches and therapeutic indications. The table below summarizes our two most advanced switch technologies.

	CaspaCIDE	GoCAR-T
Cell Type	Donor T cells (HSCT) or patient T cells (TCRs or CAR Ts)	Patient T cells
Proprietary Components	iCaspase-9 safety switch	iMC activation switch
Current Applications	HSCT, TCR and CAR T therapy	CAR T therapy
Potential Benefit	Increases therapeutic window by providing a mechanism to control toxicities through T cell apoptosis	Increases therapeutic window by providing a mechanism to control T cell activation & proliferation
Product Candidates	BPX-501 and BPX-701, CD19 CAR T collaboration	BPX-601

CaspaCIDE is our CID-based safety switch technology designed to eliminate cells in the event of toxicity. The CaspaCIDE switch consists of the CID-binding domain coupled to the signaling domain of Caspase-9, an enzyme that is an integral part of the apoptotic, cell death pathway. Infusion of rimiducid is designed to trigger dimerization and activation of this domain of Caspase-9, which in turn leads to selective apoptosis of the CaspaCIDE-expressing cells. Because CaspaCIDE is designed to be permanently incorporated into our cellular therapies, the safety switch has the potential to be available for use long after the initial therapy is delivered. This technology is applied to our lead clinical product candidate, BPX-501, an adjunct T cell therapy provided after allogeneic HSCT, and to our TCR product candidate, BPX-701.

We believe that CaspaCIDE is the optimal cell therapy safety switch technology described to-date. The only other widely reported clinically validated approach is based on the Herpes Simplex Virus thymidine kinase, or HSV-tk, a non-human immunogenic protein which can incorporate into a dividing cell's DNA, the widely-used anti-viral drug, ganciclovir, leading to cell death. Comparative nonclinical studies have demonstrated CaspaCIDE's potential benefits relative to HSV-tk, including lack of immunogenicity, effectiveness in rescuing animals from toxicities that have progressed, lack of dependence on the cell cycle for cell elimination, and most importantly, speed of elimination. In human trials, CaspaCIDE has demonstrated clinical activity beginning as soon as 30 minutes after administration of the activating drug, rimiducid. Lastly, rimiducid is bio-inert in the absence of cells containing a CID-based switch, and has no other clinical use. In contrast, ganciclovir is used to treat herpes virus family infections, and can have clinical side effects.

Other cell elimination approaches described in the literature include gene modification of cells to express truncated epidermal growth factor receptor (tEGFR) or codon-optimized CD20. Administration of the monoclonal antibodies, cetuximab or rituximab, respectively, is intended to trigger complement--dependent cytotoxicity, or CDC, or antibody-dependent cellular cytotoxicity, or ADCC, mediated cell elimination. While CaspaCIDE eliminates cells via the apoptotic pathway, the body's non-inflammatory mechanism for this important function, we believe a CDC-mediated mechanism may add to complications in patients already in an inflammatory crisis, such as seen with serious CRS, after CAR T cell therapy. Moreover, cetuximab and rituximab, both anti-cancer therapies that can have potentially serious side effects, are unlikely to be usable in a titratable manner. Lastly, these approaches have yet to

demonstrate efficacy in clinical trials.

CaspaCIDE has been evaluated in both preclinical and clinical studies, with additional clinical trials ongoing and planned. In addition to using our CaspaCIDE technology for the substantial elimination of cellular therapy, like an “off” switch, we are studying partial elimination of a cellular therapy, like a “dimmer” switch, by delivering reduced doses of rimiducid. We observed the dose response to rimiducid by measuring the viability of BPX-501 cells in culture following the addition of increasing amounts of rimiducid to the culture medium, as well as by measuring the survival of BPX-501 cells in vivo in immune-deficient mice following injection of increasing doses of rimiducid. In these preclinical studies, rimiducid rapidly and consistently reduced or eliminated CaspaCIDE-containing cells in a dose-dependent manner.

In addition to our internal preclinical and clinical development activities, we have selectively entered into agreements with renowned cancer research centers with expertise in cellular immunotherapy to allow the use of our CaspaCIDE safety switch with the collaborators’ CAR T product candidates. While we are not the sponsor of these clinical trials, we believe that they may facilitate the adoption of CaspaCIDE in the CAR T cell setting and provide opportunities for license arrangements of our technology in the future.

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### GoCAR-T

Our GoCAR-T technology incorporates a switch that activates CAR T cells when triggered by both rimiducid and the targeted antigen expressed on the surface of the cancer cells. Current generation CAR T cell constructs consist of a CD3- domain and one or more co-stimulatory molecules that are both activated when a cancer antigen binds to the portion of the CAR on the surface of the engineered T cell. This reliance on antigen for activation of the CAR T cell results in an unpredictable and inherently uncontrollable therapeutic effect. For example, CAR T cells that target the CD19 receptor have been shown to proliferate in excess of 100,000-fold in some patients, ultimately comprising over 50% of circulating lymphocytes. Solid tumor CAR T cells, on the other hand, often fail to proliferate or persist at all for more than a few days or weeks and have been largely ineffective. In each situation, the physician has no effective way to intervene to achieve greater consistency once the cells have been administered.

Our GoCAR-T technology is designed to change the current paradigm by placing our proprietary co-stimulatory domain MC under

rimiducid control. GoCAR-T cells are designed to only be fully activated when exposed to both the cancer cells and rimiducid. This separation is designed to control the degree of activation of the CAR T cells through adjustments to the schedule of rimiducid administration, but still in a tumor-dependent manner.

In a proof-of-principle in vitro study of our GoCAR-T technology, GoCAR-T cells targeting the PSCA antigen were found to be only fully activated when the GoCAR-T cells were exposed to both their target PSCA-expressing human pancreatic cancer cells and rimiducid. In further in vivo studies of GoCAR-T technology, target antigen PSCA-expressing HPAC human pancreatic tumors, which were established in immune-deficient mice, were eliminated by administration of GoCAR-T cells targeting PSCA along with weekly rimiducid administration. We believe these studies together provide proof-of-principle that GoCAR-T technology may allow rimiducid to modulate the therapeutic effect from initiation of treatment, turning CAR T cell therapy from an uncontrollable, and largely unpredictable class into a more predictable therapy which can be adjusted, like a small molecule, to the patient's therapeutic window to the appropriate level.

### Our Product Candidates

#### BPX-501: Adjunct T Cell Therapy for Allogeneic Hematopoietic Stem Cell Transplantation

BPX-501 is an adjunct T cell therapy administered after allogeneic HSCT using genetically modified donor T cells incorporating our CaspaCIDE safety switch. BPX-501, in combination with rimiducid, has been granted orphan drug designation by the FDA for the treatment of immunodeficiency and GvHD following allogeneic HSCT. We believe that BPX-501 could enable physicians to maximize the benefits of T cell therapy for allogeneic HSCT, such as immune system reconstitution and prevention or treatment of relapse of underlying disease, while mitigating some of the safety issues associated with a stem cell transplant.

The goal of our BPX-501 clinical program is to provide better overall transplant outcomes- faster immune recovery, lower rates of infection and lower rates of disease relapse-than one would generally expect from an alternative allogeneic transplant procedure. We are currently conducting multiple Phase 1/2 clinical trials of BPX-501 in Europe. In November 2014, we initiated BP-004, a Phase 1/2 clinical trial in children with leukemias, lymphomas, or orphan inherited blood disorders, such as severe combined immunodeficiency, Wiskott-Aldrich Syndrome and beta thalassemia, all fatal or chronic life-long disorders for which HSCT is curative. The trial is being conducted in both European and U.S. pediatric transplant centers. The clinical trial is evaluating whether BPX-501 T cells from a haploidentical donor, typically the child's mother or father, administered following an alpha-beta TCR T-depleted and B-cell depleted HSCT, are safe and can enhance immune reconstitution. We have reported initial outcomes from these ongoing clinical trials at several medical meetings.

Additional ongoing clinical studies include the BP-001 and BP-008 clinical trials in adult hematological cancer patients in which BPX-501 is administered after initial allogeneic HSCT. BP-001 is investigating the potential for BPX-501 in adult high-risk malignancies as a T cell addback and BP-008 is investigating the potential for BPX-501 as a donor lymphocyte infusion to address post-HSCT relapse. In addition, we are planning to initiate additional clinical trials in the U.S. and Europe, as part of our strategy to pursue global regulatory approvals and expand the potential addressable patient population for BPX-501.

In July 2016, the intellectual property for BPX-501 was strengthened with a U.S. method of use patent issued to Baylor College of Medicine, or Baylor. The patent, licensed exclusively to us, is scheduled to expire in 2031. During 2016, we discussed with the European Medicines Agency, or the EMA, clinical and regulatory plans to support the filing of Marketing Authorization Applications, or MAAs, for BPX-501 and rimiducid in Europe, initially for pediatric patients with certain orphan inherited blood disorders or treatment-refractory hematological cancers. Based on the regulatory discussions, we believe that data from the European arm of our BP-004 trial, with a primary endpoint of event-free survival (transplant-related mortality, severe GvHD and serious infection) at six months, could form the basis of MAAs for BPX-501 and rimiducid. In addition, the EMA's Committee for Medicinal Products for Human Use, or the CHMP, has agreed that review and approval under "exceptional circumstances" may be suitable, recognizing that a randomized trial may not be feasible in the pediatric haploidentical hematopoietic stem cell transplant setting. Exceptional circumstances may be granted for medicines that treat very rare diseases, or where controlled



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studies are impractical or not consistent with accepted principles of medical ethics. In place of a randomized trial, we are collecting data from a concurrent observational study in the pediatric matched unrelated donor hematopoietic stem cell transplant setting, which will include both retrospective patients and prospective patients.

We are currently planning additional clinical trials for BPX-501. In the adult malignant patient setting, we are designing a randomized, controlled trial in adults with acute myeloid leukemia, and potentially other hematological cancers, to compare outcomes in patients receiving a haplo-transplant with and without BPX-501. For the U.S. pediatric patient setting, we are designing a clinical trial, that we believe could be registrational, to evaluate BPX-501 in a distinct orphan disease population. We expect to initiate both of these clinical trials in the second half of 2018.

### BPX-601: GoCAR-T Product Candidate for Solid Tumors

We are developing BPX-601, a GoCAR-T product candidate containing Bellicum's proprietary iMC activation switch, for the treatment of solid tumors expressing PSCA. PSCA is a cancer antigen expressed in several solid tumor indications, including: gastric, esophageal, cholangiocarcinoma, glioblastoma, prostate, pancreatic and bladder cancers. Preclinical data shows enhanced T-cell proliferation, persistence and in vivo anti-tumor activity compared to traditional CAR T therapies.

A Phase 1 clinical trial in patients with non-resectable pancreatic cancer is ongoing and we expect to report initial data from this clinical trial in the second half of 2018. In addition to pancreatic cancer, we are planning to expand the clinical development of BPX-601 to include additional cancer types.

### BPX-701: CaspaCIDE TCR Product Candidate for Solid Tumors

We are developing BPX-701, a TCR-based therapy that incorporates our CaspaCIDE technology, in collaboration with Leiden University Medical Center, or Leiden. BPX-701 is designed to target malignant cells expressing PRAME. As initially reported in Clinical Cancer Research in 2011, PRAME-specific clones showed high reactivity against a panel of PRAME positive tumor cell lines, metastatic melanoma, sarcomas and neuroblastoma tissues, and no reactivity against normal cell types, with the exception of low reactivity against kidney epithelial cells and intermediate reactivity against mature dendritic cells. Based on in vitro studies, BPX-701 has demonstrated strong affinity to panels of cancer cells presenting PRAME peptides and low affinity to non-tumor cells. In other in vitro studies, BPX-701 cells containing the CaspaCIDE safety switch, have demonstrated complete elimination in response to the administration of rimiducid.

BPX-701 is a CaspaCIDE-enabled natural high affinity TCR product candidate designed to target malignant cells expressing the preferentially-expressed antigen in melanoma, or PRAME. The ongoing Phase 1 clinical trial for BPX-701 is in adult patients with refractory or relapsed AML, and myelodysplastic syndromes, or MDS. We expect to report initial data from this clinical trial in the second half of 2018.

### CD19 CAR T Program

We are working with academic collaborators to establish clinical proof of concept for CaspaCIDE in the CD19 setting. We believe that this strategy allows a cost-effective approach for clinical evaluation of CaspaCIDE in attenuating the acute toxicities of CD19-targeted therapies. As part of this strategy, in November 2016 we announced an expanded collaboration with OPBG, a leading European pediatric research center and hospital. Clinical development of a CaspaCIDE-enabled CD19 CAR T cell therapy is ongoing at OPBG.

### Manufacturing, Processing and Delivering to Patients

We have developed efficient and scalable processes to manufacture genetically modified T cells of high quality. We historically have worked with third-party contract manufacturers in both Europe and the U.S. to produce BPX-501, BPX-601 and BPX-701 for our clinical trials. In the first quarter of 2017, we completed the initial phase of the build-out of our in-house cell manufacturing and vector production capabilities in 30,400 square feet of leased space at our headquarters in Houston, Texas. This site was designed and constructed to satisfy both U.S. and European regulatory requirements. We began manufacturing clinical trial material from this site beginning in the first quarter of 2017 and completed the build-out of this facility in early 2018 and expect that it will meet our U.S. clinical trial and early commercialization requirements. For the European market, we plan to continue working with established contract manufacturers, with our U.S. manufacturing facility being available as a potential back-up site. We are leveraging the processes we have developed for BPX-501, BPX-601 and BPX-701 in combination with our proprietary cellular control technologies, resources, capabilities and expertise for the manufacture of CAR T and TCR

product candidates to create and develop first and best-in-class product candidates.

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Our product candidates require a combination of three critical components: (1) viral vectors with DNA content encoded for our proprietary switch proteins and co-stimulatory and other accessory molecules, (2) patient-specific donor T cells that are genetically modified by our viral vectors, and (3) the synthetic small molecule rimiducid, which activates the switch proteins. Each of these components requires a separate supply chain and shares the same regulatory requirements applicable for biological or chemical materials suitable for human use. Details on each of these components are described below:

**Viral Vectors.** We use a retrovirus to transduce our T cell based product candidates. We believe that the retrovirus is optimal for T cell transduction given that it is an integrating vector that induces long-term gene expression, exhibits high transduction efficiency, has sufficient capacity for DNA content, and has been safely used in clinical trials. We have recently completed facilities to enable in-house vector production, but to date have been reliant upon multiple third-party suppliers that operate under good manufacturing practices, or GMPs, procedures and requirements.

