Table of Contents

UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
Washington, DC 20549

FORM 10-K

☒ **ANNUAL REPORT UNDER SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934**

For the fiscal year ended December 31, 2017

OR

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

For the transition period from _____ to _____

Commission File Number 001-33038

ZIOPHARM Oncology, Inc.

(Exact Name of Registrant as Specified in Its Charter)

Delaware	**84-1475642**
(State or Other Jurisdiction of Incorporation or Organization)	**(IRS Employer Identification No.)**
One First Avenue, Parris Building 34, Navy Yard Plaza Boston, Massachusetts	**02129**
(Address of Principal Executive Offices)	**(Zip Code)**

(617) 259-1970
(Registrant's Telephone Number, Including Area Code)

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

Common Stock (par value $0.001 per share)

Indicate by check mark if the registrant is a well-known seasoned issuer, as defined in Rule 405 of the Securities Act. Yes ☐ No ☒

Indicate by check mark if the registrant is not required to file reports pursuant to Section 13 or 15(d) of the 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 past 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 Web site, if any, every Interactive Data File required to be submitted and posted pursuant to Rule 405 of Regulation S-T 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 incorporated by reference in Part III of this Form 10-K or any amendment to this Form 10-K. ☐

Indicate by check mark whether the registrant is a large accelerated filer, an accelerated filer, a non-accelerated filer or a smaller reporting company. See definition of "large accelerated filer," "accelerate filer" and "smaller reporting company" in Rule 12b-2 of the Exchange Act. (Check one):

Large Accelerated Filer	☒	Accelerated Filer	☐
Non-Accelerated Filer	☐	Smaller Reporting Company	☐
		Emerging growth company	☐

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

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

The aggregate market value of the registrant's common stock held by non-affiliates was $808,804,937 as of June 30, 2017 (the last business day of the registrant's most recently completed second fiscal quarter), based on a total of 130,032,948 shares of common stock held by non-affiliates and a closing price of $6.22 as reported on the Nasdaq Capital Market on June 30, 2017. For purposes of this computation, all officers, directors, and 10% beneficial owners of the registrant are deemed to be affiliates. Such determination should not be deemed to be an admission that such officers, directors or 10% beneficial owners, are, in fact, affiliates of the registrant.

As of February 21, 2018, there were 142,398,936 shares of the registrant's common stock, $0.001 par value per share, outstanding.

DOCUMENTS INCORPORATED BY REFERENCE:

Portions of the definitive proxy statement for the registrant's 2018 annual meeting of stockholders, which is to be filed within 120 days after the end of the fiscal year ended December 31, 2017, are incorporated by reference into Part III of this Form 10-K, to the extent described in Part III.

ZIOPHARM Oncology, Inc.
ANNUAL REPORT ON FORM 10-K
FOR THE FISCAL YEAR ENDED DECEMBER 31, 2017

TABLE OF CONTENTS

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Special Note Regarding Forward-Looking Statements

This Annual Report on Form 10-K contains forward-looking statements that are based on management's current beliefs and assumptions and on information currently available to management. All statements other than statements of historical facts contained in this Annual Report are forward-looking statements. In some cases, you can identify forward-looking statements by words such as: "anticipate," "believe," "estimate," "expect," "forecast," "intend," "may," "plan," "project," "target," "will" and other words and terms of similar meaning.

These statements involve risks, uncertainties and other factors that may cause actual results, levels of activity, performance or achievements to be materially different from the information expressed or implied by these forward-looking statements. Although we believe that we have a reasonable basis for each forward-looking statement contained in this report, we caution you that these statements are based on a combination of facts and factors currently known by us and our projections of the future, about which we cannot be certain. Forward-looking statements in this Annual Report include, but are not limited to, statements about:

- our ability to raise substantial additional capital to fund our planned operations and to continue as a going concern;
- our estimates regarding expenses, use of cash, timing of future cash needs and capital requirements;
- the development of our product candidates, including statements regarding the timing of initiation, completion and the outcome of clinical studies or trials and related preparatory work and the period during which the results of the trials will become available;
- our ability to advance our product candidates through various stages of development, especially through pivotal safety and efficacy trials;
- the risk that final trial data may not support interim analysis of the viability of our product candidates;
- our expectation regarding the safety and efficacy of our product candidates;
- the progress and timing of our research and development programs;
- the timing, scope or likelihood of regulatory filings and approvals from the U.S. Food and Drug Administration or equivalent foreign regulatory agencies for our product candidates and for which indications;
- our ability to license additional intellectual property relating to our product candidates from third parties and to comply with our existing license agreement;
- our ability to achieve the results contemplated by our collaboration agreements and the benefits to be derived from relationships with collaborators;
- developments and projections relating to competition from other pharmaceutical and biotechnology companies or our industry;
- our estimates regarding the potential market opportunity for our product candidates;
- the anticipated rate and degree of market acceptance of our product candidates for any indication if approved;
- the anticipated amount, timing and accounting of deferred revenues, milestones and other payments under licensing, collaboration or acquisition agreements, research and development costs and other expenses;
- our intellectual property position, including the strength and enforceability of our intellectual property rights;
- our ability to attract and retain qualified employees and key personnel;

- the impact of government laws and regulations in the United States and foreign countries; and
- other risks and uncertainties, including those listed under Part II, Item 1A, Risk Factors.

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

Unless the context requires otherwise, references in this Annual Report to “Ziopharm,” the “Company,” “we,” “us” and “our” refer to Ziopharm Oncology, Inc. and its subsidiaries.

PART I

Item 1. Business

Business Overview

Ziopharm Oncology, Inc. is a biopharmaceutical company focused on discovering, acquiring, developing and commercializing next generation immunotherapy platforms that leverage gene- and cell-based therapies to treat patients with cancer on its own and with partners. We are developing two immuno-oncology platform technologies designed to utilize the patient's immune system by employing novel, controlled gene expression and innovative cell engineering technologies to deliver safe, effective, and scalable cell- and viral-based therapies for the treatment of multiple cancer types. Our first platform is Controlled IL-12, which delivers interleukin 12 or IL-12, a master regular of the immune system, in a controlled and safe manner to focus the patient's immune system to cancer. Our second platform is referred to as Sleeping Beauty and is based on the genetic engineering of T-cells using the *Sleeping Beauty* (SB) system to rapidly reprogram T-cells outside of the body for subsequent infusion. We believe these two platforms provide or will provide unique and powerful solutions intended to advance the field of immune-oncology and address the issues associated with (1) treating heterogenous solid tumors and unknown antigens therein through control of IL-12 and (2) providing rapid and cost-effective manufacturing solutions for CAR and TCR-based cell therapies for hematologic malignancies and solid tumors against known antigens.

With our partner Precigen, Inc., or Precigen, a wholly owned subsidiary of Intrexon Corporation we are in late stage development of a gene therapy that delivers controlled IL-12 to treat patients with brain cancer, and based on technology licensed from MD Anderson Cancer Center, we are developing chimeric antigen receptor (CAR) T-cell (CAR+ T) and T-cell receptor (TCR) T-cell (TCR+ T) therapies. These programs are being advanced in collaboration with Precigen and selectively with MD Anderson Cancer Center (MD Anderson), the National Cancer Institute (NCI) and Ares Trading, or Ares, a biopharmaceutical division of Merck KGaA, Darmstadt, Germany.

Control of IL-12 is achieved from a replication-incompetent adenoviral (AD) vector administered via a single injection of virus into the brain tumor and engineered to conditionally express human IL-12 (hIL-12. The conditional expression of hIL-12 is modulated with the RheoSwitch Therapeutic System® (RTS®) by the small molecule veledimex, an activator ligand orally administered which has been shown to cross the blood-brain barrier. A Phase 1 trial in patients at high risk for death due to disease progression produced data demonstrating the safety of controlled local expression of IL-12 and showed that IL-12 by itself apparently can improve the survival of patients with recurrent glioblastoma, or rGBM. The mechanism by which these patients developed an anti-tumor effect is due to IL-12 turning "cold tumors hot" as shown from repeat biopsies that revealed a new and sustained infiltrate of activated T-cells producing interferon gamma (IFN-g) within the brain-tumor lesion. These data are consistent with biopsy data from patients with breast cancer that also showed IL-12 turning cold tumors hot, which could have a profound impact for oncology in general.

Initially, we are developing this controlled IL-12 therapy as a mono therapy entering a Phase 3 randomized control trial for the treatment of rGBM in 2018 and as Phase 1 trials that are underway to evaluate stereotactic administration and for pediatric brain tumors. In addition, we are pursuing the development of controlled IL-12 combined with a checkpoint inhibitor, for which a Phase 1 trial is currently underway.

We are using the non-viral SB transposon/transposase system to develop targeted therapies relating to novel CARs and TCRs. The SB technology reprograms T-cells to recognize and attack cancer cells with certain pre-defined antigens. We believe our manufacturing process for producing and then infusing genetically-modified T-cells holds significant potential to greatly reduce time of manufacture and cost which, we predict, will improve scalability to meet demand. SB-modified T-cells are being studied in Phase 1 studies to treat hematologic cancers, and we, together with our partners, intend to pursue other Phase 1 trials this year in additional indications, including solid tumors.

We are developing these technologies pursuant to an exclusive channel partner agreement, or Channel Agreement, with Precigen, through which we obtained certain exclusive rights to Precigen's technologies for use in the fields of oncology. In addition, we, together with Precigen, hold exclusive worldwide rights to certain additional immuno-oncology technologies owned and licensed by MD Anderson, including technologies relating to SB. The Channel Agreement and the MD Anderson License, as well as other licensing agreements and collaborations with the NCI, Merck KGaA and others are discussed in more detail below.

Recent Developments

Controlled IL-12 Platform

In January 2018, we provided updates on the continued development of our Controlled IL-12 platform and development programs for the treatment of brain cancer [at JPM?]. We announced the initiation of a Phase I clinical trial to evaluate Ad-RTS-hIL-12 plus veledimex in combination with OPDIVO® (nivolumab), an immune checkpoint, or PD-1 inhibitor, in adult patients with rGBM. We also updated guidance on our planned pivotal trial of Ad-RTS-hIL-12 plus veledimex and announced that we currently anticipate initiation in the second half of 2018, subject to regulatory approval. We have designed a Phase 3 randomized control trial to evaluate Controlled IL-12 for the treatment of patients with rGBM and following meetings with U.S. and European regulators, we are completing execution of Chemistry Manufacturing and Control (CMC) technical requirements.