**Genetically Modified T Cells.** We have completed the build-out of our facility in Houston, Texas to allow in-house manufacturing for the planned U.S. clinical and early commercial requirements for BPX-501, and the clinical supply needs of our other product candidates. We also have agreements with reputable contract manufacturing organizations, or CMOs, as a primary source in Europe, and as an alternate source in the U.S., for processing and manufacturing our genetically modified T cells. We have designed and refined a proprietary process for cell engineering that has been improved from lab-based open procedures used in academic and research settings to a functionally closed system that is more appropriate for large-scale clinical trials and commercialization. Our systems are designed to be compliant with current guidelines and regulations for cell-based manufacturing in the U.S. and Europe and have been successfully transferred and implemented by our CMOs.

**Rimiducid.** Rimiducid is a synthetic small molecule which has been rationally designed to trigger the proprietary switch proteins in our CID platform. We have separate third-party manufacturers for the active pharmaceutical ingredient, or API, and the finished drug product. Manufacturers of both the API and finished drug product are licensed to manufacture a variety of marketed drugs worldwide and have been selected based on their ability to provide supplies for our clinical trials and future commercialization.

We are focused on continuously refining our overall cell therapy process, manufacturing, processing and delivery to patients to be more efficient. Our current process cycles for our product candidates, from collection of white blood cells to infusion of the final product, can be completed in as little as two weeks and are customized to be complementary to the treatment procedure of interest in order to prevent delays or complications.

### Intellectual Property

We seek to protect proprietary technology, inventions, and improvements that are commercially important to our business by seeking, maintaining, and defending patent rights, whether developed internally or licensed from third parties. We also seek to rely on regulatory protection afforded through orphan drug designations, data exclusivity, market exclusivity and patent term extensions where available as well as contractual agreements with our academic and commercial partners.

To achieve this objective, a strategic focus for us has been to identify and license key patents and patent applications that serve to enhance our intellectual property and technology position. Our intellectual property estate includes: (1) claims directed to core CID technologies and components used in our products; (2) claims directed to methods of treatment for therapeutic indications; (3) claims directed to specific products; and (4) claims directed to innovative methods for generating new constructs for genetically engineering T cells. We believe our patent estate, together with our efforts to develop and patent next generation technologies, provides us with a substantial intellectual property position. However, the area of patent and other intellectual property rights in biotechnology is an evolving one with many risks and uncertainties.

For example, we are aware of third party patents having claims that may be considered as being directed to single-chain antibody fragments that bind to PSCA and these patents may be considered relevant to BPX-601 technologies we are developing. We currently are evaluating whether or not we need to obtain rights to these patents under a license, and if it is determined that we need to obtain such rights, whether these rights can be obtained. Please refer to the section entitled "Item 1A. Risk Factors-Risks Related to Our Intellectual Property" herein for associated risks.

To our knowledge, our patent estate, on a worldwide basis, includes 156 issued patents, 38 of which are in the U.S., and 60 pending patent applications, 17 of which are in the U.S., which we own or for which we have an exclusive, either in its entirety or within our field of use, commercial license as of February 28, 2018.

We have internally developed technology disclosed in two pending utility patent applications in the U.S. and 13 pending foreign patent applications which relates to our GoCAR-T technology. If U.S. patents issue from the U.S. applications, the estimated expiration date of the last to expire patent is in 2035. If patents are issued in foreign jurisdictions, the anticipated expiration dates will be in 2035.

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Pursuant to our licenses from Baylor, we have exclusive commercial rights to nine issued U.S. patents expiring in 2024 or later, four pending U.S. utility patent applications, nine issued foreign patents expiring in 2024 or later and 11 pending patent applications in foreign jurisdictions that relate to our GoCAR-T, BPX-501 and certain of our other technologies. If U.S. patents issue from the currently pending U.S. patent applications, the estimated expiration date of the last to expire patent is 2031. If patents from the currently pending patent applications are issued in foreign jurisdictions, the estimated expiration dates range from 2024 to 2029.

Pursuant to our license agreement with ARIAD Pharmaceuticals, Inc., or ARIAD, as amended, we have exclusive commercial rights within our field of use to 22 patents, seven in the U.S. and 15 in foreign jurisdictions, which relate to dimerizer technology. The estimated expiration date of the last to expire U.S. patent is 2032. The estimated expiration date of the last to expire foreign patent is 2032.

The provisional and pending patent applications and issued patents in the patent estate include composition of matter and method of use claims.

Composition of matter patent coverage on rimiducid, the dimerization molecule AP1903, has expired. However, we believe that additional barriers to entry exist for a competitor attempting to use rimiducid. This is significant because, if true, then potential competitors will not be able to use the abbreviated new drug application pathway for approval of rimiducid. With respect to our investigational products, the FDA has assigned combination product status to BPX-501, and we plan to submit a biologic license application, or BLA, for the combination product. We believe that this will be the case for each future product candidate of ours that incorporates rimiducid. If our investigational products incorporating rimiducid receive FDA approval through BLAs, then the FDA would not approve any biosimilar of these combination products until at least 12 years from the date that we receive FDA approval.

Additionally, although ‘biosimilar’ provisions exist for products approved through BLAs, it is not clear if the FDA will permit the biosimilar route to be used for complex biological products such as our investigational products.

Rimiducid is a relatively complex drug substance to manufacture. We have substantial experience in manufacturing rimiducid and in preparing it for patient infusion. Our manufacturing know-how is a valuable asset and we incorporate contractual confidentiality terms in all agreements with our third-party manufacturers. We believe that a competitor will face substantial obstacles with respect to time and cost in order to derive a clinically acceptable manufacturing process.

Our strategy is also to develop and obtain additional intellectual property covering manufacturing processes and methods for genetically engineering T cells expressing new constructs. To support this effort, we have established expertise and development capabilities focused in the areas of preclinical research and development, manufacturing and manufacturing process scale-up, quality control, quality assurance, product delivery and storage, regulatory affairs and clinical trial design and implementation. As appropriate, we expect to file additional patent applications to expand this layer of our intellectual property estate.

The term of individual patents depends upon the legal term of the patents in the countries in which they are obtained. In most countries in which we file, the patent term is 20 years from the date of filing of the first non-provisional application to which priority is claimed. In the U.S., a patent’s term may be lengthened by patent term adjustment, which compensates a patentee for administrative delays by the U.S. Patent and Trademark Office, or the USPTO, in granting a patent, or may be shortened if a patent is terminally disclaimed over an earlier-filed patent. The term of a patent that covers an FDA-approved drug or biologic may also be eligible for a patent term restoration of up to five years under the Hatch-Waxman Act, which is designed to compensate for the patent term lost during the FDA regulatory review process. The length of the patent term restoration is calculated based on the length of time the drug or biologic is under regulatory review. A patent term restoration under the Hatch-Waxman Act 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 or biologic may be restored. Moreover, a patent can only be restored once, and thus, if a single patent is applicable to multiple products, it can only be extended based on one product. Similar provisions are available in Europe and certain other foreign jurisdictions to extend the term of a patent that covers an approved drug or biologic. When possible, depending upon the length of clinical trials and other factors involved in the filing of a BLA we expect to apply for patent term extensions for patents covering our product candidates and their methods of use.

We may rely, in some circumstances, on trade secrets to protect our technology. We seek to protect our proprietary technology and processes, in part, by entering into confidentiality agreements with our employees, consultants, scientific advisors and contractors. We also seek to preserve the integrity and confidentiality of our data and trade secrets by maintaining physical security of our premises and physical and electronic security of our information technology systems. While 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. In addition, our trade secrets may otherwise become known or be independently discovered by competitors. To the extent that our consultants, contractors or collaborators 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.

Our Collaboration and License Agreements

Co-Development and Co-Commercialization Agreement - Adaptimmune

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In December 2016, we and Adaptimmune Therapeutics plc, or Adaptimmune entered into a Co-Development and Co-Commercialization Agreement, or the Adaptimmune Agreement, in order to facilitate a staged collaboration to evaluate, develop and commercialize next generation T cell therapies.

Under the Adaptimmune Agreement, the parties agreed to evaluate our GoTCR technology, iMC co-stimulation, with Adaptimmune's affinity-optimized SPEAR® T cells for the potential to create enhanced TCR product candidates. Depending on results of the preclinical proof-of-concept phase, the parties expect to progress to a two-target co-development and co-commercialization phase. To the extent necessary, and in furtherance of the parties' proof-of-concept and co-development efforts, the parties granted each other a royalty-free, non-transferable, non-exclusive license covering their respective technologies for purposes of facilitating such proof-of-concept and co-development efforts. In addition, as to covered therapies developed under the Adaptimmune Agreement, the parties granted each other a reciprocal exclusive license for the commercialization of such therapies.

With respect to any joint commercialization of a covered therapy, the parties agreed to negotiate in good faith the commercially reasonable terms of a co-commercialization agreement. The parties also agreed that any such agreement shall provide for, among other things, equal sharing of the costs of any such joint commercialization and the calculation of profit shares as set forth in the Adaptimmune Agreement.

The Adaptimmune Agreement will expire on a country-by-country basis once the parties cease commercialization of the T cell therapies covered by the Adaptimmune Agreement, unless earlier terminated by either party for material breach, non-performance or cessation of development, bankruptcy/insolvency, or failure to progress to co-development phase.

**Collaboration Agreement - OPBG**

In October 2016, we entered into a collaboration agreement with OPBG, or the OPBG Agreement, pursuant to which we and OPBG agreed to collaborate on research projects and early stage clinical trials for the design and development of various T cell immunotherapies, or the OPBG Research.

As consideration for OPBG's performance of the OPBG Research and grant of certain licenses to us, we agreed to fund an aggregate of up to \$4.4 million in project costs payable to OPBG or certain third-party service providers, as applicable, over the term of the OPBG Research, estimated to be four years. With respect to any inventions arising from the OPBG Research, OPBG agreed to grant us an exclusive license to any such inventions, the terms of which would be set forth in a separate agreement. In addition, OPBG granted us paid-up, worldwide co-exclusive licenses for non-commercial development of OPBG's CD19 and CAR.GD2 CAR T technologies, as well as paid-up, worldwide exclusive licenses to commercialize OPBG's CD19 and CAR.GD2 CAR T technologies, each to be governed by a separate agreement.

The initial term of the OPBG Agreement expired on June 30, 2017, and we are in the process of negotiating for a potential extension.

**Collaboration Agreement - Leiden**

In May 2016, we and Academisch Ziekenhuis Leiden, also acting under the name Leiden University Medical Centre, or Leiden, entered into a research collaboration agreement, or the Leiden Agreement, pursuant to which we will provide Leiden with financial support for research to discover and validate high-affinity TCR product candidates targeting several cancer-associated antigens, or the Research.

As consideration for Leiden's performance of the Research, we agreed to pay Leiden an aggregate of EUR 2.5 million in quarterly installments during the three-year term of the Research. With respect to any inventions arising from the Research that are relevant to or useful for any high affinity TCR that is studied in the Research, Leiden granted us an exclusive option to obtain an exclusive, worldwide license to practice and exploit such inventions. The parties agreed to negotiate in good faith the commercially reasonable terms of each such license agreement entered into between the parties, based on terms similar to those set forth in the previously executed license agreement between the parties and those specified in the Leiden Agreement.

The Research will be conducted during a three-year term, after which the Leiden Agreement will expire. We and Leiden have agreed to negotiate in good faith a potential extension of such term, dependent on Leiden's progress in the performance of the Research. Either party may terminate the Leiden Agreement upon a material breach by the other

party that remains uncured following 30 days after the date of written notice of such breach. Leiden may terminate the Leiden Agreement in the event of a failure by us to pay any amounts due under the Leiden Agreement that remains uncured on the date that is 30 days after written notice of such failure.

License Agreement - Agensys

In December 2015, we and Agensys entered into a license agreement, or the Agensys Agreement, pursuant to which (i) Agensys granted us, within the field of cell and gene therapy of diseases in humans, an exclusive, worldwide license and sublicense to its patent rights directed to PSCA and related antibodies, and (ii) we granted Agensys a non-exclusive, fully paid license to our patents directed



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to inventions that were made by us in the course of developing our licensed products, solely for use with Agensys therapeutic products containing a soluble antibody that binds to PSCA or, to the extent not based upon our other proprietary technology, to non-therapeutic applications of antibodies not used within the field.

As consideration for the rights granted to us under the Agensys Agreement, we agreed to pay to Agensys a non-refundable upfront fee of \$3.0 million. We are also required to make aggregate milestone payments to Agensys of up to (i) \$5.0 million upon the first achievement of certain specified clinical milestones for its licensed products, (ii) \$50.0 million upon the achievement of certain specified clinical milestones for each licensed product, and (iii) \$75.0 million upon the achievement of certain sales milestones for each licensed product. The Agensys Agreement additionally provides that we will pay to Agensys a royalty percentage that ranges from the mid to high single digits based on the level of annual net sales of licensed products by us, our affiliates or permitted sublicensees. The royalty payments are subject to reduction under specified circumstances.

Under the Agensys Agreement, Agensys also was granted the option to obtain an exclusive license, on a product-by-product basis, from us to commercialize in Japan each licensed product developed under the Agensys Agreement that has completed a phase 2 clinical trial. As to each such licensed product, if Agensys or its affiliate, Astellas Pharma, Inc., exercises the option, the Agensys Agreement provides that we will be paid an option exercise fee of \$5.0 million. In addition, the Agensys Agreement provides that we will be paid a royalty that ranges from the mid to high single digits based on the level of annual net sales in Japan of each such licensed product. If the option is exercised, the aggregate milestone payments payable by us to Agensys, described above with respect to each licensed product, would be reduced by up to an aggregate of \$65.0 million upon the achievement of certain specified clinical and sales milestones.

The Agensys Agreement will terminate upon the expiration of the last royalty term for the products covered by the Agensys Agreement, which is the earlier of (i) the date of expiration or abandonment of the last valid claim within the licensed patent rights covering any licensed products under the Agensys Agreement, (ii) the expiration of regulatory exclusivity as to a licensed product, and (iii) 10 years after the first commercial sale of a licensed product. Either party may terminate the Agensys Agreement upon a material breach by the other party that remains uncured following 60 days after the date of written notice of such breach (or 30 days if such material breach is related to failure to make payment of amounts due under the Agensys Agreement) or upon certain insolvency events. In addition, Agensys may terminate the Agensys Agreement immediately upon written notice to us if we or any of our affiliates or permitted sublicensees commence an interference proceeding or challenge the validity or enforceability of any of Agensys' patent rights.

License Agreement - BioVec

In June 2015, we and BioVec Pharma, Inc., or BioVec, entered into a license agreement, or the BioVec Agreement, pursuant to which BioVec agreed to supply us with certain proprietary cell lines and granted us a non-exclusive, worldwide license to certain of its patent rights and related know-how related to such proprietary cell lines.