In November 2017, during the 22nd Annual Meeting and Education Day of the Society for Neuro-Oncology (SNO) in San Francisco, we made multiple presentations on controlled IL-12. New data presented included sustained median overall survival (mOS) of 12.5 months for patients treated with Ad-RTS-hIL-12 plus 20mg of veledimex (n=15) at a longer mean follow-up time of 11.1 months as of October 18, 2017, which compares favorably to the 5- to 8-months overall survival data of approved therapies. Additional data relative to an influx of cytotoxic T-cells, increased expression levels of PD-1 and PD-L1, peripheral biomarkers and the impact of low-dose steroids on survival were presented.

In October 2017, we announced the first patient dosed in a Phase 1 trial of Ad-RTS-hIL-12 + veledimex for the treatment of pediatric brain tumors.

Sleeping Beauty Platform

In December 2017, we delivered multiple presentations on our adoptive cell therapy programs and application of the SB technology at the 59th American Society of Hematology (ASH) Annual Meeting and Exposition in Atlanta. We presented on the advancement of our SB platform towards point-of-care (P-O-C) for very rapid manufacturing of genetically modified CAR+ T cells. Data presented from first- and second-generation SB clinical trials demonstrate tolerability, disease response, long-term survival and persistence of infused CD19-specific CAR+ T cells. Preclinical studies presented at ASH and at the Keystone Symposia in February 2018 showed that P-O-C CAR+ T cells co-expressing membrane-bound interleukin-15 (mbIL15) and a control switch manufactured within two days do not require activation or propagation in tissue culture to achieve anti-tumor effects and prolonged T-cell survival in mice. Building on these data, we plan to initiate an investigator-led first P-O-C clinical trial in the second half of 2018 at MD Anderson.

We also updated guidance on the anticipated start of the NCI-led Phase 1 trial to evaluate adoptive cell transfer (ACT)-based immunotherapies genetically modified using the SB transposon/transposase system to express TCRs for the treatment of solid tumors. We, Intrexon (now Precigen), and NCI last year entered into a Cooperative Research and Development Agreement (CRADA) to develop and evaluate ACT for patients with advanced cancers using autologous peripheral blood lymphocytes (PBL) genetically modified using the non-viral SB system to express TCRs that recognize specific immunogenic mutations, or neoantigens, expressed within a patient's cancer. We expect this Phase 1 trial, which is being led by and conducted at the NCI, to be initiated in the second half of 2018.

Refocusing of Research and Development Efforts

We previously entered into an agreement with Intrexon (now Precigen) to pursue, through collaboration, the potential treatment and prevention of graft versus host disease, or GvHD. As a result of an in-depth review of our research and development portfolio, we determined that the pursuit of GvHD as an indication was not a material part of our corporate strategy and therefore have decided to stop pursuing the development of engineered cell therapy strategies, used either separately or in combination, for targeted treatment of GvHD. We have reverted our rights under the GvHD program back to Precigen [and are in the process of winding down the related activities]. We made this decision to focus our efforts and resources on the development of our Controlled IL-12 and Sleeping Beauty platforms for the treatment of oncology indications.

Platform Technologies

Immuno-oncology, which typically utilizes a patient's own immune system to treat cancer, is one of the most actively pursued areas of research by biotechnology and pharmaceutical companies today. Cancer cells contain mutated proteins and may overexpress other proteins usually found in the body at low levels. The immune system typically recognizes unusual or aberrant cell protein expression and eliminates these cells in an efficient process known as immune surveillance. Central to immune surveillance are types of white blood cells known as T-cells and NK cells. In healthy individuals, T-cells and NK cells can identify and kill infected or abnormal cells, including cancer cells. Cancer cells develop the ability to evade immune surveillance, which is a key factor in their growth, spread, and persistence. In the recent past, there has been substantial scientific progress in countering these evasion mechanisms using immunotherapies, or therapies that activate the immune system.

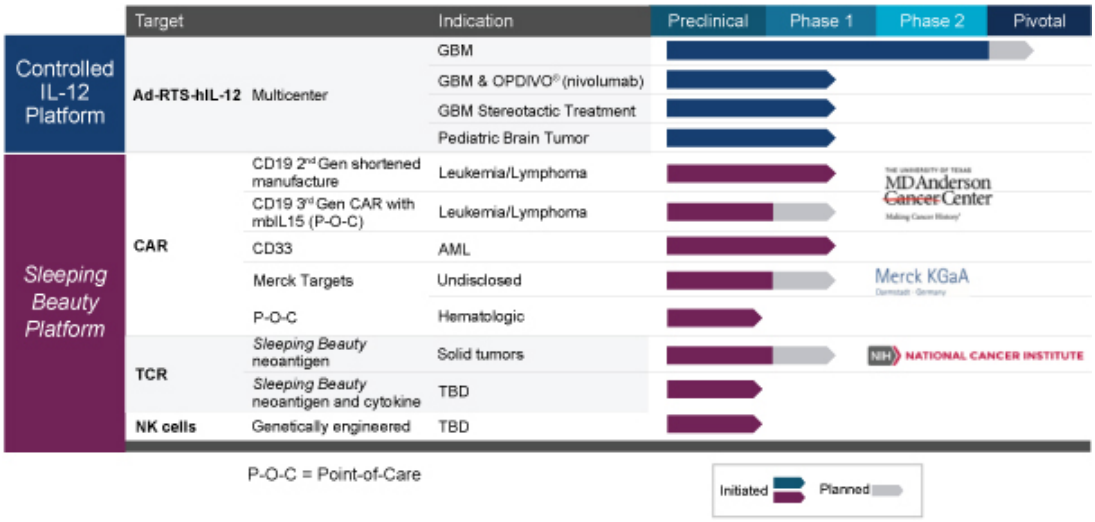
Our approach to immuno-oncology entails the application of engineering principles to biological systems for designing and constructing new biological systems or redesigning/modifying existing biological systems. Biological systems are governed by DNA, the building block of genetic programs, which control cellular processes by coding to produce proteins and other molecules that have a functional purpose and by regulating the activities of these molecules. This regulation occurs via complex biochemical and cellular reactions working through intricate cell signaling pathways, and control over these molecules modifies the output of biological systems. Our approach to immuno-oncology has been enabled by the application of information technology and advanced statistical analysis, also known as bioinformatics, to genetic engineering, as well as by improvements in DNA synthesis. This approach aims to engineer gene-based programs or codes to modify cellular function to achieve a desired biological outcome. Its application is intended to allow more precise control of drug concentration and dose, thereby improving the therapeutic index associated with the resulting drug. A further embodiment of this technology is the ability to eliminate genetically modified immune cells after infusion.

We are developing two platform technologies which we use in the implementation of our product candidates:

- Controlled IL-12: An immune system master regulator which weaponizes the immune system delivered in a tunable dose;
- *Sleeping Beauty*: A non-viral genetic manipulation that empowers and directs T-cells to fight cancer.

Product Candidates

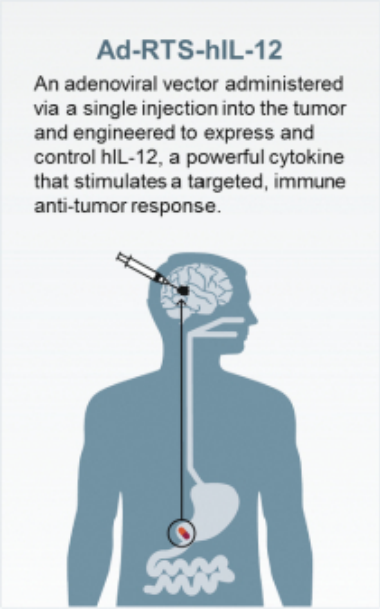
The following chart identifies our immuno-oncology product candidates and their current stage of development, each of which are described in more detail below.



Controlled IL-12 Platform

Background

Ad-RTS-hIL-12 plus veledimex, our most advanced product candidate, uses our gene delivery system to produce IL-12, a potent, naturally occurring anti-cancer protein. We have developed a replication-incompetent adenoviral vector, Ad-RTS-IL-12, administered intra-tumorally under the control of a "switch" referred to as the RTS®, expression platform. Activation of the switch and therefore conditional gene expression and subsequent IL-12 protein production is tightly controlled by the activator ligand, veledimex, delivered to the patient as an oral capsule. When veledimex is administered to a patient, the switch is turned "on" and IL-12 as well as downstream IFN-g, are produced; when veledimex is withdrawn, the switch is turned "off" and production of recombinant IL-12 ceases. IL-12 is a potent pro-inflammatory cytokine capable of reversing immune escape mechanisms and improving the function of tumor fighting natural killer, or NK, and T-cells. We have found direct evidence of infiltration of activated T-cells in previously "cold" tumors (i.e. turning cold tumors hot) following administration of Ad-RTS-IL-12 plus veledimex; the presence of such T-cells has furthermore been sustained months after administration of the Ad-RTS-hIL-12 plus veledimex. Gliomas represent a unique form of aggressive cancer that spreads loco-regionally and are particularly well suited to IL-12 local therapy.



We tested Ad-RTS-IL-12 plus veledimex in several Phase 1 and 2 clinical trials including the treatment of metastatic melanoma, breast cancer, and brain cancer patients. Since 2015, our focus has been on clinical trials of the product in rGBM, a deadly form of brain cancer with limited treatment options.

Glioblastoma Market

We are developing controlled IL-12 to treat patients with rGBM. Glioblastoma is an aggressive primary brain tumor affecting approximately 74,000 people worldwide each year; it is a fast-growing, aggressive type of central nervous system tumor, with an estimated 12,390 new adult cases predicted in the United States for 2017 according to the American Brain Tumor Association. Recurrence rates for this type of cancer are near 90 percent, and prognosis for adult patients is poor with treatment often combining multiple approaches including surgery, radiation and chemotherapy.

Recurrent glioblastoma is an aggressive cancer with one of the lowest 3-year survival rates, at 3%, among all cancers. For patients who have experienced multiple recurrences, the prognosis is particularly poor, with a mOS of 6-7 months, while overall survival in patients who have failed temozolomide and bevacizumab, or equivalent salvage chemotherapy, is approximately 3-5 months. Given the poor overall prognosis and lack of effective treatments, new therapeutic approaches for malignant gliomas are needed.

In children, the incidence of brain cancer is approximately 4.84 per 100,000, according to the NCI. Glioma in the cortex (cerebrum) of children is unusual and is treated along the same lines as in adults with occurrence common and survival poor. Glioma in the pontine region of the brain, or diffuse intrinsic pontine glioma (DIPG), accounts for approximately 15 percent of all cases of pediatric brain tumors, with a median survival time of less than one year. Because of where these tumors are situated, DIPG is inaccessible to surgery and there are no curative options.

Monotherapy: Clinical development Ad-RTS-IL-12 + veledimex for rGBM

Our multi-center Phase 1 trial in patients with rGBM, which was initiated in June 2015, continues to show promising data with preliminary evidence of a survival benefit and a good safety profile.

The primary objective of the Phase 1 trial is to determine the safety and tolerability of a single intratumoral Ad-RTS-hIL-12 injection activated upon dosing with oral veledimex. Secondary objectives are to determine the maximum tolerated dose, the immune responses elicited, and assessment of biologic response. The study has enrolled patients at doses ranging from 10 mg to 40 mg of veledimex. 20 mg has been identified as the target dose for further study; we plan to continue to enroll patients at the 20 mg dose level and are preparing for initiation of a pivotal trial later in the year.

We have presented updates of data from the ongoing Phase 1 study at a variety of major medical conferences including the annual meetings of American Society for Clinical Oncology (ASCO), American Academy of Neurological Surgery (AAcNS) and Society for Neuro-oncology (SNO).

Most recently, during the 22nd Annual Meeting and Education Day of SNO on November 16-19, 2017, we delivered an oral presentation entitled, “A Phase 1 study of Ad-RTS-hIL-12 + veledimex in adult rGBM” with new data showing median overall survival (mOS) of 12.5 months had been sustained for patients treated with Ad-RTS-hIL-12 plus 20mg of veledimex (n=15) and a longer mean follow-up time of 11.1 months in this on-going study. This mOS of 12.5 months continues to compare favorably to the 5 to 8 months survival established in historical controls for patients with rGBM. We also reported an anti-tumor effect evident with centralized review of magnetic resonance imaging showing decreasing size of brain tumor lesions in several patients.

Additionally, data linking the intra-tumor production of hIL-12 to patients’ overall survival was presented:

- Immunohistochemistry analyses from three of three patient biopsies after completion of veledimex demonstrated that IL-12 activates and sustains an immune response in rGBM;
- All three biopsies of rGBM lesions demonstrated evidence of an anti-tumor response with extensive infiltration of $CD8^+$ T cells within the rGBM;
- Biopsies all showed sustained (greater than 4 months) production of interferon-gamma, a cytokine crucial to arming an immune response in the tumor microenvironment;
- Ratio of circulating killer $CD8^+$ T cells to suppressor $FOXP3^+$ T cells appeared to correlate with survival;
- Interferon-gamma was undetectable in the blood at the time of biopsies while observed in the tumor providing further evidence of a sustained on-target response;

- Expression levels of both PD-1 and PD-L1 were upregulated in all the biopsies, which suggests added potential efficacy for combining Ad-RTS-hIL-12 plus veledimex with an immune checkpoint inhibitor;

Dr. Chiocca, the 2017 President of the Society for Neuro-Oncology, was the lead author of this presentation.

We also delivered two additional oral presentations: “Controlled expression of IL-12 improves survival in glioma by activating the immune response in mice and humans” and “Controlled local expression of IL-12 as gene therapy concomitant with systemic chemotherapy improves survival in glioma”.

In our Phase 1 trial in rGBM, Ad-RTS-hIL-12 plus veledimex continues to be safe and well tolerated, as adverse events (AE) were predictable and reversible, neurologic AEs were relatively mild and transient, and there were no drug-related deaths.

We plan to conduct a multi-center, randomized pivotal trial to evaluate Ad-RTS-hIL-12 plus veledimex as a treatment for patients with rGBM. We have met with the U.S. Food and Drug Administration (FDA) in an End-of-Phase 2 meeting as well with European regulators in multiple meetings during 2017. We have designed a pivotal trial consistent with this guidance and are completing CMC technical requirements. We continue to engage in partnership discussions for further development in this indication and are collecting additional clinical data from the open Phase 1 trial, including a combination study with an immune checkpoint inhibitor (iCPI).

Ad-RTS-IL-12 + veledimex for the treatment of malignant glioma was granted orphan drug designation by the FDA in July 2015. Orphan drug designation provides eligibility for a seven-year period of market exclusivity in the United States after product approval, an accelerated review process, accelerated approval where appropriate, grant funding, tax benefits and an exemption from user fees.

Pediatrics

On October 16, 2017, we announced the first patient dosed in a new Phase 1 trial of Ad-RTS-hIL-12 with veledimex for the treatment of pediatric brain tumors. This open label study will assess the safety and tolerability of a single intratumoral injection of Ad-RTS-hIL-12, and is conducted in two groups: the first is comprised of pediatric patients with recurrent or progressive brain tumors, while the second is comprised of pediatric patients with DIPG. This Phase 1 trial is being conducted at leading pediatric cancer centers across the United States, including Ann & Robert H. Lurie Children’s Hospital in Chicago, Dana-Farber Cancer Institute in Boston and the University of California, San Francisco. The first pediatric patient has received Ad-RTS-hIL-12 plus veledimex at Lurie Children’s Hospital. Stewart Goldman, MD, presented a poster, entitled “Phase 1 study of Ad-RTS-hIL-12 + veledimex in pediatric brain tumors” at the 2017 Annual Meeting of SNO describing the study design.

Combination therapy

Our enthusiasm about Controlled IL-12 as a platform has recently increased based on emerging clinical data demonstrating that this cytokine recruits immune cells such as T-cells into rGBM turning “cold” tumor sites “hot” for long periods of time. As the Phase 1 survival data matured over the latter half of 2017, we saw compelling evidence from biopsies, taken more than four months after administration of Ad-hIL-12 plus veledimex, demonstrating that Controlled IL-12 causes a sustained influx of activated killer T-cells into brain tumors and upregulated expression of PD-1/PDL-1 biomarkers.

We have previously reported, in May 2016 at the Annual Meeting of the American Society of Gene and Cell Therapy, or ASGCT, preclinical trials suggesting that combination of Ad-RTS-hIL-12 plus veledimex with an iCPI improves the anti-tumor effect. We believe these data support a first-in-human study combining Ad-RTS-IL-12 + veledimex with an iCPI for the investigational treatment of rGBM.

Our first study with an iCPI is with nivolumab and will explore the potentially synergistic effect of this combination. This study was initiated in 2018.

Other indications

Ad-RTS-IL-12 plus veledimex has been evaluated in four clinical trials prior to shifting our focus to brain cancer. The first, a Phase 1/2 study for the treatment of metastatic melanoma, and the second, a Phase 2 study for the treatment of unresectable recurrent or metastatic breast cancer. We have also concluded enrollment of a single-center Phase 1b/2 study, following standard chemotherapy, for the treatment of patients with locally advanced or metastatic breast cancer. In January 2017, we announced that we paused the breast cancer studies after successfully collecting the desired biomarker data demonstrating the intratumoral influx of $CD8^+$ T cells. Prospective partnership discussions include GBM, breast cancer, and melanoma indications.

SB-Modified T-cells Platform

We are actively pursuing non-viral genetic engineering technologies to develop novel CAR^+ T and TCR-therapies. The platform we, together with Intrexon (now Precigen), exclusively licensed from MD Anderson uses the SB, non-viral genetic modification system to generate and characterize new CAR^+ T and TCR designs. We believe this non-viral gene transfer using the SB system is the most advanced non-viral gene transfer system in the field of oncology and has distinct advantages in terms of cost and time to produce compared with viral gene transfer, *e.g.*, retrovirus and lentivirus. First, it may reduce the manufacturing expense and challenges associated with viral gene transfer systems in creating T-cells engineered to express CAR and TCR. The SB system simply uses DNA plasmid and does not require time-consuming and laborious manufacture of virus.

Furthermore, the T-cell manufacturing process with SB has the potential to significantly shorten virus-based manufacturing time. Our technology referred to as P-O-C enables rapid manufacture of autologous (patient-derived) genetically modified T-cells in near real time. In the preclinical setting, the time to administration of third-generation SB-modified T-cells co-expressing mbIL15 and kill switch has been reduced to less than two days through elimination of the need for *in vitro* T-cell activation and propagation which avoids the need to culture T-cells. The addition of our proprietary mbIL15 likely enables the administration of CAR-expressing “younger” T-cells with an ability to be long-lived after infusion in animals. The ability of CAR^+ T cells to signal via recombinant IL-15 increases CAR persistence and has the potential to eliminate lymphodepletion.

Non-viral gene transfer and our P-O-C technology also enables the potential for a hospital-based, manufacturing model rather than the centralized manufacturing approach currently being employed for other CAR^+ T products, including Kymriah and Yescarta. For example, patient-derived cells may no longer need to be shipped to and from the manufacturing site, thereby eliminating cumbersome and time-consuming shipment and receipt.

Finally, the use of the SB platform may be significantly more customizable, therefore enabling us to prepare personalized TCR therapies against unique, and potentially multiple, patient-specific neoantigens. This approach would be cost prohibitive with viral gene transfer and may allow us to develop TCR therapies against both hematologic malignancies and solid tumors.

We expect to build upon these data to co-express immunoreceptors with cytokines and to leverage its ability to control expression with the RTS® and/or kill switches. The IL-12 data arising from the brain cancer trial with Ad-RTS-hIL-12 + veledimex firmly establishes that the RTS® is a controllable switch in humans. The RTS® technology is being further developed for use in T-cells. In addition, kill switches have been developed to eliminate gene-modified T-cells in the event of adverse events.

The improvements our P-O-C technology may bring to both the reduction in vein-to-vein time as well as the personalization of treatment will be significant advances in the field of immuno-oncology. The development technology platform is focused on (1) shortening the time the patient must wait for treatment with engineered T-cells, (2) increasing the access of hospitals to deliver, and patients to receive, cell therapies, and (3) providing safe and efficacious personalized cell therapies to patients across a wide range of cancers.

Hematologic and solid tumor malignancy market

According to the Leukemia and Lymphoma Society, an estimated 1,237,824 people in the U.S. are living with, or are in remission from leukemia, lymphoma, or myeloma. New diagnoses for such hematologic malignancies in the U.S. were estimated to be 171,500 and represented approximately 10% of the new cancer cases in the U.S. in 2016. Acute myeloid leukemia (AML) is the most common form of acute leukemia in adults and has a particularly poor prognosis with a relative 5-year survival rate of only 26% overall. An estimated 19,950 new cases of AML were estimated in the US in 2016.