As consideration for the products supplied and rights granted to us under the BioVec Agreement, we agreed to pay to BioVec an upfront fee of \$100,000 within ten business days of the effective date of the BioVec Agreement and a fee of \$300,000 within ten business days of its receipt of the first release of GMP lot of the products licensed under the BioVec Agreement. In addition, we agreed to pay to BioVec an annual fee of \$150,000, commencing 30 days following the first filing of an IND, or its foreign equivalent, for a product covered by the license; with such annual fees being creditable against any royalties payable by us to BioVec under the BioVec Agreement. We also are required to make a \$250,000 milestone payment to BioVec for each of the first three licensed products to enter into a clinical phase trial and one-time milestone payments of \$2.0 million upon receipt of a registration granted by the FDA or EMA on each of our first three licensed products. The BioVec Agreement additionally provides that we will pay to BioVec a royalty in the low single digits on net sales of products covered by the BioVec Agreement. We may also grant sublicenses under the licensed patent rights and know-how to third parties for limited purposes related to the use, sale and other exploitation of the products licensed under the BioVec Agreement. The BioVec Agreement will continue until terminated. The BioVec Agreement may be terminated by us, in our sole discretion, at any time upon 90 days written notice to BioVec. Either party may terminate the BioVec Agreement in the event of a breach by the other party of any material provision of the BioVec Agreement that remains uncured on the date that is 60 days after

written notice of such failure or upon certain insolvency events that remain uncured following the date that is 30 days after the date of written notice to a party regarding such insolvency event.

License Agreement - Leiden

In April 2015, we and Leiden, entered into a license agreement, or the 2015 Leiden Agreement, pursuant to which Leiden granted to us an exclusive, worldwide license to its patent rights covering high affinity T-cell receptors targeting PRAME, and POU2AF1 epitopes. The license granted under the 2015 Leiden Agreement is subject to certain restrictions and to Leiden's retained right to use the licensed patents solely for academic research and teaching purposes, including research collaborations by Leiden with academic, non-profit research third parties; provided that Leiden provides 30 days advance written notice to us of such academic research collaborations.

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As consideration for the rights granted to us under the 2015 Leiden Agreement, we agreed to pay to Leiden an aggregate of EUR 75,000 in upfront fees within 30 days of the effective date of the 2015 Leiden Agreement. In addition, we agreed to pay to Leiden, beginning on the eighth anniversary of the effective date of the 2015 Leiden Agreement, annual minimum royalty payments of EUR 30,000. We are also required to make milestone payments to Leiden of up to an aggregate of EUR 1,025,000 for each of the first licensed product that is specific to PRAME and to POU2AF1. The 2015 Leiden Agreement additionally provides that we will pay to Leiden a royalty in the low single digits on net sales of products covered by the 2015 Leiden Agreement. If we enter into a sublicensing agreement with a third party related to a product covered by the Leiden Agreement, we have agreed to pay Leiden a percentage ranging in the low double digits on all non-royalty income received from sublicensing revenue directly attributable to the sublicense, dependent on whether we are in phase 1/2, phase 2 or phase 3 at the time that we enter into any such sublicensing agreement.

Under the 2015 Leiden Agreement, we and Leiden entered into a sponsored research agreement, pursuant to which we are required to pay Leiden up to EUR 300,000 over a three-year period during the term of the sponsored research agreement. The 2015 Leiden Agreement will expire upon the expiration of the last patent included in the licensed patent rights. The 2015 Leiden Agreement may be terminated earlier upon mutual written agreement between us and Leiden, and at any time by us upon six months written notice to Leiden. Leiden may terminate the 2015 Leiden Agreement in the event of a failure by us to pay any amounts due under the 2015 Leiden Agreement that remains uncured on the date that is 30 days after written notice of such failure. Either party may terminate the 2015 Leiden Agreement upon a material breach by the other party that remains uncured following 30 days after the date of written notice of such breach or upon certain insolvency events that remain uncured following the date that is 45 days after the date of written notice to a party of such insolvency event.

License Agreement - ARIAD Pharmaceuticals, Inc.

2011 License Agreement

In March 2011, we entered into an amended and restated exclusive license agreement, or restated ARIAD license, with ARIAD which restated a license agreement entered into in 2006. Under the restated ARIAD license, ARIAD granted to us an exclusive, even as to ARIAD, license, with the right to grant sublicenses, under ARIAD's patent rights relating to dimerizers, genetic constructs coding for dimerizer binding domains, vectors containing said constructs, cells containing said constructs and methods of inducing biological processes in cells containing said constructs. These licensed patent rights were limited in the 2011 restated license to defined products in the fields of cell transplantation and certain types of cancer.

In connection with the original license from ARIAD, in 2006 we issued 121,242 shares of our common stock to ARIAD which were subject to antidilution protection that ultimately resulted in additional issuances to ARIAD by us of 556,221 shares of our common stock, such that ARIAD received a total of 677,463 shares of our common stock under the original license agreement. In addition, we paid ARIAD a license fee of \$250,000 in connection with the restated license in 2011. The restated ARIAD license also provided for certain royalty and milestone payments, which were subsequently terminated pursuant to an omnibus amendment agreement with ARIAD.

Under the restated ARIAD license, we are required to diligently proceed with the development, manufacture and sale of licensed products. The restated ARIAD license is subject at all times to restrictions and obligations under a license agreement by and between ARIAD Gene Therapeutics, Inc., an ARIAD affiliate that merged into ARIAD, and the academic institution from with ARIAD obtained its license to the underlying technology. While we are not required to pay royalties or fees to such academic institution, no sublicensee of ours may enter into a sublicense with respect to any intellectual property owned by the academic institution without its consent, which terms must be consistent with those included in the agreement between ARIAD and such academic institution.

The restated ARIAD license will expire upon expiration of the last license term of a licensed product covered by the agreement, which is the later of (1) 12 years from the date of the first commercial sale of the licensed product, or (2) the expiration of the last to expire valid patent claim on the licensed product. Either party to the license may terminate or modify the restated ARIAD license upon a material breach by the other party that remains uncured following the date that is 30 days after written notice of a payment breach and 90 days for any other breach, and

effective immediately upon bankruptcy of the other party. We may terminate the restated ARIAD license in our sole discretion at any time if we determine not to develop or commercialize any licensed product. In addition, upon termination of the restated ARIAD license prior to expiration, we must transfer any ownership and any beneficial ownership in any orphan drug designation or any similar designation in any jurisdiction of orphan drug status of the ARIAD dimerizer to ARIAD.

2014 Amendment

In October 2014, we entered into an omnibus amendment agreement with ARIAD, which in part amended the restated ARIAD license to expand the license to cover a broader scope of dimerizers and licensed products for use and exploitation in any human therapeutic field of use other than in vivo administration of genetic material directly into a human being using viral vectors for the purpose of producing proteins or other macromolecules that are expressed or secreted for therapeutic or prophylactic purposes.

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In connection with the amendment, we made an initial payment of \$15.0 million and we issued a promissory note to ARIAD for a principal amount of \$35.0 million in return for the broader scope of the license and the termination of all obligations to make milestone and royalty payments to ARIAD in the future. On December 23, 2014, the closing of our initial public offering triggered an acceleration of the payment of \$15.0 million due to ARIAD under the amendment and the promissory note. As a result of such acceleration, on December 29, 2014, we paid to ARIAD an aggregate amount of \$35.0 million, which included an additional payment of \$20.0 million to extinguish the promissory note. In exchange, ARIAD returned to us all of the 677,463 shares of our common stock then held by ARIAD and all of the agreements related to ARIAD's rights as a stockholder were terminated.

License Agreements - Baylor College of Medicine

2008 Baylor License Agreement

Pursuant to an Exclusive License Agreement with Baylor College of Medicine, or Baylor, dated March 20, 2008, or the 2008 Baylor license agreement, we obtained an exclusive, worldwide and fully paid up license to certain intellectual property, including intellectual property related to methods for activating antigen presenting cells and to genetic constructs coding for membrane bound inducible cytoplasmic CD40.

As consideration for the 2008 Baylor license agreement, we issued to Baylor 23,529 shares of our common stock and assumed responsibility for all legal fees and expenses, filing or maintenance fees, assessments and all other costs and expenses related to prosecuting, obtaining and maintaining patent protection on the patents subject to the 2008 Baylor license agreement.

The 2008 Baylor license agreement is subject to certain restrictions and is nonexclusive with respect to (1) the making or use of the licensed intellectual property for use in non-commercial research, patient care, teaching, and other educational purposes; (2) any non-exclusive license covering the licensed intellectual property that Baylor grants to other academic or research institutions for noncommercial research purposes; (3) any non-exclusive licenses that Baylor is required to grant to the U.S. or foreign state pursuant to an existing or future treaty with the U.S.; and (4) a non-exclusive license granted to ARIAD under the terms of a materials transfer agreement between Baylor and ARIAD.

Baylor may terminate or modify the 2008 Baylor license agreement in the event of a material breach by us that remains uncured following the date that is 90 days after written notice of such breach or upon certain insolvency events that remain uncured following the date that is 30 days following written notice of such insolvency event. We may terminate the 2008 Baylor license agreement, or any portion thereof, at our sole discretion at any time upon 30 days' written notice to Baylor. Upon termination of the 2008 Baylor license agreement, all rights to the intellectual property immediately revert to Baylor.

2010 Baylor License Agreement

Pursuant to an Exclusive License Agreement with Baylor, dated June 27, 2010, or the 2010 Baylor license agreement, we obtained an exclusive, worldwide license to certain intellectual property, including intellectual property related to methods for treating prostate cancer, methods of administering T cells to a patient, and methods of activating antigen presenting cells with constructs comprising MyD88 and CD40.

Pursuant to the terms of the 2010 Baylor license agreement, we paid Baylor a license execution fee of \$30,000. In addition, we are required to pay a low annual maintenance fee on each anniversary of the agreement date.

The terms of the 2010 Baylor license agreement also require us to make royalty payments of less than one percent, subject to certain annual minimums, on net sales of products covered by the license. In addition, to the extent we enter into a sublicensing agreement relating to a licensed product, we are required to pay Baylor a percentage in the mid-single digits on all non-royalty income received from sublicensing revenue. Bellicum is required to make milestone payments, of up to \$735,000 in aggregate, upon successful completion of clinical and regulatory milestones regarding the first two products covered by this license.

The 2010 Baylor license agreement will expire upon expiration of the last patent contained in the licensed patent rights, on a country-by-country basis, upon which we will have a perpetual, paid-in-full license in such country.

Baylor may terminate or modify the 2010 Baylor license agreement in the event of a material breach by us that remains uncured following the date that is 90 days after written notice of such breach or upon certain insolvency events that remain uncured following the date that is 30 days following written notice of such insolvency event. We

may terminate the 2010 Baylor license agreement, or any portion thereof, at our sole discretion at any time upon 60 days' written notice to Baylor. Upon termination of the 2010 Baylor license agreement for any reason prior to expiration, we must assign to Baylor each authorized sublicense agreement that is currently in effect on the date of termination.

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### 2014 Baylor License Agreement

Pursuant to an Exclusive License Agreement with Baylor, effective November 1, 2014, or the 2014 Baylor license agreement, we obtained an exclusive, worldwide license to certain intellectual property, including intellectual property related to methods for inducing selective apoptosis.

Pursuant to the terms of the 2014 Baylor license agreement, we paid Baylor a license execution fee of \$25,000. In addition, we are required to pay Baylor a low annual maintenance fee on each anniversary of the agreement date. The terms of the 2014 Baylor license agreement also require us to make royalty payments in the low single digits, subject to certain annual minimums, on net sales of products covered by the license. To the extent we enter into a sublicensing agreement relating to a licensed product, Bellicum is also required to pay Baylor a percentage in the low double-digits on all non-royalty income received from sublicensing revenue. We are required to make milestone payments, of up to \$275,000 in aggregate, upon successful completion of clinical and regulatory milestones regarding the first product covered by this license. The 2014 Baylor license agreement will expire upon expiration of the last patent contained in the licensed patent rights, on a country-by-country basis, upon which we will have a perpetual, paid-in-full license in each such country.

Baylor may terminate or modify the 2014 Baylor license agreement in the event of a material breach by us that remains uncured following the date that is 90 days after written notice of such breach or upon certain insolvency events that remain uncured following the date that is 30 days following written notice of such insolvency event. We may terminate the 2014 Baylor license agreement, or any portion thereof, at our sole discretion at any time upon 60 days' written notice to Baylor.

### 2016 Baylor License Agreements

In March 2016, we and Baylor entered into two additional license agreements pursuant to which we obtained exclusive rights to technologies and patent rights owned by Baylor. We paid Baylor a non-refundable license fee of \$100,000, and could incur additional payments upon the achievement of certain milestone events as set forth in the agreements. If we are successful in developing any of the licensed technologies under either agreement, resulting sales would be subject to a royalty payment in the low single digits.

### Grant Agreement

#### Grant Agreement with Cancer Prevention and Research Institute of Texas

In July 2011, we entered into a Cancer Research Grant Contract, or the First Grant Contract, with the Cancer Prevention and Research Institute of Texas, or CPRIT, under which CPRIT awarded a grant not to exceed approximately \$5.7 million to be used for the execution of defined clinical development of BPX-501. To date, we have received approximately \$4.9 million under the grant. The Grant Contract terminated on June 30, 2014, but obligations exist as to licensing, royalty payments, and indemnification provisions.

In November 2016, we announced that the Company received notice of a product development award totaling approximately \$16.9 million from CPRIT, the terms of which have been formalized in a contract. The CPRIT award is expected to fund a portion of a three-year global clinical program comprising clinical trials for adult and pediatric patients with high-risk and intermediate-risk AML, and potentially other hematologic cancers. The proposed studies are designed to evaluate the benefit of BPX-501 and rimiducid in the context of in vivo and ex vivo T cell depleted haploidentical HSCT. The CPRIT oversight committee met in February 2017 and agreed to move forward with the proposed terms of the grant agreement, and a second grant, or the Second Grant Contract was entered into in August 2017. Additionally, the First Grant Contract was amended in order to align revenue sharing terms, discussed below, with the Second Grant Contract. We are currently in the process of finalizing the clinical trial design(s) and expect to initiate the development program supported by the CPRIT funding in the second half of 2018.

Pursuant to the terms of each of the Grant Contracts, we grant to CPRIT a non-exclusive, irrevocable, royalty-free, perpetual, worldwide license to any technology and intellectual property resulting from the grant-funded activities and any other intellectual property that is owned by us and necessary for the exploitation of the technology and intellectual property resulting from the grant-funded activities, or the Project Results, for and on behalf of CPRIT and other governmental entities and agencies of the State of Texas and private or independent institutions of higher education located in Texas for education, research and other non-commercial purposes only. The terms of each of the Grant Contracts require that we pay tiered royalties in the low- to mid-single digit percentages on revenues from sales and

licenses of products or services that are based upon, utilize, are developed from or materially incorporate Project Results. Such royalties reduce to less than one percent after a mid-single-digit multiple of the grant funds have been repaid to CPRIT in royalties. Such royalties are payable for so long as we have marketing exclusivity or patents covering the applicable product or service (or twelve years from first commercial sale of such product or service in certain countries if there is no such exclusivity or patent protection).