In 2016 more than 15.5 million people in the U.S. were living with, or are in remission from some form of cancer. Approximately 1,688,780 new cancer cases were expected to be diagnosed in the US in 2017 according to the American Cancer Society. Of these, the majority were caused by solid tumors. Malignancies of epithelial tissue, or carcinomas, represent 80 to 90 percent of all cancer cases according to the Surveillance, Epidemiology, and End Results (SEER) Program of the National Cancer Institute. These diseases include colorectal, non-small cell lung, skin, bladder and head and neck cancers, among others. Despite significant advances in immunotherapy many patients with metastatic carcinomas will die from disease progression. Cancer is the second most common cause of death in the US, accounting for nearly 1 of every 4 deaths.

Clinical Development CAR+ T

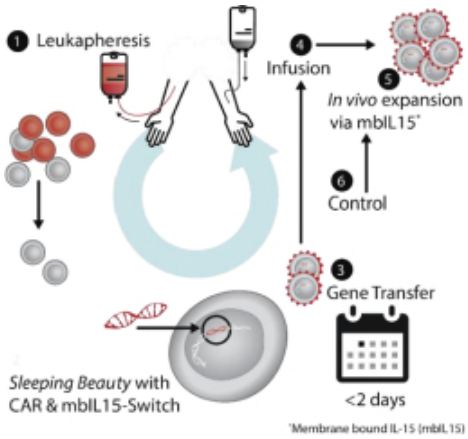
Through the MD Anderson License, we entered the clinic with three CAR+ T therapies in 2015 utilizing the non-viral genetic modification capabilities of the SB system. Two of these trials are with “first generation” technologies, the results from which were published in the *Journal of Clinical Investigation* in September 2016. An update on patients in the first-generation trials was presented in a poster at the 2017 Annual Meeting of ASH. The trials demonstrated that first-generation SB-modified CD19-specific CAR+ T cells appear to provide long term cancer control when infused after hematopoietic stem-cell transplantation (HSCT) for patients with advanced CD19+ malignancies and could be detected years after administration in some recipients. All seven patients with advanced CD19+ non-Hodgkin’s lymphoma (NHL) that received autologous T-cells were alive at a median survival of 40 months since infusion, with progression-free survival (PFS) reported at 86% and overall survival (OS) at 100%. For 19 patients with advanced CD19+ acute lymphoblastic leukemia (ALL) and NHL infused with allogeneic T-cells following HSCT, nine patients were alive with a median survival of 31 months. The PFS rate and OS rates are 32% and 49%, respectively. Of the subset of eight patients who received donor-derived T-cells after haploidentical HSCT, PFS and OS rates are 50% and 63%, respectively. Persistence of circulating SB-modified CAR+ T cells was demonstrated at two years in an autologous and allogeneic patient and for four years in two autologous patients.

We are currently enrolling patients in an investigator-led Phase 1 study using second-generation CD19-specific CAR+ T cells with a revised CAR structure in patients with advanced lymphoid malignancies at MD Anderson. Our second-generation CD19 trial employs a revised CAR design and shortened manufacturing process advancement, with culturing times as short as two weeks. A summary of this ongoing trial was presented by Dr. Partow Kebriaei of MDACC in a presentation at the 2017 Annual Meeting of ASH in December. Interim data from the trial demonstrated that autologous T-cells infused after lymphodepleting chemotherapy could be detected, and exhibited anti-tumor effects and an encouraging safety profile in patients with relapsed/refractory CD19+ malignancies. Complete responses at one month were reported in four of eight patients with either ALL (n=5), chronic lymphocytic leukemia (n=1), or diffuse large B-cell lymphoma (n=2), with two morphologic complete responses at three months. Follow up blood tests demonstrated sustained persistence of infused T-cells and targeting of malignant and normal B cells. There were no dose limiting toxicities with only grade 1 or 2 adverse events being reported. T-cell dose escalation continues. We anticipate stopping enrollment in this trial in 2018 as our third-generation trial moves forward in the clinic.

In the preclinical setting, the time to manufacture and administration of third-generation SB-modified CAR+ T cells co-expressing mbIL15 has been reduced to less than two days. This shortened very rapid manufacturing

process, referred to as P-O-C, delivers genetically modified T-cells with superior proliferative potential *in vivo*. Preclinical studies of third generation SB CAR+ T cells, presented at the 2017 Annual Meeting of ASH, demonstrated that a single low-dose of T-cells co-expressing a CD19-specific CAR, mbIL15, and kill switch resulted in sustained *in vivo* persistence that produced potent anti-tumor effects and superior leukemia-free survival in mice. These preclinical data support our P-O-C plans to very rapidly infuse SB CAR+ T cells in a Phase 1 trial in 2018. Our intent to administer clinical-grade SB CAR+ T cells in less than 48 hours, this non-viral CAR+ T approach has the potential to outpace viral-based methods in terms of time to the administration of therapy concomitant with a reduction in cost. The P-O-C technology is based on the non-viral gene transfer to stably integrate both CAR and mbIL15 with a kill switch.

Overview of the "Point-of-Care" (P-O-C) using the *Sleeping Beauty* (SB) system to very rapidly generate CAR+ T cells against known tumor antigens.



We are also progressing an ongoing Phase 1 adoptive cellular therapy clinical trial at MD Anderson infusing autologous T-cells transduced with lentivirus to express a CD33-specific CAR co-expressed with a kill switch in patients with relapsed or refractory AML. Preclinical studies, presented at the 2017 annual meeting of ASH, demonstrated that lentiviral transduced CAR-T cells targeting CD33 exhibit specific cytotoxic activity for CD33+ AML cells. A proof-of-concept study utilizing an *in vivo* mouse model for AML showed that these CAR-T cells could reduce disease burden and significantly enhance survival as compared to control groups. These positive preliminary results indicated biological activity and are suggestive of potential therapeutic effect for the treatment of AML. This Phase 1 clinical trial is now open for enrollment at MD Anderson. The anticipated clinical data may establish that CD33 can be targeted by CAR on genetically modified T-cells, which will provide a foundation for considering then to advance this program under the P-O-C approach.

Clinical Development TCR

Many of these genetic engineering technologies can also be applied toward targeting intracellular antigens with one or more tumor-specific TCRs. This approach is particularly important for addressing the complexity of solid tumors. We believe that the SB non-viral platform is ideally suited for targeting intracellular antigens by TCR as it may be more cost-effective, should allow for rapid manufacturing, and is expected to be customizable for individual patient therapies with the ability to include multiple TCRs in a single therapy. We are pursuing a discovery program in TCR therapies for neoantigen targets. The development of an approach to create a truly personalized therapy for each cancer patient based on his/her unique neoantigens is a strategic goal of ours.

On January 10, 2017, we announced the signing of a CRADA with the NCI for the development of ACT-based immunotherapies genetically modified using the SB transposon/transposase system to express TCRs for the

treatment of solid tumors. The principal goal of the CRADA is to develop and evaluate ACT for patients with advanced cancers using autologous PBL genetically modified using the non-viral SB system to express TCRs that recognize specific immunogenic mutations, or neoantigens, expressed within a patient's cancer. Clinical evaluations of the ability of these SB-engineered PBL to express TCRs reactive against cancer mutations to mediate cancer regression in patients with metastatic disease will be performed. Research conducted under the CRADA will be at the direction of Steven A. Rosenberg, M.D., Ph.D., Chief of the Surgery Branch at the NCI, in collaboration with researchers at Ziopharm and Precigen. Preparations for the clinical trial are underway at the NCI. Following validation of the manufacturing process, we anticipate submission of the IND and initiation of the clinical trial in 2018.

Preclinical Development

In collaboration with Precigen, we continue to develop additional CAR+ T targets, using our Sleeping Beauty platform. Under the collaboration, Ares Trading has elected two CAR+ T targets for which we will perform certain research activities that will, in part, be funded by Ares Trading. We and Precigen will also independently conduct research and development on other CAR+ T candidates, with Ares Trading having the opportunity during clinical development to opt-in to these candidates for additional payments to us and Precigen. We anticipate further advancement of at least one target toward the clinic in 2018.

In addition, we will continue efforts to genetically modify allogeneic NK cells to improve their persistence and anti-tumor efficacy.

License Agreements, Intellectual Property and Other Agreements

Our goal is to obtain, maintain, and enforce patent protection for our products, formulations, processes, methods, and other proprietary technologies to preserve our trade secrets and to operate without infringing upon the proprietary rights of other parties. Our policy is to actively seek the broadest possible intellectual property protection for our product candidates through a combination of contractual arrangements and patents, both in the United States and abroad.

Exclusive Channel Partner Agreement with Precigen for the Cancer Programs

On January 6, 2011, we entered into the Channel Agreement with Intrexon (now Precigen), that governs a "channel partnering" arrangement in which we use Precigen's technology to research, develop and commercialize products in which DNA is administered to humans for expression of anti-cancer effectors for treatment or prophylaxis of cancer, which we collectively refer to as the Cancer Program. This Channel Agreement establishes committees comprising representatives of us and Precigen that govern activities related to the Cancer Program in the areas of project establishment, chemistry, manufacturing and controls, clinical and regulatory matters, commercialization efforts and intellectual property.

The Channel Agreement grants us a worldwide license to use patents and other intellectual property of Precigen in connection with the research, development, use, importing, manufacture, sale, and offer for sale of products involving DNA administered to humans for expression of anti-cancer effectors for the purpose of treatment or prophylaxis of cancer, which are collectively referred to as the Ziopharm Products. Such license is exclusive with respect to any clinical development, selling, offering for sale or other commercialization of Ziopharm Products, and otherwise is non-exclusive. Subject to limited exceptions, we may not sublicense these rights without Precigen's written consent.

Under the Channel Agreement, and subject to certain exceptions, we are responsible for, among other things, the performance of the Cancer Program, including the development, commercialization and certain aspects of manufacturing of Ziopharm Products. Precigen is responsible for establishing manufacturing capabilities and facilities for the bulk manufacture of products developed under the Cancer Program, certain other aspects of manufacturing and costs of discovery-stage research with respect to platform improvements and costs of filing, prosecution and maintenance of Precigen's patents.

After the 2016 Exclusive Channel Partner (ECP) Amendment, discussed below, and subject to certain expense allocations and other offsets provided in the Channel Agreement, we are obligated to pay Precigen on a quarterly basis 20% of net profits derived in that quarter from the sale of Ziopharm Products, calculated on a Ziopharm Product-by- Ziopharm Product basis. We likewise agreed to pay Precigen on a quarterly basis 50% of revenue obtained in that quarter from a sublicensor in the event of a sublicensing arrangement. In addition, in partial consideration for each party's execution and delivery of the Channel Agreement, we entered into a stock purchase agreement with Precigen.

Upon termination of the Channel Agreement, we may continue to develop and commercialize any Ziopharm Product that, at the time of termination:

- Is being commercialized by us;
- Has received regulatory approval;
- Is a subject of an application for regulatory approval that is pending before the applicable regulatory authority; or
- Is the subject of at least an ongoing Phase 2 clinical trial (in the case of a termination by Precigen due to an uncured breach or a voluntary termination by us), or an ongoing Phase 1 clinical trial in the field (in the case of a termination by us due to an uncured breach or a termination by Precigen following an unconsented assignment by us or its election not to pursue development of a Superior Therapy (as defined in the Channel Agreement)).

With respect to these "retained" Ziopharm Products, our obligation to pay 20% of net profits derived from the sale of Ziopharm Products and 50% of revenue derived from a sublicensor will survive termination of the Channel Agreement.

Amendment of Collaborations with Precigen

On March 27, 2015, we, together with Intrexon, now Precigen, entered into an ECP Amendment, amending the Channel Agreement. The ECP Amendment modifies the scope of the parties' collaboration under the Channel Agreement in connection with the Ares Trading Agreement discussed below. Pursuant to the ECP Amendment, the chimeric antigen receptor T-cell products to be developed and commercialized pursuant to the Ares Trading Agreement shall be included within the Precigen/ Ziopharm collaboration under the Channel Agreement. The ECP Amendment provides that Precigen will pay us fifty percent of all payments Precigen receives for upfronts, milestones and royalties under the Ares Trading Agreement.

On June 29, 2016, we entered into (1) the 2016 ECP Amendment with Intrexon (now Precigen), amending the Channel Agreement, and (2) the 2016 GvHD Amendment, amending our Exclusive Channel Collaboration Agreement we entered into with Intrexon (now Precigen) in September 2015, or the GvHD Agreement. The 2016 ECP Amendment reduced the royalty percentage that we will pay to Precigen under the Channel Agreement on a quarterly basis from 50% to 20% of net profits derived in that quarter from the sale of Ziopharm Products, calculated on a Ziopharm Product-by- Ziopharm Product basis, subject to certain expense allocations and other offsets provided in the Channel Agreement. The 2016 GvHD Amendment reduced the royalty percentage that we would pay to Precigen under the GvHD Agreement on a quarterly basis from 50% to 20% of net profits derived in that quarter from the sale of Products (as defined in the GvHD Agreement), subject to certain expense allocations and other offsets provided in the GvHD Agreement. The reductions in the royalty percentages provided by the 2016 ECP Amendment and the 2016 GvHD Amendment do not apply to sublicensing revenue or royalties under the Channel Agreement and GvHD Agreement, nor do they apply to any royalties or other payments made with respect to sublicensing revenue from our existing collaboration with Ares Trading S.A., or Ares Trading, a subsidiary of the biopharmaceutical business of Merck KGaA. We have recently announced our decision to stop pursuing the development of engineered cell therapy strategies for targeted treatment of GvHD. We have reverted our rights under the GvHD Agreement back to Precigen [and are in the process of winding down the related activities].

In consideration for the execution and delivery of the 2016 ECP Amendment and the 2016 GvHD Amendment, we agreed to issue to Intrexon 100,000 shares of its Series 1 preferred stock. Each share of our Series 1 preferred stock has a stated value of $1,200, subject to appropriate adjustment in the event of any stock dividend, stock split, combination or other recapitalization, and certain other rights, preferences, privileges and obligations (see Note 9 to the accompanying financial statements).

Exclusive Channel Collaboration Agreement with Precigen for GvHD

On September 28, 2015, we entered into the GvHD Agreement with Intrexon (now Precigen), whereby we would use Precigen's technology directed towards *in vivo* expression of effectors to research, develop and commercialize products for use in the treatment or prevention of GvHD. The GvHD Agreement granted us a worldwide license to use specified patents and other intellectual property of Precigen in connection with the research, development, use, importing, manufacture, sale, and offer for sale of products developed under the GvHD Agreement.

We paid Intrexon a technology access fee of $10.0 million in cash in October 2015 and agreed to reimburse Intrexon for all related research and development costs pursuant to the GvHD Agreement. We have determined that the rights acquired in the GvHD Agreement represent in-process research and development with no alternative future use. Accordingly, we recorded a charge of $10.0 million to research and development expense in September 2015.

As a result of an in-depth review of our research and development portfolio, we determined that the pursuit of GvHD as an indication was not a material part of our corporate strategy and therefore have decided to stop pursuing the development of engineered cell therapy strategies, used either separately or in combination, for targeted treatment of GvHD. We have reverted our rights under the GvHD program back to Precigen [and are in the process of winding down the related activities]. We made this decision to focus our efforts and resources on the development of our Controlled IL-12 and Sleeping Beauty platforms for the treatment of oncology indications.

License Agreement—The University of Texas MD Anderson Cancer Center

On January 13, 2015, we, together with Intrexon (now Precigen), entered into a License Agreement, or the MD Anderson License, with The University of Texas MD Anderson Cancer Center, or MD Anderson. Pursuant to the MD Anderson License, we, together with Precigen, hold an exclusive, worldwide license to certain technologies owned and licensed by MD Anderson including technologies relating to novel chimeric antigen receptor, or CAR, T cell therapies, non-viral gene transfer systems, genetic modification and/or propagation of immune cells and other cellular therapy approaches, Natural Killer, or NK Cells, and T-cell receptors, or TCRs, arising from the laboratory of Laurence Cooper, M.D., Ph.D., who became our Chief Executive Officer in May 2015 and was formerly a tenured professor of pediatrics at MD Anderson and is now currently a visiting scientist under that institution's policies, as well as either co-exclusive or non-exclusive licenses under certain related technologies.

Pursuant to the terms of the MD Anderson License, MD Anderson received consideration consisting of $50.0 million in shares of our common stock (or 10,124,561 shares), and $50.0 million in shares of Intrexon's common stock, in each case based on a trailing 20 day volume weighted average of the closing price our and Intrexon's common stock ending on the date prior to the announcement of the entry into the MD Anderson License, collectively referred to as the License Shares, pursuant to the terms of the License Shares Securities Issuance Agreement described below. The License Shares were issued to MD Anderson on March 11, 2015, pursuant to the terms of the MD Anderson License.

On January 9, 2015, in order to induce MD Anderson to enter into the MD Anderson License on an accelerated schedule, we, together with Intrexon entered into a letter agreement, or the Letter Agreement, pursuant to which MD Anderson received consideration of $7.5 million in shares of our common stock (or 1,597,602 shares), and

$7.5 million in shares of Intrexon's common stock, in each case based on a trailing 20-day volume-weighted average of the closing price of our and Intrexon's common stock ending on the date prior to the execution of the Letter Agreement, collectively referred to as the Incentive Shares, in the event that the MD Anderson License was entered into on January 14, 2015. The Incentive Shares were issued to MD Anderson on March 11, 2015, pursuant to the terms of the Incentive Shares Securities Issuance Agreement described below.

On August 17, 2015, we, Intrexon (now Precigen) and MD Anderson entered into a research and development agreement, or the Research and Development Agreement, to formalize the scope and process for the transfer by MD Anderson, pursuant to the terms of the MD Anderson License, of certain existing research programs and related technology rights, as well as the terms and conditions for future collaborative research and development of new and ongoing research programs.

Pursuant to the Research and Development Agreement, we, Intrexon (now Precigen) and MD Anderson have agreed to form a joint steering committee that will oversee and manage the new and ongoing research programs. As provided under the MD Anderson License, we provided funding for research and development activities in support of the research programs under the Research and Development Agreement for a period of three years and in an amount of no less than $15.0 million and no greater than $20.0 million per year. During the twelve months ended December 31, 2017, we made payments in the aggregate amount of $13.0 million to MD Anderson compared to $15.0 million during the twelve months ended December 31, 2016. The decrease in cash paid to MD Anderson during 2017 is a result of approved expenditures incurred by us being deducted from the April, July, and October quarterly payments. As of December 31, 2017, MD Anderson had used $7.3 million to offset costs incurred pursuant to the MD Anderson License and the Research and Development Agreement. The net balance of cash resources on hand at MD Anderson is $31.9 million, of which $18.5 million is included in other current assets and the remaining $13.4 million is included in non-current assets at December 31, 2017. Subsequent to the balance sheet date, the final payment to MD Anderson was made in January 2018 for $2.7 million.

The term of the MD Anderson License expires on the last to occur of (a) the expiration of all patents licensed thereunder, or (b) the twentieth anniversary of the date of the MD Anderson License; provided, however, that following the expiration of the term of the MD Anderson License, we, together with Precigen, shall then have a fully-paid up, royalty free, perpetual, irrevocable and sublicensable license to use the licensed intellectual property thereunder. After ten years from the date of the MD Anderson License and subject to a 90-day cure period, MD Anderson will have the right to convert the MD Anderson License into a non-exclusive license if we and Precigen are not using commercially reasonable efforts to commercialize the licensed intellectual property on a case-by-case basis. After five years from the date of the MD Anderson License and subject to a 180-day cure period, MD Anderson will have the right to terminate the MD Anderson License with respect to specific technology(ies) funded by the government or subject to a third-party contract if we and Precigen are not meeting the diligence requirements in such funding agreement or contract, as applicable. MD Anderson may also terminate the agreement with written notice upon material breach by us and Precigen, if such breach has not been cured within 60 days of receiving such notice. In addition, the MD Anderson License will terminate upon the occurrence of certain insolvency events for both us and Precigen and may be terminated by the mutual written agreement of us, Precigen and MD Anderson.

In connection with the MD Anderson License and the issuance of the License Shares and the Incentive Shares, on January 13, 2015, we, together with MD Anderson, entered into a Registration Rights Agreement, or the Registration Rights Agreement, pursuant to which the we agreed to file a "resale" registration statement, or the Registration Statement, registering the resale of the License Shares, the Incentive Shares and any other shares of the our common stock held by MD Anderson on the date that the Registration Statement is filed. Under the terms of the Registration Rights Agreement, we are obligated to maintain the effectiveness of the Registration Statement until all securities therein are sold or are otherwise can be sold pursuant to Rule 144, without any restrictions. A prospectus supplement under our already effective registration statement on Form S-3 (File No. 333-201826) was filed on April 1, 2015 in satisfaction of our obligations under the Registration Rights Agreement.