If we abandon patent applications or patents covering Project Results in certain major market countries, CPRIT can, at its own cost, take over the prosecution and maintenance of such patents and is granted a non-exclusive, irrevocable, royalty-free, perpetual license with right to sublicense in such country to the applicable Project Results. We are required to use diligent and commercially reasonable efforts to commercialize at least one commercial product or service or otherwise bring to practical application the Project Results. If



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CPRIT notifies us of our failure with respect to the foregoing, and such failure is not owing to material safety concerns, then, at CPRIT's option, the applicable Project Results would be transferred to CPRIT and CPRIT would be granted a non-exclusive license to any other intellectual property that is owned by us and necessary for the exploitation of the Project Results, and CPRIT, at its own cost, can commercialize products or services that are based upon, utilize, are developed from or materially incorporate Project Results. CPRIT's option is subject to our ability to cure any failures identified by CPRIT within 60 days and a requirement to negotiate in good faith with us with respect to an alternative commercialization strategy for a period of 180 days.

### Competition

The biopharmaceutical industry is characterized by intense and dynamic competition to develop new technologies and proprietary therapies. 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 CID platform, differentiated product candidates and scientific expertise in the field of cellular immunotherapy provide us with competitive advantages, we face potential competition from various sources, including larger and better-funded pharmaceutical, specialty pharmaceutical and biotechnology companies, as well as from academic institutions, governmental agencies and public and private research institutions.

Our lead product candidate, BPX-501, is an adjunct therapy for HSCT with alternative donors that is designed to provide improved outcomes through enhanced time to reconstitution of the immune system and address the safety risks of GvHD and susceptibility to infections. The current standard-of-care that addresses some of the safety challenges associated with HSCT, primarily GvHD, is high-dose steroids. We are aware of other companies that are developing product candidates to improve the outcome of HSCT, including Kiadis Pharma Netherlands B.V. and MolMed S.p.A.

T-cell based treatments for cancer, such as CAR T and TCR therapies, have recently been an area of significant research and development by academic institutions and biopharmaceutical companies. BPX-601 and BPX-701 based on our GoCAR-T and CaspaCIDE technologies may compete with product candidates from a number of companies that are currently focused on this therapeutic modality, including Adaptimmune, bluebird bio, Inc., Celgene Corporation, Cellectis SA, Cell Medica Limited, GlaxoSmithKline plc, Intrexon Corporation, Immune Design Corp., Gilead Sciences, Inc., Iovance Biotherapeutics, Inc., Juno Therapeutics, Inc., Kiadis Pharma B.V., Medigene AG, MolMed S.p.A., Novartis AG, Pfizer Inc., Unum Therapeutics, Precision Biosciences, Inc. and Ziopharm Oncology. Many of our competitors, either alone or with their strategic partners, have substantially greater financial, technical and human resources than we do and significantly greater experience in the discovery and development of product candidates, obtaining FDA and other regulatory approvals of treatments and commercializing those treatments. Accordingly, our competitors may be more successful than us in obtaining approval for treatments and achieving widespread market acceptance. Our competitors' treatments may be more effective, or more effectively marketed and sold, than any treatment we may commercialize and may render our treatments obsolete or non-competitive before we can recover the expenses of developing and commercializing any of our treatments.

Mergers and acquisitions in the biotechnology and pharmaceutical industries may result in even more resources being concentrated among a smaller number of our competitors. These competitors also compete with us in recruiting and retaining qualified scientific and management personnel and establishing clinical study sites and subject registration for clinical studies, as well as in 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.

We anticipate that we will face intense and increasing competition as new drugs enter the market and advanced technologies become available. We expect any treatments that we develop and commercialize to compete on the basis of, among other things, efficacy, safety, convenience of administration and delivery, price, the level of generic competition and the availability of reimbursement from government and other third-party payers. For example, if a third party is able to obtain a stand-alone new drug application for rimiducid, then potential generic manufacturers may be able to file abbreviated new drug applications for that product.

Our commercial opportunity could be reduced or eliminated if our competitors develop and commercialize products that are safer, more effective, have fewer or less severe side effects, are more convenient or are less expensive than

any products that we may develop. Our competitors also may obtain FDA or other regulatory approval for their products more rapidly than we may obtain approval for ours, which could result in our competitors establishing a strong market position before we are able to enter the market. In addition, we expect that our therapeutic products, if approved, will be priced at a significant premium over competitive generic products and our ability to compete may be affected in many cases by insurers or other third-party payers seeking to encourage the use of generic products.

#### Research & Development Expenses

Information about our research and development expenses is incorporated herein by reference to Item 8 of Part II of this Annual Report.

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### Government Regulation and Product Approval

As a biopharmaceutical company that operates in the U.S., we are subject to extensive regulation. Our cell products will be regulated as biologics. With this classification, commercial production of our products will need to occur in registered and licensed facilities in compliance with the current good manufacturing practice, or cGMP, for biologics. The FDA regulates human cells, tissues, and cellular and tissue-based products, or HCT/Ps, under a two-tiered framework, based on risk categorization. Higher-risk HCT/Ps are regulated as biologics. Manufacturers of biologics are subject to extensive government regulation. For example, such products must complete extensive clinical trials, which must be conducted pursuant to an effective IND. The FDA must review and approve a BLA before a new biologic may be marketed.

The FDA considers our investigational products to be “combination products” because our products involve a biologic, the engineered cells, that is intended to be used with a small molecule chemical drug, rimiducid. In general, biologics such as our engineered cells are regulated through the FDA’s Center for Biologics Evaluation and Research, or CBER, while synthetic drugs are regulated through the FDA’s Center for Drug Evaluation and Research. When the FDA encounters a combination product such as our products, the agency determines which of the two centers will have primary responsibility for regulating the product by determining the primary mode of action for the product. The cellular component of our combination contributes the primary mode of action and, as a result, the FDA will regulate our investigational products as biologics, through CBER.

Government authorities in the U.S., at the federal, state and local levels, and in other countries extensively regulate, among other things, the research, development, testing, manufacturing, quality control, approval, labeling, packaging, storage, record-keeping, promotion, advertising, distribution, post-approval monitoring and reporting, marketing and export and import of biopharmaceutical products such as those we are developing. Our product candidates must be approved by the FDA before they may be legally marketed in the U.S. and by the appropriate foreign regulatory agency before they may be legally marketed in foreign countries. Generally, our activities in other countries will be subject to regulation that is similar in nature and scope as that imposed in the U.S., although there can be important differences. Additionally, some significant aspects of regulation in Europe are addressed in a centralized way, but country-specific regulation remains essential in many respects. The process for obtaining regulatory marketing approvals and the subsequent compliance with appropriate federal, state, local and foreign statutes and regulations require the expenditure of substantial time and financial resources.

### U.S. Product Development Process

In the U.S., the FDA regulates new drugs and biological products under the Federal Food, Drug and Cosmetic Act, or FDCA, the Public Health Service Act, or PHSA, and implementing regulations. Products are also subject to other federal, state and local statutes and regulations. The process of obtaining regulatory approvals and the subsequent compliance with appropriate federal, state, local and foreign statutes and regulations require the expenditure of substantial time and financial resources. Failure to comply with the applicable U.S. requirements at any time during the product development process, approval process or after approval, may subject an applicant to administrative, criminal, or civil sanctions. The FDA sanctions could include, among other actions, refusal to approve pending applications, withdrawal of an approval, a clinical hold, warning letters, product recalls or withdrawals from the market, product seizures, total or partial suspension of production or distribution injunctions, fines, refusals of government contracts, restitution, disgorgement or civil or criminal penalties. Any administrative, criminal, or civil enforcement action could have a material adverse effect on us. The FDA has limited experience with commercial development of T cell therapies for cancer. The process required by the FDA before a biological product may be marketed in the U.S. generally involves the following:

- completion of nonclinical laboratory tests and animal studies according to good laboratory practices, or GLPs, and applicable requirements for the humane use of laboratory animals or 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 the FDA’s regulations commonly referred to as good clinical practices, or GCPs, and any additional requirements for the protection of human research patients and their health information, to establish the safety and efficacy of the proposed biological product for its

intended use;

• submission to the FDA of a BLA for marketing approval that includes substantial evidence of safety, purity, and potency from results of nonclinical testing and clinical trials;

• satisfactory completion of an FDA inspection of the manufacturing facility or facilities where the biological product is produced to assess compliance with cGMP, to assure that the facilities, methods and controls are adequate to preserve the biological product's identity, strength, quality and purity and, if applicable, the FDA's current good tissue practices, or GTPs, for the use of HCT/Ps;

• potential FDA audit of the nonclinical study and clinical trial sites that generated the data in support of the BLA; and  
• FDA review and approval, or licensure, of the BLA.

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Before testing any biological product candidate, including our product candidates, in humans, the product candidate enters the preclinical testing stage. Preclinical tests, also referred to as nonclinical studies, include laboratory evaluations of product chemistry, toxicity and formulation, as well as animal studies to assess the potential safety and activity of the product candidate. The conduct of the preclinical tests must comply with federal regulations and requirements including GLPs. The clinical trial sponsor must submit the results of the preclinical tests, together with manufacturing information, analytical data, any available clinical data or literature and a proposed clinical protocol, to the FDA as part of the IND. Some preclinical testing may continue even after the IND is submitted. The IND automatically becomes effective 30 days after receipt by the FDA unless the FDA raises concerns or questions regarding the proposed clinical trials and places the trial on a clinical hold within that 30-day time period. In such a case, the IND sponsor must resolve FDA's outstanding concerns before the clinical trial can begin. The FDA may also impose clinical holds on a biological product candidate at any time before or during clinical trials due to safety concerns or non-compliance. If the FDA imposes a clinical hold, trials may not recommence without FDA authorization and then only under terms authorized by the FDA. Accordingly, we cannot be sure that submission of an IND will result in the FDA allowing clinical trials to begin, or that, once begun, issues will not arise that suspend or terminate such clinical trials. Gene therapy clinical trials conducted at institutions that receive funding for recombinant DNA research from the NIH, are also subject to review by the RAC. Although the FDA decides whether individual gene therapy protocols may proceed, the RAC review process can delay the initiation of a clinical trial, even if the FDA has reviewed the trial design and details and approved its initiation. Conversely, the FDA can put an IND on clinical hold even if the RAC has provided a favorable review of the drug.

Clinical trials involve the administration of the biological product candidate to healthy volunteers or patients under the supervision of qualified investigators, generally physicians not employed by or under the trial sponsor's control.

Clinical trials are conducted under protocols detailing, among other things, the objectives of the clinical trial, dosing procedures, subject selection and exclusion criteria, and the parameters to be used to monitor subject safety, including stopping rules that assure a clinical trial will be stopped if certain adverse events should occur. Each protocol and any amendments to the protocol must be submitted to the FDA as part of the IND. Clinical trials must be conducted and monitored in accordance with the FDA's regulations comprising the GCP requirements, including the requirement that all research patients provide informed consent. Further, each clinical trial must be reviewed and approved by an institutional review board, or IRB, at or servicing each institution at which the clinical trial will be conducted. An IRB is independent from the trial sponsor and is charged with protecting the welfare and rights of clinical trial participants and considers such items as whether the risks to individuals participating in the clinical trials are minimized and are reasonable in relation to anticipated benefits. The IRB also approves the form and content of the informed consent that must be signed by each clinical trial subject or his or her legal representative and must monitor the clinical trial until completed. Clinical trials also must be reviewed by an institutional biosafety committee, or IBC, a local institutional committee that reviews and oversees basic and clinical research conducted at that institution. The IBC assesses the safety of the research and identifies any potential risk to public health or the environment.

Human clinical trials for biologic products are typically conducted in three sequential phases that may overlap or be combined:

Phase 1. The biological product is initially introduced into healthy human subjects and tested for safety. In the case of some products for severe or life-threatening diseases, especially when the product may be too inherently toxic to ethically administer to healthy volunteers, the initial human testing is often conducted in patients.

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

Phase 3. Clinical trials are undertaken to further evaluate dosage, clinical efficacy, potency, and safety in an expanded patient population at geographically dispersed clinical trial sites. These clinical trials are intended to establish the overall risk to benefit ratio of the product and provide an adequate basis for product labeling.

Post-approval clinical trials, sometimes referred to as Phase 4 clinical trials, may be conducted after initial marketing approval. These clinical trials are used to gain additional experience from the treatment of patients in the intended therapeutic indication, particularly for long-term safety follow-up.

During all phases of clinical development, regulatory agencies require extensive monitoring and auditing of all clinical activities, clinical data, and clinical trial investigators. Annual progress reports detailing the progress of the clinical trials must be submitted to the FDA. Written IND safety reports must be promptly submitted to the FDA, the NIH and the investigators for serious and unexpected adverse events, any findings from other studies, tests in laboratory animals or in vitro testing that suggest a significant risk for human patients, or any clinically important increase in the rate of a serious suspected adverse reaction over that listed in the protocol or investigator brochure. The sponsor must submit an IND safety report within 15 calendar days after the sponsor determines that the information qualifies for reporting. The sponsor also must notify the FDA of any unexpected fatal or life-threatening suspected adverse reaction within seven calendar days after the sponsor's initial receipt of the information. Phase 1, Phase 2 and Phase 3 clinical trials may not be completed successfully within any specified period, if at all. The FDA or the sponsor or its data safety monitoring

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board may suspend or terminate a clinical trial at any time on various grounds, including a finding that the research patients are being exposed to an unacceptable health risk, including risks inferred from other unrelated immunotherapy trials. 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 biological product has been associated with unexpected serious harm to patients.

Human immunotherapy products are a new category of therapeutics. This is a relatively new and expanding area of novel therapeutic interventions, and therefore there is uncertainty as to the length of the trial period, the number of patients the FDA will require to be enrolled in the clinical trials in order to establish the safety, efficacy, purity and potency of immunotherapy products, and the eventual quality of data to be generated in these clinical trials for the FDA to support marketing approval.

Concurrently with clinical trials, companies usually complete additional studies and must also develop additional information about the physical characteristics of the biological product, as well as finalize a process for manufacturing the product in commercial quantities in accordance with cGMP requirements. 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 things, 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. Federal law requires that we register all of our clinical trials on a publicly accessible website, and accordingly we disclose information on our clinical trials on [www.clintrials.gov](http://www.clintrials.gov). We must also provide results information for most of our clinical trials, other than Phase 1 clinical trials.

### U.S. Review and Approval Processes

After the completion of clinical trials of a biological product, FDA approval of a BLA must be obtained before commercial marketing of the biological product. The BLA must include results of product development, laboratory and animal studies, human trials, information on the manufacture and composition of the product, proposed labeling and other relevant information. The FDA may grant deferrals for submission of certain data or full or partial waivers. The testing and approval processes require substantial time and effort and there can be no assurance that the FDA will accept the BLA for filing and, even if filed, that any approval will be granted on a timely basis, if at all.

Under the Prescription Drug User Fee Act, or PDUFA, as amended, each BLA must be accompanied by a significant user fee. The FDA adjusts the PDUFA user fees on an annual basis. The PDUFA also imposes an annual product fee for biological products and an annual establishment fee on facilities used to manufacture prescription biological products. Fee waivers or reductions are available in certain circumstances, including a waiver of the application fee for the first application filed by a small business. Additionally, no user fees are assessed on BLAs for products designated as orphan drugs, unless the application also includes a non-orphan indication.

Within 60 days following submission of the application, the FDA reviews a BLA submitted to determine if it is substantially complete before the agency accepts it for filing. The FDA may refuse to file any BLA that it deems incomplete or not properly reviewable at the time of submission and may request additional information. In this event, the BLA 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. 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 whether the product is being manufactured in accordance with cGMP to assure and preserve the product's identity, safety, strength, quality, potency and purity. The FDA may refer applications for novel biological products or biological 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 biological product approval process, the FDA also will determine whether a Risk Evaluation and Mitigation Strategy, or REMS, is necessary to assure the safe use

of the biological product. If the FDA concludes a REMS is needed, the sponsor of the BLA must submit a proposed REMS. The FDA will not approve a BLA without a REMS, if required.

Before approving a BLA, 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. For immunotherapy products, the FDA also will not approve the product if the manufacturer is not in compliance with the GTPs, to the extent applicable. These are FDA regulations and guidance documents that govern the methods used in, and the facilities and controls used for, the manufacture of HCT/Ps. The primary intent of the GTP requirements is to ensure that cell and tissue based products are manufactured in a manner designed to prevent the introduction, transmission and spread of communicable disease. FDA regulations also require HCT/P establishments to register and list their HCT/Ps with the FDA and, when applicable, to evaluate donors through screening and testing. Additionally, before approving



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a BLA, 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 maintain compliance with CGMPs, GTPs, and GCPs, 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 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 in its present form, the FDA will issue a complete response letter that describes all of the specific deficiencies in the BLA 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, addressing all of the deficiencies identified in the letter, or withdraw the application.

If a product receives regulatory approval, the approval may be significantly limited to specific diseases 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 REMS or other 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.

In addition, under the Pediatric Research Equity Act, or PREA, a BLA or supplement to a BLA must contain data to assess the safety and effectiveness of the product for the claimed indications in all relevant pediatric subpopulations and to support dosing and administration for each pediatric subpopulation for which the product is safe and effective. The FDA may grant deferrals for submission of data or full or partial waivers. Unless otherwise required by regulation, the PREA does not apply to any product for an indication for which orphan designation has been granted. However, if only one indication for a product has orphan designation, a pediatric assessment may still be required for any applications to market that same product for the non-orphan indication(s). Sponsors in satisfaction of this obligation may receive an additional six months of marketing exclusivity for all dosage forms and all indications with the same active moiety as the drug studied.

### Orphan Drug Designation

Under the Orphan Drug Act, the FDA may grant orphan designation to a drug or biologic intended to treat a rare disease or condition, which is generally a disease or condition that affects fewer than 200,000 individuals in the U.S., or 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 drug or biologic for this type of disease or condition will be recovered from sales in the U.S. for that drug or biologic. Orphan drug designation must be requested before submitting a BLA. After the FDA grants orphan drug designation, the generic identity of the therapeutic agent and its potential orphan use are disclosed publicly by the FDA. The orphan drug designation does not shorten the duration of the regulatory review or approval process, but does provide certain advantages, such as a waiver of PDUFA fees, enhanced access to FDA staff, and potential waiver of the PREA requirements discussed above.

If a product that has orphan drug designation subsequently receives the first FDA approval for the disease for which it has such designation, the product is entitled to orphan product exclusivity, which means that the FDA may not approve any other applications, including a full BLA, to market the same biologic for the same indication for seven years, except in limited circumstances, such as a showing of clinical superiority to the product with orphan drug exclusivity. Orphan drug exclusivity does not prevent FDA from approving a different drug or biologic for the same disease or condition, or the same drug or biologic for a different disease or condition. Among the other benefits of orphan drug designation are tax credits for certain research and a waiver of the BLA application user fee.

A designated orphan drug may not receive orphan drug exclusivity if it is approved for a use that is broader than the indication for which it received orphan designation. In addition, exclusive marketing rights in the U.S. may be lost if

the FDA later determines that the request for designation was materially defective or if the manufacturer is unable to assure sufficient quantities of the product to meet the needs of patients with the rare disease or condition. On February 22, 2016, we announced that the FDA granted orphan drug designation for the combination of BPX-501 genetically modified T cells and activator agent rimiducid as "replacement T-cell therapy for the treatment of immunodeficiency and graft versus host disease(GvHD) after allogeneic hematopoietic stem cell transplant." BPX-501 is an adjunct T-cell therapy incorporating our proprietary CaspaCIDE safety switch.

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### Expedited Development and Review Programs

The FDA has a Fast Track program that is intended to expedite or facilitate the process for reviewing new products that meet certain criteria. Specifically, new products are eligible for Fast Track designation if they are intended to treat a serious or life-threatening disease or condition and demonstrate the potential to address unmet medical needs, or if the drug has been designated as a qualified infectious disease product. Fast Track designation applies to the combination of the product and the specific indication for which it is being studied. Under Fast Track, the FDA may consider for review sections of the BLA on a rolling basis before the complete application is submitted, if the sponsor provides a schedule for the submission of the sections of the BLA, the FDA agrees to accept sections of the BLA and determines that the schedule is acceptable, and the sponsor pays any required user fees upon submission of the first section of the BLA. Even if Fast Track designation is granted, it may be rescinded if the product no longer meets the qualifying criteria.

Any product, submitted to the FDA for approval, including a product with a Fast Track designation, may also be eligible for other types of FDA programs intended to expedite development and review, such as priority review and accelerated approval. A product is eligible for priority review if it treats a serious condition and, if approved, would provide a significant improvement in safety and efficacy. The FDA will attempt to direct additional resources to the evaluation of an application for a new product designated for priority review in an effort to facilitate the review.

Additionally, a product may be eligible for accelerated approval. Products studied for their safety and effectiveness in treating serious or life-threatening diseases or conditions may receive accelerated approval upon a determination that the product treats a serious condition, provides a meaningful advantage over available therapies, and demonstrates an effect on 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, that is reasonably likely to predict an effect on irreversible morbidity or mortality or other clinical benefit, taking into account the severity, rarity, or prevalence of the condition and the availability or lack of alternative treatments. As a condition of approval, the FDA may require that a sponsor of a drug or biological product receiving accelerated approval perform appropriate post-marketing clinical studies to verify and describe the predicted effect on irreversible morbidity or mortality or other clinical benefit. In addition, the FDA currently requires as a condition for accelerated approval pre-approval of promotional materials, which could adversely impact the timing of the commercial launch of the product. The FDCA also provides expedited procedures for FDA withdrawal of approval of a product approved through accelerated approval. Fast Track designation, priority review and accelerated approval do not change the standards for approval but may expedite the development or approval process.

In 2012, the FDA established a Breakthrough Therapy Designation which is intended to expedite the development and review of products that treat serious or life-threatening conditions. The designation requires preliminary clinical evidence that may demonstrate substantial improvement on a clinically significant endpoint over available therapies. The designation includes all of the Fast Track program features, as well as more intensive FDA interaction and guidance, organizational commitment, and other potential actions to expedite review. The Breakthrough Therapy Designation is a distinct status from both accelerated approval and priority review, which can also be granted to the same product if relevant criteria are met. If a product is designated as breakthrough therapy, the FDA will expedite the development and review of such product. Even if a Breakthrough Therapy Designation is granted, it may be rescinded if the product no longer meets the qualifying criteria.

Where applicable, we plan to request Fast Track and Breakthrough Therapy Designation for our product candidates, including BPX-501, BPX-601 and BPX-701. Even if we receive one or both of these designations for our product candidates, the FDA may later decide that our product candidates no longer meet the conditions for qualification. In addition, these designations may not provide us with a material commercial advantage.

### Post-Approval Requirements

Any product for which we receive FDA approval is subject to continuing regulation by the FDA, including, among other things, record-keeping requirements, reporting of adverse experiences with the product, providing the FDA with updated safety and efficacy information, product sampling and distribution requirements, and complying with FDA promotion and advertising requirements, which include, among others, standards for direct-to-consumer advertising, restrictions on promoting products for uses or in patient populations that are not described in the product's approved

uses, known as “off-label use,” limitations on industry-sponsored scientific and educational activities, and requirements for promotional activities involving the internet. Although physicians may prescribe legally available products for off-label uses, if the physicians deem it to be appropriate in their professional medical judgment, manufacturers may not market or promote such off-label uses.

In addition, quality control and manufacturing procedures must continue to conform to applicable manufacturing requirements after approval to ensure the long-term stability of the product. We rely, and expect to continue to rely, on third parties for the production of clinical and commercial quantities of our products in accordance with cGMP regulations. cGMP regulations require among other things, quality control and quality assurance as well as the corresponding maintenance of records and documentation and the obligation to investigate and correct any deviations from cGMP. Manufacturers and other entities involved in the manufacture and distribution of approved products are required to register their establishments with the FDA and certain state agencies, and are subject

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to periodic unannounced inspections by the FDA and certain state agencies for compliance with cGMP and other laws. Accordingly, manufacturers must continue to expend time, money, and effort in the area of production and quality control to maintain cGMP compliance. Discovery of problems with a product after approval may result in restrictions on a product, manufacturer, or holder of an approved BLA, including, among other things, recall or withdrawal of the product from the market, seizure of product manufactured not in accordance with GMPs, suspension or termination of manufacturing activities at one or more facilities, or other civil or criminal sanctions. In addition, changes to the manufacturing process are strictly regulated, and depending on the significance of the change, may require prior FDA approval before being implemented. Other types of changes to the approved product, such as adding new indications and claims, are also subject to further FDA review and approval.

The FDA also may require post-marketing testing, known as Phase 4 testing, and surveillance to monitor the effects of an approved product. Discovery of previously unknown problems with a product or the failure to comply with applicable FDA requirements can have negative consequences, including adverse publicity, judicial or administrative enforcement, warning letters from the FDA, mandated corrective advertising or communications with doctors, and civil or criminal penalties, among others. Newly discovered or developed safety or effectiveness data may require changes to a product's approved labeling, including the addition of new warnings and contraindications, and also may require the implementation of a REMS or other risk management measures. Also, new government requirements, including those resulting from new legislation, may be established, or the FDA's policies may change, which could delay or prevent regulatory approval of our products under development.

### U.S. Patent Term Restoration and Marketing Exclusivity

The Biologics Price Competition and Innovation Act, or BPCIA, amended the PHSA to authorize the FDA to approve similar versions of innovative biologics, commonly known as biosimilars. Among other requirements, a competitor seeking approval of a biosimilar must file an application to establish its molecule as highly similar to an approved innovator biologic, without any clinically meaningful differences in terms of safety, purity, and potency. The BPCIA, however, bars the FDA from approving biosimilar applications for 12 years after an innovator biological product receives initial marketing approval. This 12-year period of data exclusivity may be extended by six months, for a total of 12.5 years, if the FDA requests that the innovator company conduct pediatric clinical investigations of the product. It remains to be seen how FDA will apply the statutory biosimilar provisions to biological products such as ours.

Depending upon the timing, duration and specifics of the FDA approval of the use of our product candidates, some of our U.S. patents, if granted, may be eligible for limited patent term extension under the Drug Price Competition and Patent Term Restoration Act of 1984, commonly 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's approval date. The patent term restoration period is generally one-half the time between the effective date of an IND and the submission date of a BLA, plus the time between the submission date of a BLA and the approval of that application. Only one patent applicable to an approved product is eligible for the extension and the application for the extension must be submitted prior to the 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 may intend to apply for restoration of patent term for one of our currently owned or licensed patents to add patent life beyond its current expiration date, depending on the expected length of the clinical trials and other factors involved in the filing of the relevant BLA.

### Other U.S. Healthcare Laws and Compliance Requirements

In the U.S., our activities are potentially subject to regulation by various federal, state and local authorities in addition to the FDA, including but not limited to, the Centers for Medicare and Medicaid Services, or CMS, other divisions of the U.S. Department of Health and Human Services, or HHS, such as the Office of Inspector General, the U.S. Department of Justice, or DOJ, and individual U.S. Attorney offices within the DOJ, and state and local governments. For example, sales, marketing and scientific/educational grant programs must comply with the anti-fraud and abuse provisions of the Social Security Act, the false claims laws, the privacy provisions of the Health Insurance Portability and Accountability Act, or HIPAA, the sunshine provisions of the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act, collectively, the Affordable Care Act, and similar

state laws, each as amended.

The federal Anti-Kickback Statute prohibits, among other things, any person or entity, from knowingly and willfully offering, paying, soliciting or receiving any remuneration, directly or indirectly, overtly or covertly, in cash or in kind, to induce or in return either the referral of an individual for, or the for purchasing, leasing, ordering or arranging for the purchase, lease or order of any good, facility, item or service reimbursable, in whole or in part, under Medicare, Medicaid or other federal healthcare programs. The term remuneration has been interpreted broadly to include anything of value. The Anti-Kickback Statute has been interpreted to apply to arrangements between biologic manufacturers on one hand and prescribers, purchasers, and formulary managers on the other. There are a number of statutory exceptions and regulatory safe harbors protecting some common activities from prosecution. The exceptions and safe harbors are drawn narrowly and practices that involve remuneration that may be alleged to be intended to induce prescribing, purchasing or recommending may be subject to scrutiny if they do not qualify for an exception or safe harbor. Failure to meet all of

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the requirements of a particular applicable statutory exception or regulatory safe harbor does not make the conduct per se illegal under the Anti-Kickback Statute. Instead, the legality of the arrangement will be evaluated on a case-by-case basis based on a cumulative review of all of its facts and circumstances.

Additionally, the intent standard under the Anti-Kickback Statute was amended by the Affordable Care Act to a stricter standard such that a person or entity no longer needs to have actual knowledge of the statute or specific intent to violate it in order to have committed a violation. The Anti-Kickback Statute may be violated if only one purpose of the remuneration is to induce referrals. In addition, the Affordable Care Act codified case law that a claim including items or services resulting from a violation of the federal Anti-Kickback Statute constitutes a false or fraudulent claim for purposes of the federal civil False Claims Act.

The civil monetary penalties law imposes penalties against any person or entity who, among other things, is determined to have presented or caused to be presented a claim to a federal health program that the person knows or should know is for an item or service that was not provided as claimed or is false or fraudulent.