We determined that the rights acquired in the MD Anderson License represented in process research and development with no alternative future use. Accordingly, we recorded a charge of $67.3 million to research and development expense in 2015, representing the fair value of the 11,722,163 shares of its common stock on the date the MD Anderson License was executed.

Ares Trading License and Collaboration Agreement

On March 27, 2015, we, together with Intrexon (now Precigen), signed a worldwide License and Collaboration Agreement, or the Ares Trading Agreement, with Ares Trading S.A., or Ares Trading, a subsidiary of the biopharmaceutical business of Merck KGaA, Darmstadt, Germany, through which the parties established a collaboration for the research and development and commercialization of certain products for the prophylactic, therapeutic, palliative or diagnostic use for cancer in humans.

Under the collaboration, Ares Trading has elected two CAR$^+$ T targets for which we will perform certain research activities that will, in part, be funded by Ares Trading. Once these candidates reach investigational new drug, or IND, stage, the programs will be transferred to Ares Trading for clinical development and commercialization. We expect to perform multiple preclinical development programs, each consisting of the development of one product candidate, pursuant to the agreement. We, together with Precigen, will also independently conduct research and development on other CAR$^+$ T candidates, with Ares Trading having the opportunity during clinical development to opt-in to these candidates for additional payments to us and Precigen.

Precigen is entitled to receive $5.0 million, from Ares Trading, payable in equal quarterly installments over two years for each identified product candidate, which will be used to fund discovery work. We are responsible for costs exceeding the quarterly installments and all other costs of the preclinical research and development. For the twelve months ended December 31, 2017, we have expensed $1.6 million under the Ares Trading Agreement, respectively.

Ares Trading paid a non-refundable upfront fee of $115.0 million to Intrexon as consideration for entry into the Ares Trading Agreement. Pursuant to the ECP Amendment, we were entitled to receive 50% of the upfront fee, or $57.5 million, which we received from Intrexon in July 2015.

The Ares Trading Agreement provides for up to $60.0 million in development milestone payments, up to $148.0 million in regulatory milestone payments and up to $205.0 million in commercial milestone payments for each product candidate. Development milestone payments are triggered upon initiation of a defined phase of clinical research for a product candidate. Regulatory milestone payments are triggered upon approval to market a product candidate by the FDA, or other global regulatory authorities. Commercial milestone payments are triggered when an approved pharmaceutical product reaches certain defined levels of net sales by the licensee. The Ares Trading Agreement also provides for up to $50.0 million of one-time payments upon the achievement of certain technical milestones evidenced by the initiation of a defined phase of clinical research. All development, regulatory and technical milestones are considered substantive based on the contingent nature of the milestone, specifically reviewing factors such as the scientific, clinical, regulatory, commercial and other risks that must be overcome to achieve the milestone as well as the level of effort and investment required. Accordingly, such amounts will be recognized as revenue in full in the period in which the associated milestone is achieved, assuming all other revenue recognition criteria are met. All commercial milestones will be accounted for in the same manner as royalties and recorded as revenue upon achievement of the milestone, assuming all other revenue recognition criteria are met. The next potential milestone payment that Precigen could be entitled to receive under the Ares Trading Agreement is a $15.0 million substantive milestone for the initiation of a Phase 1 clinical trial. In addition, to the extent any of the product candidates licensed by Ares Trading are commercialized, Precigen would be entitled to receive royalties ranging from the lower-single digits to the low-teens of net sales derived from the sale of products developed under agreement. Precigen will pay 50% of all milestone and royalty payments that it receives under the Ares Trading Agreement to us pursuant to the ECP Amendment.

The term of the Ares Trading Agreement commenced in May 2015 and may be terminated by either party in the event of a material breach as defined in the agreement and may be terminated voluntarily by Ares Trading upon 90 days written notice to us.

We considered FASB Accounting Standards Codification 605-25, *Multiple-Element Arrangements*, in evaluating the appropriate accounting for the Ares Trading Agreement. In accordance with this guidance, we identified the license and research and development services as our deliverables in the arrangement. We concluded that the license does not have standalone value independent from the research and development services. Accordingly, the Ares Trading Agreement is accounted for by us as a single unit of accounting. The $57.5 million upfront payment received by us was recorded as deferred revenue and is being recognized over the estimated period of performance of the research and development services which are currently estimated to be nine years, beginning with the commencement of the research and development services. During the three and twelve months ended December 31, 2017 and 2016, we recognized $1.6 million, each quarter, of revenue related to the Ares Trading Agreement. As of December 31, 2017, the remaining balance of deferred revenue associated with the upfront payment is $41.5 million, of which $6.4 million is current and $35.1 million is classified as long-term. As of December 31, 2016, the remaining balance of deferred revenue associated with the upfront payment was $47.9 million, of which $6.4 million was current and $41.5 million was classified as long term.

Patent and Technology License Agreement—The University of Texas MD Anderson Cancer Center and the Texas A&M University System

On August 24, 2004, we entered into a patent and technology license agreement with MD Anderson and the Texas A&M University System, which we refer to, collectively, as the Licensors. Under this agreement, we were granted an exclusive, worldwide license to rights (including rights to U.S. and foreign patent and patent applications and related improvements and know-how) for the manufacture and commercialization of two classes of organic arsenicals (water- and lipid-based) for human and animal use. The class of water-based organic arsenicals includes darinaparsin.

We issued options to purchase 50,222 shares outside of our stock option plans following the successful completion of certain clinical milestones, of which 37,666 shares have vested. The remaining 12,556 shares vested upon enrollment of the first patient in a multi-center pivotal clinical trial *i.e.* a human clinical trial intended to provide the substantial evidence of efficacy necessary to support the filing of an approvable New Drug Application, or NDA. An expense of $87 thousand was charged to research and development expense for the vesting event which occurred in March 2016. This trial was initiated by Solasia Pharma K.K., or Solasia, on March 28, 2016 and triggered a $1.0 million milestone payment to us from Solasia which was received in May 2016. An equivalent of $1.0 million milestone payment was subsequently made to MD Anderson and reported net. In addition, the Licensors are entitled to receive certain milestone payments. In addition, we may be required to make additional payments to the Licensors (as defined in the MD Anderson License) upon achievement of certain other milestones in varying amounts which, on a cumulative basis could total up to an additional $4.5 million. In addition, the Licensors are entitled to receive single digit percentage royalty payments on sales from a licensed product and will also be entitled to receive a portion of any fees that we may receive from a possible sublicense under certain circumstances.

Collaboration Agreement with Solasia Pharma K.K.

On March 7, 2011, we entered into a License and Collaboration Agreement with Solasia. Pursuant to the License and Collaboration Agreement, we granted Solasia an exclusive license to develop and commercialize darinaparsin in both intravenous and oral forms and related organic arsenic molecules, in all indications for human use in a pan-Asian/Pacific territory comprising Japan, China, Hong Kong, Macau, Republic of Korea, Taiwan, Singapore, Australia, New Zealand, Malaysia, Indonesia, Philippines and Thailand.

As consideration for the license, we received an upfront payment of $5.0 million to be used exclusively for further clinical development of darinaparsin outside of the pan-Asian/Pacific territory and will be entitled to

receive additional payments of up to $32.5 million in development-based milestones and up to $53.5 million in sales-based milestones. We will also be entitled to receive double digit royalty payments from Solasia based upon net sales of licensed products in the applicable territories, once commercialized, and a percentage of sublicense revenues generated by Solasia. The $5.0 million upfront payment received in March 2011 was amortized over the period of the research and development effort, which was completed in March 2016.

On July 31, 2014, we entered into an amendment and restatement of the License and Collaboration Agreement granting Solasia an exclusive worldwide license to develop and commercialize darinaparsin, and related organoarsenic molecules, in both intravenous and oral forms in all indications for human use. In exchange, we will be eligible to receive from Solasia development- and sales-based milestones, a royalty on net sales of darinaparsin, once commercialized, and a percentage of any sublicense revenues generated by Solasia.

Solasia will be responsible for all costs related to the development, manufacturing and commercialization of darinaparsin. Our Licensors, as defined in the agreement, will receive a portion of all milestone and royalty payments made by Solasia to us in accordance with the terms of our license agreement with the Licensors.

On March 28, 2016, Solasia initiated a multi-center pivotal clinical trial intended to provide substantial evidence of efficacy necessary to support the filing of an application for an NDA for darinaparsin in certain of the territories assigned to Solasia. The initiation of the trial on March 28, 2016 triggered a $1.0 million milestone payment from Solasia to us which was received in May 2016. We subsequently made an equivalent payment to MD Anderson as the ultimate licensor of darinaparsin (see above).

License Agreement with Baxter Healthcare S.A.

On November 3, 2006, we entered into a definitive Asset Purchase Agreement for indibulin and a License Agreement to proprietary nanosuspension technology with affiliates of Baxter Healthcare S.A. The purchase included the entire indibulin intellectual property portfolio as well as existing drug substance and capsule inventories. The terms of the Asset Purchase Agreement included an upfront cash payment and an additional payment for existing inventory. During the year ending December 31, 2017, we made the final payment of $250 thousand under the asset agreement. We are not actively pursuing the development of indibulin.

Patents and Other Intellectual Property Rights and Protection

Patents extend for varying periods according to the date of patent filing or grant and the legal term of patents in the various countries where patent protection is obtained. The actual protection offering by a patent, which can vary from country to country, depends of the type of patent, the scope of its coverage and the availability of legal remedies in the country.

Pursuant to the Drug Price Competition and Patent Term Restoration Act of 1984, referred to as the Hatch-Waxman Amendments, some of our patents, under certain conditions, may be eligible for limited patent term extension for a period of up to five years as compensation for patent term lost during drug development and the FDA regulatory review process. However, this extension period cannot be extended beyond 14 years from the drug's approval date. The patent term restoration period is generally one-half the period of time elapsed between the effective date of an IND application or the issue date of the patent, whichever is later, and the submission date of an NDA, plus the period of time between the submission date of the NDA or the issue date of the patent, whichever is later, and FDA approval. The United States Patent and Trademark Office, in consultation with the FDA, reviews and approves applications for any patent term extension or restoration. We intend to seek the benefits of this statute, but there can be no assurance that we will be able to obtain any such benefits.