The federal false claims laws, including but not limited to the federal civil False Claims Act, prohibit, among other things, any person or entity from knowingly presenting, or causing to be presented, a false claim for payment to, or approval by, the federal government. Pharmaceutical and other healthcare companies have been prosecuted under these laws for allegedly providing free product to customers with the expectation that the customers would bill federal programs for the product. Other companies have been prosecuted for causing false claims to be submitted because of the companies' marketing of the product for unapproved, that is, off-label, and thus non-reimbursable, uses.

HIPAA created new federal criminal statutes that prohibit knowingly and willfully executing, or attempting to execute, a scheme to defraud or to obtain, by means of false or fraudulent pretenses, representations or promises, any money or property owned by, or under the control or custody of, any healthcare benefit program, including private third-party payors and knowingly and willfully falsifying, concealing or covering up by trick, scheme or device, a material fact or making any materially false, fictitious or fraudulent statement in connection with the delivery of or payment for healthcare benefits, items or services.

Also, many states have similar fraud and abuse statutes or regulations that apply to items and services reimbursed under Medicaid and other state programs, or, in several states, apply regardless of the payor.

We may be subject to data privacy and security regulations by both the federal government and the states in which we conduct our business. HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act, or HITECH, and their implementing regulations, imposes requirements relating to the privacy, security and transmission of individually identifiable health information. Among other things, HITECH makes HIPAA's security standards directly applicable to business associates independent contractors or agents of covered entities that receive or obtain protected health information in connection with providing a service on behalf of a covered entity. HITECH also created four new tiers of civil monetary penalties, amended HIPAA to make civil and criminal penalties directly applicable to business associates, and gave state attorneys general new authority to file civil actions for damages or injunctions in federal courts to enforce the federal HIPAA laws and seek attorneys' fees and costs associated with pursuing federal civil actions. In addition, state laws govern the privacy and security of health information in specified circumstances, many of which differ from each other in significant ways and may not have the same effect, thus complicating compliance efforts.

Additionally, the federal Physician Payments Sunshine Act, and its implementing regulations, require that certain manufacturers of drugs, devices, biological and medical supplies for which payment is available under Medicare, Medicaid or the Children's Health Insurance Program, with certain exceptions, to report annually information related to certain payments or other transfers of value made or distributed to physicians and teaching hospitals, or to entities or individuals at the request of, or designated on behalf of, the physicians and teaching hospitals and require that certain manufacturers and group purchasing organizations report annually certain ownership and investment interests held by physicians and their immediate family members.

We will also be required to begin satisfying the product tracing, verification, and reporting requirements set out in the Drug Quality and Security Act.

In order to distribute products commercially, we must also comply with state laws that require the registration of manufacturers and wholesale distributors of drug and biological products in a state, including, in certain states,

manufacturers and distributors who ship products into the state even if such manufacturers or distributors have no place of business within the state.

Several states have enacted legislation requiring pharmaceutical and biotechnology companies to, among other things, establish marketing compliance programs, file periodic reports with the state, make periodic public disclosures on sales, marketing, pricing, clinical trials and other activities, and/or register their sales representatives, as well as to prohibit pharmacies and other healthcare entities from providing certain physician prescribing data to pharmaceutical and biotechnology companies for use in sales and marketing, and to prohibit certain other sales and marketing practices. All of our activities are potentially subject to federal and state consumer protection and unfair competition laws.



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If our operations are found to be in violation of any of the federal and state healthcare laws described above or any other governmental regulations that apply to us, we may be subject to penalties, including without limitation, civil, criminal and/or administrative penalties, damages, fines, disgorgement, individual imprisonment, additional reporting requirements and oversight if we become subject to a corporate integrity agreement or similar agreement to resolve allegations of non-compliance with these laws, exclusion from participation in government programs, such as Medicare and Medicaid, injunctions, private “qui tam” actions brought by individual whistleblowers in the name of the government, or refusal to allow us to enter into government contracts, contractual damages, reputational harm, administrative burdens, diminished profits and future earnings, and the curtailment or restructuring of our operations, any of which could adversely affect our ability to operate our business and our results of operations.

### Coverage, Pricing and Reimbursement

Significant uncertainty exists as to the coverage and reimbursement status of any product candidates for which we obtain regulatory approval. In the U.S. and markets in other countries, sales of any products for which we receive regulatory approval for commercial sale will depend, in part, on the extent to which third-party payors provide coverage and establish adequate reimbursement levels for such products. In the U.S., third-party payors include federal and state healthcare programs, private managed care providers, health insurers and other organizations. The process for determining whether a third-party payor will provide coverage for a product may be separate from the process for setting the price of a product or for establishing the reimbursement rate that such a payor will pay for the product. Third-party payors may limit coverage to specific products on an approved list, also known as a formulary, which might not include all of the FDA-approved products for a particular indication. Third-party payors are increasingly challenging the price, examining the medical necessity and reviewing the cost-effectiveness of medical products, therapies and services, in addition to questioning their safety and efficacy. We may need to conduct expensive pharmaco-economic studies in order to demonstrate the medical necessity and cost-effectiveness of our products, in addition to the costs required to obtain the FDA approvals. Our product candidates may not be considered medically necessary or cost-effective. A payor’s decision to provide coverage for a product does not imply that an adequate reimbursement rate will be approved. Further, one payor’s determination to provide coverage for a product does not assure that other payors will also provide coverage for the product. Adequate third-party reimbursement may not be available to enable us to maintain price levels sufficient to realize an appropriate return on our investment in product development.

Different pricing and reimbursement schemes exist in other countries. In the EU, governments influence the price of pharmaceutical products through their pricing and reimbursement rules and control of national health care systems that fund a large part of the cost of those products to consumers. Some jurisdictions operate positive and negative list systems under which products may only be marketed once a reimbursement price has been agreed. To obtain reimbursement or pricing approval, some of these countries may require the completion of clinical trials that compare the cost-effectiveness of a particular product candidate to currently available therapies. Other member states allow companies to fix their own prices for medicines, but monitor and control company profits. The downward pressure on health care costs has become very intense. As a result, increasingly high barriers are being erected to the entry of new products. In addition, in some countries, cross-border imports from low-priced markets exert a commercial pressure on pricing within a country.

The marketability of any product candidates for which we receive regulatory approval for commercial sale may suffer if the government and third-party payors fail to provide adequate coverage and reimbursement. In addition, emphasis on managed care in the U.S. has increased and we expect will continue to increase the pressure on healthcare pricing. Coverage policies and third-party reimbursement rates may change at any time. Even if favorable coverage and reimbursement status is attained for one or more products for which we receive regulatory approval, less favorable coverage policies and reimbursement rates may be implemented in the future.

### Healthcare Reform

In March 2010, President Obama signed the Affordable Care Act, which was intended to broaden access to health insurance, improve quality, and reduce or constrain the growth of healthcare spending among other health policy reforms. The Affordable Care Act has substantially changed healthcare financing and delivery by both governmental and private insurers, and continues to significantly impact the pharmaceutical and biotechnology industry. The

Affordable Care Act has changed existing government healthcare programs and resulted in the development of new programs.

Among the Affordable Care Act's provisions of importance to the pharmaceutical and biotechnology industries, in addition to those otherwise described above, are the following:

an annual, nondeductible fee on any entity that manufactures or imports certain specified branded prescription drugs and biologic agents apportioned among these entities according to their market share in some government healthcare programs;

an increase in the statutory minimum rebates a manufacturer must pay under the Medicaid Drug Rebate Program, retroactive to January 1, 2010, to 23.1% and 13% of the average manufacturer price for most branded and generic drugs, respectively and capped the total rebate amount for innovator drugs at 100% of the Average Manufacturer Price, or AMP;

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a new Medicare Part D coverage gap discount program, in which manufacturers must agree to offer 50% point-of-sale discounts off negotiated prices of applicable brand drugs to eligible beneficiaries during their coverage gap period, as a condition for the manufacturers' outpatient drugs to be covered under Medicare Part D;

extension of manufacturers' Medicaid rebate liability to covered drugs dispensed to individuals who are enrolled in Medicaid managed care organizations;

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

expansion of the entities eligible for discounts under the Public Health Service pharmaceutical pricing program; and

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

Since January 2017, President Trump has signed two Executive Orders designed to delay the implementation of certain provisions of the PPACA or otherwise circumvent some of the requirements for health insurance mandated by the PPACA. Concurrently, Congress has considered legislation that would repeal, or repeal and replace, all or part of the PPACA. While Congress has not passed comprehensive repeal legislation, two bills affecting the implementation of certain taxes under the PPACA have been signed into law. The Tax Cuts and Jobs Act of 2017 includes a provision repealing, effective January 1, 2019, the tax-based shared responsibility payment imposed by the PPACA on certain individuals who fail to maintain qualifying health coverage for all or part of a year that is commonly referred to as the "individual mandate". Additionally, on January 22, 2018, President Trump signed a continuing resolution on appropriations for fiscal year 2018 that delayed the implementation of certain PPACA-mandated fees, including the so-called "Cadillac" tax on certain high cost employer-sponsored insurance plans, the annual fee imposed on certain health insurance providers based on market share, and the medical device excise tax on non-exempt medical devices. Congress may consider other legislation to replace elements of the PPACA.

There have also been changes to the reimbursement landscape in the U.S. since the passage of the Affordable Care Act. On August 2, 2011, President Obama signed into law the Budget Control Act of 2011, which, among other things, created the Joint Select Committee on Deficit Reduction to recommend to Congress proposals in spending reductions. The Joint Select Committee did not achieve a targeted deficit reduction of at least \$1.2 trillion for the years 2013 through 2021, triggering the legislation's automatic reduction to several government programs. This includes reductions to Medicare payments to providers of 2% per fiscal year, which went into effect on April 1, 2013, and, due to subsequent legislative amendments will stay in effect through 2025 unless additional Congressional action is taken. On January 2, 2013, President Obama signed into law the American Taxpayer Relief Act of 2012, which, among other things, reduced Medicare payments to several providers, including hospitals, imaging centers and cancer treatment centers and increased the statute of limitations period for the government to recover overpayments to providers from three to five years. Further, there has been heightened governmental scrutiny recently over the manner in which manufacturers set prices for their marketed products. For example, there have been several recent Congressional inquiries and proposed bills designed to, among other things, bring more transparency to drug pricing, review the relationship between pricing and manufacturer patient programs, reduce the cost of drugs under Medicare, and reform government program reimbursement methodologies for drug products. We expect that additional state and federal healthcare reform measures will be adopted in the future, any of which could limit the amounts that federal and state governments will pay for healthcare products and services, which could result in reduced demand for our products and/or additional pricing pressure. In addition, it is possible that there will be further legislation or regulation that could harm our business, financial condition, and results of operations.

The Foreign Corrupt Practices Act

The Foreign Corrupt Practices Act, or FCPA, prohibits any U.S. individual or business from paying, offering, or authorizing payment or offering of anything of value, directly or indirectly, to any foreign official, political party or candidate for the purpose of influencing any act or decision of the foreign entity in order to assist the individual or business in obtaining or retaining business. The FCPA also obligates companies whose securities are listed in the U.S. to comply with accounting provisions requiring the company to maintain books and records that accurately and fairly reflect all transactions of the corporation, including international subsidiaries, and to devise and maintain an adequate

system of internal accounting controls for international operations.

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### Additional Regulation

In addition to the foregoing, state and federal laws regarding environmental protection and hazardous substances, including the Occupational Safety and Health Act, the Resource Conservancy and Recovery Act and the Toxic Substances Control Act, affect our business. These and other laws govern our use, handling and disposal of various biological, chemical and radioactive substances used in, and wastes generated by, our operations. If our operations result in contamination of the environment or expose individuals to hazardous substances, we could be liable for damages and governmental fines. We believe that we are in material compliance with applicable environmental laws and that continued compliance therewith will not have a material adverse effect on our business. We cannot predict, however, how changes in these laws may affect our future operations.

### Europe / Rest of World Government Regulation

In addition to regulations in the U.S., we will be subject to a variety of regulations in other jurisdictions governing, among other things, clinical trials and any commercial sales and distribution of our products. Whether or not we obtain FDA approval of a product, we must obtain the requisite approvals from regulatory authorities in foreign countries prior to the commencement of clinical trials or marketing of the product in those countries. Certain countries outside of the U.S. have a similar process that requires the submission of a clinical trial application much like the IND prior to the commencement of human clinical trials. In the EU, for example, a clinical trial application must be submitted to each country's national health authority and an independent ethics committee, much like the FDA and IRB, respectively. Once the clinical trial application is approved in accordance with a country's requirements, clinical trial development may proceed. Because biologically sourced raw materials are subject to unique contamination risks, their use may be restricted in some countries. The requirements and process governing the conduct of clinical trials, product licensing, pricing and reimbursement vary from country to country. In all cases, the clinical trials are conducted in accordance with GCP and the applicable regulatory requirements and the ethical principles that have their origin in the Declaration of Helsinki.

To obtain regulatory approval of an investigational drug or biological product under EU regulatory systems, we must submit a marketing authorization application. The application used to file the BLA in the U.S. is similar to that required in the EU, with the exception of, among other things, country-specific document requirements.

For other countries outside of the EU, such as countries in Eastern Europe, Latin America or Asia, the requirements governing the conduct of clinical trials, product licensing, pricing and reimbursement vary from country to country. In all cases, again, the clinical trials are conducted in accordance with GCP and the applicable regulatory requirements and the ethical principles that have their origin in the Declaration of Helsinki.

### Employees

As of December 31, 2017, we had 137 employees, all of whom were full-time, 117 of whom were engaged in research and development activities and 20 of whom were engaged in business development, finance, information systems, facilities, human resources or administrative support. None of our employees is subject to a collective bargaining agreement. We consider our relationship with our employees to be good.

### Corporate Information

We were incorporated in Delaware in July 2004. Our principal executive offices are located at 2130 W. Holcombe Blvd., Ste. 800, Houston, Texas and our telephone number is (832) 384-1100. Our corporate website address is [www.bellicum.com](http://www.bellicum.com). Our Annual Report on Form 10-K, Quarterly Reports on Form 10-Q, Current Reports on Form 8-K, and amendments to reports filed pursuant to Sections 13(a) and 15(d) of the Securities Exchange Act of 1934, as amended, or the Exchange Act, will be made available free of charge on our website as soon as reasonably practicable after we electronically file such material with, or furnish it to, the Securities and Exchange Commission, or the SEC. The contents of our website are not incorporated into this Annual Report and our reference to the URL for our website is intended to be an inactive textual reference only.

We are an "emerging growth company," as defined in the JOBS Act. We will remain an emerging growth company until the earlier of (a) December 31, 2019, (b) the last day of the fiscal year in which we have total annual gross revenue of at least \$1.0 billion (c) the last day of the fiscal year in which we are deemed to be a large accelerated filer, which means the market value of our common stock that is held by non-affiliates exceeded \$700.0 million as of the prior June 30th, or (d) the date on which we have issued more than \$1.0 billion in non-convertible debt during the prior

three-year period. References to “emerging growth company” in this Annual Report on Form 10-K have the meaning associated with it in the JOBS Act.