We also depend upon the skills, knowledge, and experience of our scientific and technical personnel, as well as those of our advisors, consultants, and other contractors, none of which is patentable. To help protect proprietary know-how, which is not patentable, and for inventions for which patents may be difficult to enforce, we currently

rely, and in the future, will continue to rely, on trade secret protection and confidentiality agreements to protect our interests. To this end, we generally require employees, consultants, advisors and other contractors to enter into confidentiality agreements that prohibit the disclosure of confidential information and, where applicable, require disclosure and assignment to us of the ideas, developments, discoveries and inventions important to our business.

Our patent position and proprietary rights are subject to certain risks and uncertainties. Please read the “Risk Related to Our Intellectual Property” section for further information about certain risks and uncertainties that may affect our patent position and proprietary rights.

Additional information as of December 31, 2017 about material patents and other proprietary rights covering our product candidates is set forth below.

Ad-RTS-IL-12 + veledimex and DC-RTS-IL-12 + veledimex

The patent estate licensed to us by Precigen covering Ad-RTS-IL-12 + activator ligands, such as veledimex and DC-RTS-IL-12 + activator ligand compositions, methods of use, methods of manufacture, and formulations includes over one hundred patents and applications. This portfolio also includes issued and pending foreign patents in Europe, Canada, Japan, Australia and other countries. The term of one or more of the issued patents may be extended due to the regulatory approval process.

CAR+ T

In January 2015, we in-licensed from MD Anderson a technology portfolio that includes intellectual property directed to certain non-viral SB system and CAR+ T cell and bioprocessing technology. Under the terms of the agreement, we have an exclusive license to certain of the intellectual property, a co-exclusive license to certain of the intellectual property technology and a non-exclusive license to certain of the intellectual property technology. Our rights to the MD Anderson intellectual property flow to us via our agreement with Precigen.

Governmental Regulation and Product Approval

As a biopharmaceutical company, we are subject to extensive regulation. Our programmed T-cell product candidates, if approved, 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 current Good Manufacturing Practices, or cGMPs, for biologics.

Human immunotherapy products are a new category of therapeutics. The FDA categorizes human cell- or tissue-based products as either minimally manipulated or more than minimally manipulated, and has determined that more than minimally manipulated products require clinical trials to demonstrate product safety and efficacy and the submission of a Biologics License Application, or BLA, for marketing authorization.

Government authorities in the United States (at the federal, state and local level) and in other countries and jurisdictions, including the European Union, extensively regulate, among other things, the research, development, preclinical and clinical testing, manufacturing, quality control, labeling, packaging, storage, record-keeping, promotion, advertising, sale, 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 United States 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 United States, 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 applicable federal, state, local and foreign statutes and regulations require the expenditure of substantial time and financial resources.

U.S. Product Development Process

In the United States, the FDA regulates biological products under the Public Health Service Act, or PHSA, and the Federal Food, Drug and Cosmetic Act, or FDCA, 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 or judicial sanctions. FDA sanctions could include, among other actions, refusal to approve pending applications, withdrawal of an approval, a clinical hold, warning letters and similar public notice of alleged non-compliance with laws, product recalls or withdrawals from the market, product seizures, total or partial suspension of production or distribution, fines, refusals of government contracts, restitution, disgorgement of profits, or civil or criminal penalties. Any agency or judicial enforcement action could have a material adverse effect on us. The process required by the FDA before a biological product may be approved for marketing in the United States generally involves the following:

- completion of preclinical 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 Investigational New Drug Application, or 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 subjects and their health information, to establish the safety and efficacy of the proposed biological product for its intended use;
- preparation and submission to the FDA of a Biologics License Application, or BLA, for marketing approval that includes substantive evidence of safety, purity, and potency from results of nonclinical testing and clinical trials;
- satisfactory completion of one or more FDA inspections 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 used in product manufacture 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 human cellular and tissue products;
- potential FDA audit of the nonclinical study and clinical trial sites that generated the data in support of the BLA;
- payment of user fees for FDA review of the BLA; and
- FDA acceptance, review and approval, or licensure, of the BLA, which might include review by an advisory committee, a panel typically consisting of independent clinicians and other experts who provide recommendations as to whether the application should be approved and under what conditions.

Before testing any biological product candidate, including our product candidates, in humans, the product candidate must undergo rigorous the preclinical testing. Preclinical tests, also referred to as nonclinical studies, include laboratory evaluations as well as *in vitro* and animal studies to assess the potential safety and efficacy of the product candidate. After sufficient preclinical testing has been conducted, the conduct of the preclinical tests must comply with federal regulations and requirements including GLPs. The clinical trial sponsor must submit an IND to the FDA before clinical testing can begin in the United States. An IND must contain the results of the preclinical tests, manufacturing information, analytical data, any available clinical data or literature, a proposed clinical protocol, an investigator's brochure, a sample informed consent form, and other materials. Clinical trial protocols detail, 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. Some preclinical testing, such as toxicity studies, 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 or places the trial on a clinical hold within that 30-day time period. In such a case, the IND sponsor and the FDA must resolve any 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 trials.

Further, each clinical trial must be reviewed and approved by an independent institutional review board, or IRB, at or servicing each institution at which the clinical trial will be conducted. An IRB is charged with protecting the welfare and rights of 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 involving recombinant or synthetic nucleic acid molecules 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.

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 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.

Human clinical trials 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 with the target disease or condition.
- *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, generally at geographically dispersed clinical trial sites. These clinical trials are intended to generate enough data to statistically evaluate the efficacy and safety of the product for approval, to establish the overall risk to benefit profile of the product and to provide an adequate basis for product labeling.

Phase 1, Phase 2 and Phase 3 clinical trials may not be completed successfully within any specified period, if at all.

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 results 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. The FDA or the sponsor or its data safety monitoring board, an independent group of experts that evaluates study data for safety and makes recommendations concerning continuation, modification, or termination of clinical trials, 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.

Because this is a relatively new and expanding area of novel therapeutic interventions, there can be no assurance as to the length of the trial period, the number of patients the FDA will require to be enrolled in the trials in order to establish the safety, efficacy, purity and potency of immunotherapy products, or that the data generated in these trials will be acceptable to the FDA to support marketing approval.

Concurrently with clinical trials, companies usually complete additional nonclinical 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.

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 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 as the FDA has significant discretion to approve or reject the BLA and to require additional preclinical or clinical trials.

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. PDUFA also imposes an annual program fee for approved 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 product 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 ensure that the benefits of the product outweigh its risks and to assure the safe use of the biological product, which could include medication guides, physician communication plans, or elements to assure safe use, such as restricted distribution methods, patient registries and other risk minimization tools. FDA determines the requirement for a REMS, as well as the specific REMS provisions, on a case-by-case basis. 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 human cells, tissues, and cellular and tissue based products, or HCT/Ps, which are human cells or tissue intended for implantation, transplant, infusion, or transfer into a human recipient. 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 GTP regulations also require tissue establishments to register and list their HCT/Ps with the FDA and, when applicable, to evaluate donors through screening and testing. Additionally, before approving 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 assure cGMP, GTP and GCP compliance, an applicant must incur significant expenditure of time, money and effort in the areas of training, recordkeeping, 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. If the agency decides not to approve the BLA in its present form, the FDA will issue a Complete Response Letter, which generally outlines the specific deficiencies in the BLA identified by the FDA and may require additional clinical or other data or impose other conditions that must be met in order to secure final approval of the application. The deficiencies identified may be minor, for example, requiring labeling changes, or major, for example, requiring additional clinical trials. Even with the submission of additional information, the FDA may ultimately decide that the application does not satisfy the regulatory criteria 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 is limited to the conditions of use (*e.g.*, patient population, indication) described in the application.

Further, the FDA may require that certain contraindications, warnings or precautions be included in the product labeling, 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. After approval, many types of changes to the approved product, such as adding new indications, manufacturing changes and additional labeling claims, are subject to further testing requirements and FDA review and approval.

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.

Post-Approval Requirements

Any products for which we receive FDA approvals are 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 that important safety information and material facts related to the product be disclosed. Although physicians may prescribe legally available products for off-label uses, if the physicians deem to be appropriate in their professional medical judgment, manufacturers may not market or promote such off-label uses. The FDA and other agencies actively enforce the laws and regulations prohibiting the promotion of off-label uses, and a company that is found to have improperly promoted off-label uses may be subject to significant liability.

In addition, 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 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.

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, including adverse events of unanticipated severity or frequency, with manufacturing processes, or the failure to comply with applicable FDA requirements can have negative consequences, including adverse publicity, judicial or administrative enforcement, complete withdrawal from the market, product recalls, warning letters from the FDA, mandated corrective advertising or communications with doctors, product seizure or detention, injunctions, 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 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. 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. Biosimilars are approved pursuant to an abbreviated pathway whereby applicants need not submit the full slate of preclinical and clinical data, and approval is based in part on the FDA's findings of safety, purity, and potency for the original biologic (i.e., the reference product). Original BLAs are eligible to receive 12 years of exclusivity from the time of first

licensure of the product, which prevents the FDA from approving any biosimilars to the reference product through the abbreviated pathway, but does not prevent approval of BLAs that are accompanied by a full data package and that do not rely on the reference product. A biosimilar may be approved if the product is highly similar to the reference product notwithstanding minor differences in clinically inactive components and there are no clinically meaningful differences with the reference product in terms of the safety, purity, and potency.

Pediatric exclusivity is another type of regulatory market exclusivity in the United States. Pediatric exclusivity, if granted, adds six months to existing exclusivity periods and patent terms. This six-month exclusivity, which runs from the end of other exclusivity protection or patent term, may be granted based on the voluntary completion of a pediatric trial in accordance with an FDA-issued "Written Request" for such a trial.

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 United States and markets in other countries, sales of any products for which we receive regulatory approval for commercial sale will depend, in significant part, on the extent to which third-party payors provide coverage, and establish adequate reimbursement levels for such products. In the United States, 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 of and reviewing the cost-effectiveness of medical products, therapies and services, in addition to questioning their safety and efficacy.

Reimbursement may impact the demand for, and/or the price of, any product candidate which obtains marketing approval. Even if coverage and reimbursement is obtained for a given product candidate by a third-party payor, the resulting reimbursement payment rates may not be adequate or may require co-payments that patients find unacceptably high. Patients who are prescribed medications for the treatment of their conditions, and their prescribing physicians, generally rely on third-party payors to reimburse all or part of the costs associated with those medications. Patients are unlikely to use a product, and physicians may be less likely to prescribe a product, unless coverage is provided and reimbursement is adequate to cover all or a significant portion of the cost of the product. Therefore, coverage and adequate reimbursement is critical to new drug product acceptance.