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ITEM 1A. Risk Factors

You should carefully consider the following risk factors, as well as the other information in this report, and in our other public filings. The occurrence of any of the following risks could harm our business, financial condition, results of operations and/or growth prospects or cause our actual results to differ materially from those contained in forward-looking statements we have made in this report and those we may make from time to time. You should consider all of the risk factors described when evaluating our business.

**Risks Related to Our Business and Industry**

We have incurred net losses in every year since our inception and anticipate that we will continue to incur net losses in the future.

We are a clinical stage biopharmaceutical company with a limited operating history. We are not profitable, have no products approved for commercial sale and have incurred significant losses since our inception in 2004. To date, we have financed our operations primarily through equity and debt financings. For the fiscal years ended December 31, 2017 and 2016, we reported a net loss of \$91.8 million and \$69.2 million, respectively.

As of December 31, 2017, we had an accumulated deficit of \$322.5 million. We expect to continue to incur significant losses for the foreseeable future, and we expect these losses to increase as we continue our research and development of, and seek regulatory approvals for, our product candidates.

In addition, if we obtain regulatory approval of and seek to commercialize any of our product candidates, we will likely incur significant sales, marketing and manufacturing expenses and may continue to incur substantial research and development expenses for additional post-marketing approval development requirements related to such product. We may encounter unforeseen expenses, difficulties, complications, delays and other unknown factors that may adversely affect our business. The size of our future net losses will depend, in part, on the rate of future growth of our expenses and our ability to generate revenue. Our prior losses and expected future losses have had and will continue to have an adverse effect on our stockholders' equity and working capital.

We will require significant funding to complete the development and commercialization of BPX-501 and any of our other product candidates. If we fail to obtain additional financing, we may have to delay, reduce or eliminate our development programs or commercialization efforts.

Our operations have consumed substantial amounts of cash since our inception. We expect to continue to spend substantial amounts to continue the preclinical and clinical development of our product candidates and other research and development programs.

As of December 31, 2017, we had cash and cash equivalents of approximately \$45.0 million and total investments in marketable securities of \$61.5 million. We maintain our cash, cash equivalents, and marketable securities with high quality, accredited financial institutions. These amounts at times may exceed federally insured limits. We believe that cash and cash equivalents and investments in marketable securities, or a total of \$106.5 million, will be sufficient to fund our operations through the first quarter of 2019. However, changing circumstances may cause us to consume capital significantly faster than we currently anticipate.

We expect to finance future cash needs through public or private equity offerings, debt financings, strategic partnerships and alliances or licensing arrangements. We cannot be certain that additional funding will be available on acceptable terms, or at all. Subject to limited exceptions, our loan agreement with Oxford Finance prohibits us from incurring indebtedness without the prior written consent of Oxford. If we are unable to raise additional capital in sufficient amounts or on terms acceptable to us we will need to significantly delay, scale back or discontinue the development or commercialization of our product candidates. We also could be required to:

- seek collaborators for one or more of our current or future product candidates on terms that are less favorable than might otherwise be available;
- relinquish or license on unfavorable terms our rights to technologies or product candidates that we otherwise would seek to develop or commercialize ourselves; or
- seek a third party to acquire us or our assets.

Any of the above events could significantly harm our business, prospects, financial condition and results of operations and cause the price of our common shares to decline.





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Our U.S. IND for BPX-501 has been placed on clinical hold by the FDA after three cases of encephalopathy possibly related to BPX-501 were reported. We may not conduct any clinical trials under this IND until such clinical hold is lifted by the FDA. Foreign regulatory authorities may similarly impose clinical holds on our ongoing trials of BPX-501, which would significantly delay our development and could end our development of BPX-501.

We have received notice from the FDA that U.S. studies of BPX-501 have been placed on a clinical hold following three cases of encephalopathy deemed as possibly related to BPX-501. We are working on revising the clinical trial protocols and other actions required by the FDA for it to lift the clinical hold. If the clinical hold is not lifted, it is unlikely that we will be able to pursue any further development of this product candidate in the United States which will significantly reduce the potential market for this product candidate. While the clinical hold does not affect the ongoing BP-004 trial in Europe, foreign regulatory authorities, including in Europe, may follow the FDA and place holds on the clinical development of this product candidate, which would harm our business.

Biopharmaceutical product development is a highly speculative undertaking and involves a substantial degree of uncertainty. We have never generated any revenue from product sales and may never be profitable.

We have devoted substantially all of our financial resources and efforts to developing our proprietary CID technology platform, identifying potential product candidates and conducting preclinical studies and clinical trials. We are in the early stages of developing our product candidates, and we have not completed development of any products. Our ability to generate revenue and achieve profitability depends in large part on our ability, alone or with partners, to successfully complete the development of, obtain the necessary regulatory approvals for, and commercialize, product candidates. We do not anticipate generating revenues from sales of products for the foreseeable future. Our ability to generate future revenues from product sales depends heavily on our success in:

- completing requisite clinical trials through all phases of clinical development of BPX-501 and our other current product candidates;
- seeking and obtaining marketing approvals for BPX-501 and any other product candidates that successfully complete clinical trials, if any;
- launching and commercializing BPX-501 and other product candidates for which we obtain marketing approval, if any, with a partner or, if launched independently, successfully establishing a sales force, marketing and distribution infrastructure;
- identifying and developing new product candidates;
- progressing our pre-clinical programs into human clinical trials;
- establishing and maintaining supply and manufacturing relationships with third parties;
- developing new molecular switches based on our proprietary CID technology platform;
- maintaining, protecting, expanding and enforcing our intellectual property; and
- attracting, hiring and retaining qualified personnel.

Because of the numerous risks and uncertainties associated with biologic product development, we are unable to predict the likelihood or timing for when we may receive regulatory approval of BPX-501 or any of our other current or future product candidates or when we will be able to achieve or maintain profitability, if ever. If we do not receive regulatory approvals, our business, prospects, financial condition and results of operations will be adversely affected. Even if we obtain the regulatory approvals to market and sell one or more of our product candidates, we may never generate significant revenues from any commercial sales for several reasons, including because the market for our products may be smaller than we anticipate, or products may not be adopted by physicians and payors or because our products may not be as efficacious or safe as other treatment options. If we fail to successfully commercialize one or more products, we may be unable to generate sufficient revenues to sustain and grow our business and our business, prospects, financial condition and results of operations will be adversely affected. In addition, our expenses could increase beyond expectations if we are required by the European Medicines Agency, or EMA, the FDA, or other foreign regulatory agencies, to perform studies and clinical trials in addition to those that we currently anticipate for BPX-501 and our other product candidates, or if there are any delays in our or our partners completing clinical trials or the development of any of our product candidates. Further, if one or more of the product candidates that we independently develop is approved for commercial sale, we expect to incur significant costs associated with commercializing any such product candidates. Finally, even if we do achieve profitability, we may not be able to

sustain or increase profitability on a quarterly or annual basis.

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Our CID technology is novel and largely unproven.

Our proprietary CID technology platform is novel and there are no approved products or third-party product candidates in late-stage clinical trials based on this technology. Additionally, the safety and efficacy profile of rimiducid has not been subject to large scale clinical testing. If rimiducid is found to have a poor safety profile in clinical trials, or if our technology is not effective, we may be required to redesign all of our product candidates, which would require significant time and expense. In addition, our CID platform technology may not be applicable or effective in the development of additional cellular immunotherapies beyond our current programs which would adversely affect our business and prospects.

CAR T cell therapies are novel and present significant challenges.

CAR T and TCR product candidates represent a relatively new field of cellular immunotherapy. Advancing this novel and personalized therapy creates significant challenges for us, including:

- obtaining regulatory approval, as the EMA, FDA and other regulatory authorities have limited experience with commercial development of T-cell therapies for cancer;
- sourcing clinical and, if approved, commercial supplies for the materials used to manufacture and process our product candidates;
- developing a consistent and reliable process, while limiting contamination risks, for engineering and manufacturing T cells ex vivo and infusing the engineered T cells into the patient;
- educating medical personnel regarding the potential safety benefits, as well as the challenges, of incorporating our product candidates into their treatment regimens;
- establishing sales and marketing capabilities upon obtaining any regulatory approval to gain market acceptance of a novel therapy; and
- the availability of coverage and adequate reimbursement from third-party payors for our novel and personalized therapy.

Our inability to successfully develop CAR T and TCR cell therapies or develop processes related to the manufacture, sales and marketing of these therapies would adversely affect our business, results of operations and prospects.

The EMA and/or FDA may disagree with our regulatory plans and we may fail to obtain regulatory approval of our product candidates.

Our business and future success depends, in part, on our ability to obtain regulatory approval of and then successfully commercialize BPX-501 and our other clinical product candidates. All of our product candidates, including BPX-501, will require additional clinical and non-clinical development, regulatory review and approval in multiple jurisdictions, substantial investment, and access to sufficient commercial manufacturing capacity and significant marketing efforts before we can expect to generate any revenue from product sales.

BPX-501 and our other product candidates could fail to receive regulatory approval for many reasons, including the following:

- the EMA, FDA or comparable foreign regulatory authorities may disagree with the design or implementation of our clinical trials;
- we may be unable to demonstrate to the satisfaction of the EMA, FDA or comparable foreign regulatory authorities that our product candidates have the necessary safety, purity, and potency for any of their proposed indications;
- the results of clinical trials may not meet the level of statistical significance required by the EMA, FDA or comparable foreign regulatory authorities for approval;
- we may be unable to demonstrate that our product candidates' clinical and other benefits outweigh their safety risks;
- we may encounter serious and unexpected adverse events during clinical trials that render our products unsafe for use in humans;
- the EMA, FDA or comparable foreign regulatory authorities may disagree with our interpretation of data from preclinical studies or clinical trials;

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the data collected from clinical trials of our product candidates may not be sufficient to the satisfaction of the EMA, FDA or comparable foreign regulatory authorities to support the submission of an MAA, BLA or other comparable submission in foreign jurisdictions or to obtain regulatory approval in Europe, the U.S. or elsewhere; the EMA, FDA or comparable foreign regulatory authorities may fail to approve our manufacturing processes and/or facilities of third-party manufacturers with which we contract for clinical and commercial supplies; and the approval policies or regulations of the EMA, FDA or comparable foreign regulatory authorities may significantly change in a manner rendering our clinical data insufficient for approval.

We plan to initially seek approval for BPX-501 and rimiducid from the EMA for the treatment of pediatric patients undergoing haploidentical (partial match) hematopoietic stem cell transplants, or HSCT, and to submit the marketing authorization applications, or MAAs, for this indication in 2019. While we expect that the European arm of our BP-004 trial could serve as the registrational trial for these MAAs, this clinical trial was not originally designed for that purpose. We cannot be certain that our preclinical and clinical trial package for the MAAs will be sufficient for approval of BPX-501 for multiple reasons including issues related to trial conduct and analysis; limitations of data available from pre-clinical and Phase 1/2 studies; or issues related to CMC efforts to date. We have sought to avoid or remediate potential issues but we cannot be sure that such efforts will be effective or sufficient. Further, we cannot assure you that the EMA or any other regulatory agency will agree that BPX-501 provides a clinically meaningful and differentiated therapeutic benefit or that the side effects experienced in our clinical trials yield an acceptable benefit/risk ratio in the opinion of the EMA or other regulatory agencies. If the MAAs for BPX-501 are deficient, we will incur additional expenses to address the deficiencies, which may require additional clinical trials, and the commercialization of BPX-501 will be delayed. This would adversely affect our business, results of operations and prospects.

We, or our institutional collaborators, are conducting and planning additional clinical trials of BPX-501 designed to support FDA approval of our therapy in multiple indications. In each case, we plan to conduct one clinical trial to support registration in that indication. However, the general approach for FDA approval of a new biologic or drug is dispositive data from two adequate and well-controlled, Phase 3 clinical trials of the relevant biologic or drug in the relevant patient population. Phase 3 clinical trials typically involve hundreds of patients, have significant costs and take years to complete. We believe that a single Phase 3 clinical trial strategy is warranted given the limited alternatives for patients for which BPX-501 therapy is potentially beneficial, but the FDA may ultimately require more than one Phase 3 clinical trial and may limit clinical trial designs allowed to serve as a registration trial. In addition, because BPX-501 is our most advanced product candidate, and because many of our other product candidates are based on similar technology, if BPX-501 encounters safety or efficacy problems, developmental delays, regulatory issues or other problems, our development plans and business for our other product candidates would be significantly harmed.

Our clinical trials may fail to adequately demonstrate the safety and efficacy of any of our product candidates, which would prevent or delay regulatory approval and commercialization.

Clinical testing is expensive, takes many years to complete, and its outcome is inherently uncertain. Failure can occur at any time during the clinical trial process and our product candidates are subject to the risks of failure inherent in biologic drug development. Success in early clinical trials does not mean that later clinical trials will be successful because product candidates in later-stage clinical trials may fail to demonstrate sufficient safety or efficacy despite having progressed through initial clinical testing, even at statistically significant levels. We will be required to demonstrate through clinical trials that our product candidates are safe and effective for use in the target indication before we can obtain regulatory approvals for commercial sale. Companies frequently suffer significant setbacks in late-stage clinical trials, even after earlier clinical trials have shown promising results and most product candidates that commence clinical trials are never approved as products. We expect there may be greater variability in results for cellular immunotherapy products processed and administered on a patient-by-patient basis, like all of our CID technology-based development and product candidates, than for “off-the-shelf” products, like many drugs.

If any of our product candidates fail to demonstrate sufficient safety or efficacy, we would experience potentially significant delays in, or be required to abandon our development of the product candidate, which would have a material and adverse impact on our business, prospects, financial condition and results of operations.

Many of our current product candidates are in early stage clinical trials, and we may experience unfavorable results in the future.

We have begun enrolling patients in Phase 1 clinical trials of BPX-601 for the treatment of non-resectable pancreatic cancer and BPX-701 for the treatment of refractory or relapsed acute myeloid leukemia, or AML, and myelodysplastic syndromes, or MDS. We have not initiated clinical trials for any additional preclinical product candidates and we may not be able to commence clinical trials on the time frames we expect. As these product candidates are in early stages of development, we face significant

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uncertainty regarding how effective and safe they will be in human patients and the results from preclinical studies, such as in vitro and in vivo studies, of BPX-601 and BPX-701 and our other preclinical programs may not be indicative of the results of clinical trials of these product candidates. Preclinical and clinical data are often susceptible to varying interpretations and analyses, and many companies that have believed their product candidates performed satisfactorily in preclinical studies and clinical trials have nonetheless failed to obtain marketing approval for their products.

Even if clinical trials are successfully completed, the FDA or foreign regulatory authorities may not interpret the results as we do, and more clinical trials could be required before we submit our product candidates for approval. To the extent that the results of our clinical trials are not satisfactory to the FDA or foreign regulatory authorities for support of a marketing application, approval of our product candidates may be significantly delayed, or we may be required to expend significant additional resources, which may not be available to us, to conduct additional clinical trials in support of potential approval of our product candidates.

We may not be successful in our efforts to use and expand our CID platform to build a pipeline of product candidates and develop marketable products.

We believe that our CID platform, which serves as the foundation of our CaspaCIDE and GoCAR-T technologies, can be further leveraged to discover other novel technologies, therapeutic applications and market opportunities. For example, we are currently conducting research in applying our platform TCR therapies for solid tumors, where immune toxicities associated with treatment can be even more severe than CAR T therapies. We are also developing new molecular switches and dual-switch systems to provide greater control over cellular immunotherapy. We are at an early stage of development and our platform has not yet, and may never lead to, approved or marketable products.

Even if we are successful in continuing to build our pipeline, the potential product candidates that we identify may not be suitable for clinical development, including for reasons related to their harmful side effects, limited efficacy or other characteristics that indicate that they are unlikely to be products that will receive marketing approval and achieve market acceptance. If we do not successfully develop and commercialize product candidates based upon our technological approach, we may not be able to obtain product or partnership revenues in future periods, which would adversely affect our business, prospects, financial condition and results of operations.

We rely and will continue to rely on third parties to conduct our clinical trials. If these third parties do not successfully carry out their contractual duties or meet expected deadlines, we may not be able to obtain regulatory approval of or commercialize our product candidates.

We depend and will continue to depend upon independent investigators and collaborators, such as universities, medical institutions, and strategic partners to conduct our preclinical and clinical trials under agreements with us. Negotiations of budgets and contracts with study sites may result in delays to our development timelines and increased costs. We will rely heavily on these third parties over the course of our clinical trials, and we control only certain aspects of their activities. Nevertheless, we are responsible for ensuring that each of our studies is conducted in accordance with applicable protocol, legal, regulatory and scientific standards, and our reliance on third parties does not relieve us of our regulatory responsibilities. We and these third parties are required to comply with current good clinical practices, or cGCPs, which are regulations and guidelines enforced by the FDA and comparable foreign regulatory authorities for product candidates in clinical development. Regulatory authorities enforce these cGCPs through periodic inspections of clinical trial sponsors, principal investigators and clinical trial sites. If we or any of these third parties fail to comply with applicable cGCP regulations, the clinical data generated in our clinical trials may be deemed unreliable and the FDA or comparable foreign regulatory authorities could require us to perform additional clinical trials before approving our marketing applications. It is possible that, upon inspection, such regulatory authorities could determine that any of our clinical trials fail to comply with the cGCP regulations. In addition, our clinical trials must be conducted with biologic product produced under cGMPs, regulations and will require a large number of test patients. Our failure or any failure by these third parties to comply with these regulations or to recruit a sufficient number of patients may require us to repeat clinical trials, which would delay the regulatory approval process. Moreover, our business may be implicated if any of these third parties violates federal or state fraud and abuse or false claims laws and regulations or healthcare privacy and security laws.

Any third parties conducting our clinical trials are and will not be our employees and, except for remedies available to us under our agreements with these third parties, we cannot control whether or not they devote sufficient time and resources to our ongoing preclinical, clinical and nonclinical programs. These third parties may also have relationships with other commercial entities, including our competitors, for whom they may also be conducting clinical trials or other drug development activities, which could affect their performance on our behalf. If these third parties do not successfully carry out their contractual duties or obligations or meet expected deadlines, if they need to be replaced or if the quality or accuracy of the clinical data they obtain is compromised due to the failure to adhere to our clinical protocols or regulatory requirements or for other reasons, our clinical trials may be extended, delayed or terminated and we may not be able to complete development of, obtain regulatory approval of or successfully commercialize our product candidates. As a result, our financial results and the commercial prospects for our product candidates would be harmed, our costs could increase and our ability to generate revenue could be delayed.

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Switching or adding third parties to conduct our clinical trials involves substantial cost and requires extensive management time and focus. In addition, there is a natural transition period when a new third party commences work. As a result, delays occur, which can materially impact our ability to meet our desired clinical development timelines. Also, we are conducting multiple clinical trials in Europe and may plan additional testing of our technology and product candidates in other foreign jurisdictions. We currently have limited staffing and capabilities in foreign countries, and may not be able to effectively resolve potential disputes with our independent investigators and collaborators.

If we encounter difficulties enrolling patients in our clinical trials, our clinical development activities could be delayed or otherwise adversely affected.

We may experience difficulties in patient enrollment in our clinical trials for a variety of reasons. The timely completion of clinical trials in accordance with their protocols depends, among other things, on our ability to enroll a sufficient number of patients who remain in the study until its conclusion. The enrollment of patients depends on many factors, including:

- the patient eligibility criteria defined in the protocol;
- the size of the patient population required for analysis of the trial's primary endpoints;
- the proximity of patients to study sites;
- the design of the clinical trial;
- our ability to recruit clinical trial investigators with the appropriate competencies and experience;
- our ability to obtain and maintain patient consents;
- the risk that patients enrolled in clinical trials will drop out of the clinical trials before completion; and
- competing clinical trials and approved therapies available for patients.

In particular, some of our clinical trials will look to enroll patients with characteristics which are found in a very small population, for example, patients with rare cancers with specific attributes that are targeted with our product candidates and patients with orphan inherited blood disorders. Our clinical trials will compete with other companies' clinical trials for product candidates that are in the same therapeutic areas as our product candidates, and this competition will reduce the number and types of patients available to us, because some patients who might have opted to enroll in our clinical trials may instead opt to enroll in a trial being conducted by one of our competitors. Since the number of qualified clinical investigators is limited, we expect to conduct some of our clinical trials at the same clinical trial sites that some of our competitors use, which will reduce the number of patients who are available for our clinical trials in these clinical trial sites. Moreover, because our product candidates represent a departure from more commonly used methods for cancer treatment, potential patients and their doctors may be inclined to use conventional therapies, such as chemotherapy and antibody therapy, rather than enroll patients in any of our future clinical trials. Patients may also be unwilling to participate in our clinical trials because of negative publicity from adverse events in the biotechnology or gene therapy industries.

Delays in patient enrollment may result in increased costs or may affect the timing or outcome of the planned clinical trials, which could prevent completion of these clinical trials and adversely affect our ability to advance the development of our product candidates.

Any adverse developments that occur during any clinical trials conducted by academic investigators, our collaborators or other entities conducting clinical trials under independent INDs may affect our ability to obtain regulatory approval or commercialize our product candidates.

Rimiducid, BPX-501 and certain of our other CaspaCIDE product candidates are being used by third parties in clinical trials for which we are collaborating or in clinical trials which are completely independent of our development programs. We have little to no control over the conduct of those clinical trials. If serious adverse events occur during these or any other clinical trials using our product candidates, the FDA and other regulatory authorities may delay, limit or deny approval of our product candidate or require us to conduct additional clinical trials as a condition to marketing approval, which would increase our costs. If we receive regulatory approval for any product candidate and a new and serious safety issue is identified in connection with clinical trials conducted by third parties, the applicable regulatory authorities may withdraw their approval of the product or otherwise restrict our ability to market and sell



our product. In addition, treating physicians may be less willing to administer our product due to concerns over such adverse events, which would limit our ability to commercialize our product.

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Adverse side effects or other safety risks associated with our product candidates could delay or preclude approval, cause us to suspend or discontinue clinical trials, abandon product candidates, limit the commercial profile of an approved label, or result in significant negative consequences following marketing approval, if any.

In third party clinical trials involving CAR T cells, the most prominent acute toxicities included symptoms thought to be associated with the release of cytokines, such as fever, low blood pressure and kidney dysfunction. Some patients also experienced toxicity of the central nervous system, such as confusion, cranial nerve dysfunction and speech impairment. Adverse side effects attributed to CAR T cells were severe and life-threatening in some patients. The life-threatening events were related to kidney dysfunction and toxicities of the central nervous system. Severe and life-threatening toxicities occurred primarily in the first two weeks after cell infusion and generally resolved within three weeks. In the past, several patients have also died in clinical trials by others involving CAR T cells.

Undesirable side effects observed in our clinical trials, whether or not they are caused by our product candidates, could result in the delay, suspension or termination of clinical trials by us, the FDA or other regulatory authorities for a number of reasons. In addition, because the patients in our clinical trials are suffering from life-threatening diseases, are often suffering from multiple complicating conditions and, in the case of transplant patients, are in a position of extreme immune deficiency at the time that they receive our therapy, it may be difficult to accurately assess the relationship between our product candidates and adverse events experienced by very ill patients. In January 2018, we received notice from the FDA that all clinical trials of BPX-501 in the United States have been placed on a clinical hold following three cases of encephalopathy deemed as possibly related to BPX-501, and we are currently unable to continue to enroll additional patients in these trials until the FDA lifts the clinical hold. If we elect or are required to delay, suspend or terminate any clinical trial of any product candidates that we develop, the commercial prospects of such product candidates will be harmed and our ability to generate product revenues from any of these product candidates will be delayed or eliminated. Serious adverse events observed in clinical trials could hinder or prevent market acceptance of the product candidate at issue. Any of these occurrences may harm our business, prospects, financial condition and results of operations significantly.

Clinical trials are expensive, time-consuming and difficult to design and implement.

Human clinical trials are expensive and difficult to design and implement, in part because they are subject to rigorous regulatory requirements. Because our product candidates are based on relatively new technology and engineered on a patient-by-patient basis, we expect that they will require extensive research and development and have substantial manufacturing and processing costs. In addition, costs to treat patients with relapsed/refractory cancer and to treat potential side effects that may result from therapies such as our current and future product candidates can be significant. Accordingly, our clinical trial costs are likely to be significantly higher than for more conventional therapeutic technologies or drug products. In addition, our proposed personalized product candidates involve several complex and costly manufacturing and processing steps, the costs of which will be borne by us. The costs of our clinical trials may increase if the FDA does not agree with our clinical development plans or requires us to conduct additional clinical trials to demonstrate the safety and efficacy of our product candidates.

We face significant competition from other biotechnology and pharmaceutical companies, and our operating results will suffer if we fail to compete effectively.

The biopharmaceutical industry is characterized by intense competition and rapid innovation. Our competitors may be able to develop other compounds or drugs that are able to achieve similar or better results. Our potential competitors include major multinational pharmaceutical companies, established biotechnology companies, specialty pharmaceutical companies and universities and other research institutions. Many of our competitors have substantially greater financial, technical and other resources, such as larger research and development staff and experienced marketing and manufacturing organizations and well-established sales forces. Smaller or early-stage companies may also prove to be significant competitors, particularly through collaborative arrangements with large, established companies. Mergers and acquisitions in the biotechnology and pharmaceutical industries may result in even more resources being concentrated in our competitors. Competition may increase further as a result of advances in the commercial applicability of technologies and greater availability of capital for investment in these industries. Our competitors, either alone or with collaborative partners, may succeed in developing, acquiring or licensing on an exclusive basis drug or biologic products that are more effective, safer, more easily commercialized or less costly than

our product candidates or may develop proprietary technologies or secure patent protection that we may need for the development of our technologies and products. We believe the key competitive factors that will affect the development and commercial success of our product candidates are efficacy, safety, tolerability, reliability, convenience of use, price and reimbursement.

Specifically, genetically engineering T cells faces significant competition in both the CAR and TCR technology space from multiple companies, including Adaptimmune, bluebird bio, Inc., Celgene Corporation, Collectis SA, GlaxoSmithKline plc, Intrexon Corporation, Juno Therapeutics, Inc., Kite Pharma, Inc., Novartis AG, Pfizer Inc. and Ziopharm Oncology. BPX-501, is an adjunct therapy for HSCT with alternative donors that potentially improves stem cell engraftment, accelerates host immune

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system recovery and treats GvHD. Even if we obtain regulatory approval of our product candidates, the availability and price of our competitors' products could limit the demand and the price we are able to charge for our product candidates. We may not be able to implement our business plan if the acceptance of our product candidates is inhibited by price competition or the reluctance of physicians to switch from existing methods of treatment to our product candidates, or if physicians switch to other new drug or biologic products or choose to reserve our product candidates for use in limited circumstances. For additional information regarding our competition, see "Item 1. Business—Competition."

BPX-501 and rimiducid have received orphan drug designation, but we may be unable to maintain or receive the benefits associated with orphan drug status, including market exclusivity.

The FDA or EMA grant orphan designation to a drug or biologic intended to treat a rare disease or condition or for which there is no reasonable expectation that the cost of developing and making available in that jurisdiction a drug or biologic for a disease or condition will be recovered from sales in that jurisdiction for that drug or biologic. If a product that has orphan drug designation subsequently receives the first FDA or EMA approval for the disease for which it has such designation, the product is entitled to orphan product exclusivity, which means that the FDA or EMA may not approve any other applications, including a full authorization to market the same biologic for the same indication for seven years in the U.S. and for 10 years in Europe, except in limited circumstances, such as a showing of clinical superiority to the product with orphan drug exclusivity.

The EMA has granted orphan drug designations to BPX-501 for treatment in HSCT, and for activator agent rimiducid for the treatment of GvHD. Additionally, BPX-501 and rimiducid have received orphan drug designation from the FDA, as a combination replacement T-cell therapy for the treatment of immunodeficiency and GvHD after allogeneic HSCT. However, in each case, exclusive marketing rights may be limited if we seek approval for an indication broader than the orphan designated indication and may be lost if the EMA or FDA, as applicable, later determines that the request for designation was materially defective or if we are unable to assure the availability of sufficient quantities of the product to meet the needs of patients with the rare disease or condition. Although the respective designations may provide seven years of market exclusivity in the U.S. and 10 years of market exclusivity in Europe, the designations are subject to certain limited exceptions. Therefore, even though we have obtained orphan drug designation for certain indications, we may be unable to obtain orphan drug designation for our future product candidates and we may not be the first to obtain marketing approval for any particular orphan indication.

We are highly dependent on our key personnel, and if we are not successful in attracting and retaining highly qualified personnel, we may not be able to successfully implement our business strategy.

Our ability to compete in the highly competitive biotechnology and pharmaceutical industries depends upon our ability to attract and retain highly qualified managerial, scientific and medical personnel. We are highly dependent on our management, scientific and medical personnel, including our President and Chief Executive Officer, our Chief Financial Officer and Treasurer, our Chief Medical Officer and our Executive Vice President of Technical Operations. The loss of the services of any of our executive officers, other key employees, and other scientific and medical advisors, and our inability to find suitable replacements could result in delays in product development and harm our business.

To induce valuable employees to remain at our company, in addition to salary and cash incentives, we have provided stock options and restricted stock units (RSUs) that vest over time. The value to employees of stock options and RSUs that vest over time may be significantly affected by movements in our stock price that are beyond our control, and may at any time be insufficient to counteract more lucrative offers from other companies. Despite our ef