The downward pressure on health care costs in general, particularly prescription drugs and biologics, has become very intense. Governments have shown significant interest in implementing cost-containment programs, including price controls, restrictions on reimbursement and requirements for substitution of generic products. As a result, increasingly high barriers are being erected to the entry of new products. 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 favorable coverage and adequate reimbursement. In addition, emphasis on managed care in the United States 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.

Health Care Laws Governing Interactions with Healthcare Providers

In addition to FDA restrictions on marketing of pharmaceutical products, several other types of state and federal laws restrict our business activities, including certain marketing practices. These laws include, without limitation, anti-kickback laws, false claims laws, data privacy and security laws, as well as transparency laws regarding payments or other items of value provided to healthcare providers.

The federal healthcare program Anti-Kickback Statute prohibits, among other things, knowingly and willfully offering, paying, soliciting or receiving remuneration, directly or indirectly, in cash or in kind, to induce or reward, or in return for, purchasing, leasing, ordering or arranging for the purchase, lease or order of any healthcare item, good, facility or service reimbursable, in whole or in part, under Medicare, Medicaid or other federal healthcare programs. The term ‘‘remuneration’’ has been broadly interpreted to include anything of value. This statute has been interpreted to apply to arrangements between pharmaceutical manufacturers on the one hand and prescribers, purchasers and formulary managers on the other hand. Although there are a number of statutory exceptions and regulatory safe harbors protecting certain common activities from prosecution or other regulatory sanctions, the exceptions and safe harbors are drawn narrowly, and practices that involve remuneration that are alleged to be intended to induce prescribing, purchases or recommendations may be subject to scrutiny if they do not qualify for an exception or safe harbor. Failure to meet all of the requirements of a particular applicable statutory exception or regulatory safe harbor does not make the conduct per se illegal under the federal healthcare program 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 its facts and circumstances. Several courts have interpreted the statute’s intent requirement to mean that if any one purpose of an arrangement involving remuneration is to induce referrals of federal healthcare covered business, the federal healthcare program Anti-Kickback Statute has been violated. Additionally, the intent standard under the federal healthcare program Anti-Kickback Statute was amended by the Patient Protection and Affordable Care Act of 2010, as amended by the Health Care and Education Reconciliation Act of 2010, collectively the Affordable Care Act, or ACA, 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. In addition, the ACA codified case law that a claim including items or services resulting from a violation of the federal healthcare program Anti-Kickback Statute constitutes a false or fraudulent claim for purposes of the federal civil False Claims Act.

Federal civil and criminal false claims laws, including the civil False Claims Act, and civil monetary penalties laws, prohibit any person or entity from, among other things, knowingly presenting, or causing to be presented, a false claim for payment to the federal government, or knowingly making, or causing to be made, a false statement to have a false claim paid. Pharmaceutical and other healthcare companies have been prosecuted under these laws for, among other things, allegedly inflating drug prices they report to pricing services, which in turn were used by the government to set Medicare and Medicaid reimbursement rates, and for allegedly providing free product to customers with the expectation that the customers would bill federal programs for the product. In addition, certain marketing practices, including off-label promotion, may also violate false claims laws. Further, pharmaceutical manufacturers can be held liable under the False Claims Act even when they do not submit claims directly to government payors if they are deemed to “cause” the submission of false or fraudulent claims.

The federal Health Insurance Portability and Accountability Act of 1996, or HIPAA, created new federal criminal statutes that prohibit among other actions, knowingly and willfully executing, or attempting to execute, a scheme to defraud any healthcare benefit program, including private third- party payors, knowingly and willfully embezzling or stealing from a healthcare benefit program, willfully obstructing a criminal investigation of a healthcare offense, and knowingly and willfully falsifying, concealing or covering up a material fact or making any materially false, fictitious or fraudulent statement in connection with the delivery of or payment for healthcare benefits, items or services. Like the federal healthcare program Anti-Kickback Statute, the ACA amended the intent standard for certain healthcare fraud under HIPAA 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.

In addition, we may be subject to data privacy and security regulation by both the federal government and the states in which we conduct our business. HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act, or HITECH, and its implementing regulations, imposes certain requirements on “covered entities,” including healthcare providers, health plans and healthcare clearinghouses, as well as their respective “business associates” that create, receive, maintain or transmit individually identifiable health information for or on behalf of a covered entity, relating to the privacy, security, transmission and breach of

individually identifiable health information. Further, 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.

Additionally, the federal Physician Payments Sunshine Act, created under the ACA, and its implementing regulations, require certain manufacturers of drugs, devices, biologics and medical supplies for which payment is available under Medicare, Medicaid or the Children's Health Insurance Program (with certain exceptions) to report information related to certain payments or other transfers of value provided to physicians (defined to include doctors, dentists, optometrists, podiatrists and chiropractors) and teaching hospitals, or to entities or individuals at the request of, or designated on behalf of, the physicians and teaching hospitals and to report annually certain ownership and investment interests held by physicians and their immediate family members.

Finally, the majority of states also have statutes or regulations similar to the aforementioned federal laws, some of which are broader in scope and apply to items and services reimbursed under Medicaid and other state programs, or, in several states, apply regardless of the payor. Some state laws require pharmaceutical companies to comply with the pharmaceutical industry's voluntary compliance guidelines and the relevant compliance guidance promulgated by the federal government in addition to requiring drug manufacturers to report information related to payments to clinicians and other healthcare providers or marketing expenditures. State and foreign laws also govern the privacy and security of health information in some circumstances, many of which differ from each other in significant ways and often are not preempted by HIPAA, thus complicating compliance efforts.

Because of the breadth of these laws and the narrowness of their exceptions and safe harbors, it is possible that business activities can be subject to challenge under one or more of such laws. The scope and enforcement of each of these laws is uncertain and subject to rapid change in the current environment of healthcare reform, especially in light of the lack of applicable precedent and regulations. Federal and state enforcement bodies have recently increased their scrutiny of interactions between healthcare companies and healthcare providers, which has led to a number of investigations, prosecutions, convictions and settlements in the healthcare industry.

Ensuring that business arrangements with third parties comply with applicable healthcare laws and regulations is costly and time consuming. If business operations are found to be in violation of any of the laws described above or any other applicable governmental regulations a pharmaceutical manufacturer may be subject to penalties, including civil, criminal and administrative penalties, damages, fines, disgorgement, individual imprisonment, exclusion from governmental funded healthcare programs, such as Medicare and Medicaid, additional reporting obligations and oversight if subject to a corporate integrity agreement or other agreement to resolve allegations of non-compliance with these laws, contractual damages, reputational harm, diminished profits and future earnings, and curtailment or restructuring of operations, any of which could adversely affect a pharmaceutical manufacturer's ability to operate its business and the results of its operations.

Healthcare Reform Efforts

A primary trend in the United States healthcare industry and elsewhere is cost containment. Over the last several years, there have been federal and state proposals and legislation enacted regarding the pricing of pharmaceutical and biopharmaceutical products, limiting coverage and reimbursement for drugs and other medical products, and making changes to healthcare financing and the delivery of care in the United States.

In March 2010, the ACA was enacted, which includes measures that have significantly changed health care financing by both governmental and private insurers. The provisions of the ACA of importance to the pharmaceutical and biotechnology industry are, among others, the following:

- an annual, nondeductible fee on any entity that manufactures or imports certain branded prescription drug agents or biologic agents, which is apportioned among these entities according to their market share in certain government healthcare programs;

- an increase in the rebates a manufacturer must pay under the Medicaid Drug Rebate Program to 23.1% and 13% of the average manufacturer price for branded and generic drugs, respectively;
- a new Medicare Part D coverage gap discount program, in which manufacturers must agree to offer 50% (and 70% commencing January 1, 2019) point-of-sale discounts to negotiated prices of applicable brand drugs to eligible beneficiaries during their coverage gap period, as a condition for the manufacturer's outpatient drugs to be covered under Medicare Part D;
- extension of manufacturers' Medicaid rebate liability to covered drugs dispensed to individuals who are enrolled in Medicaid managed care organizations, unless the drug is subject to discounts under the 340B drug discount program;
- a new methodology by which rebates owed by manufacturers under the Medicaid Drug Rebate Program are calculated for drugs that are inhaled, infused, instilled, implanted or injected;
- expansion of eligibility criteria for Medicaid programs by, among other things, allowing states to offer Medicaid coverage to additional individuals and by adding new mandatory eligibility categories for certain 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;
- new requirements under the federal Physician Payments Sunshine Act for drug manufacturers to report information related to payments and other transfers of value made to physicians and teaching hospitals as well as ownership or investment interests held by physicians and their immediate family members;
- a new Patient-Centered Outcomes Research Institute to oversee, identify priorities in, and conduct comparative clinical effectiveness research, along with funding for such research;
- establishment of a Center for Medicare and Medicaid Innovation at CMS to test innovative payment and service delivery models to lower Medicare and Medicaid spending, potentially including prescription drug spending; and
- a licensure framework for follow on biologic products.

Some of the provisions of the ACA have yet to be implemented, and there have been legal and political challenges to certain aspects of the ACA. Since January 2017, President Trump has signed two executive orders and other directives designed to delay, circumvent or loosen certain requirements mandated by the ACA. Concurrently, Congress has considered legislation that would repeal or repeal and replace all or part of the ACA. While Congress has not passed repeal legislation, two bills affecting the implementation of certain taxes under the ACA 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 ACA 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 ACA- 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. Further, the Bipartisan Budget Act of 2018, or the BBA, among other things, amends the ACA, effective January 1,2019, to close the coverage gap in most Medicare drug plans, commonly referred to as the "donut hole". Congress may consider other legislation to repeal or replace elements of the ACA.

In addition, other federal health reform measures have been proposed and adopted in the United States since the ACA was enacted. For example, as a result of the Budget Control Act of 2011, providers are subject to Medicare payment reductions of 2% per fiscal year, which went into effect on April 1, 2013 and, due to subsequent legislative amendments to the statute, including the BBA, will remain in effect through 2027 unless additional

Congressional action is taken. Further, the American Taxpayer Relief Act of 2012 reduced Medicare payments to several providers and increased the statute of limitations period for the government to recover overpayments from providers from three to five years. The Medicare Access and CHIP Reauthorization Act of 2015 also introduced a quality payment program under which certain individual Medicare providers will be subject to certain incentives or penalties based on new program quality standards. Payment adjustments for the Medicare quality payment program will begin in 2019. At this time, it is unclear how the introduction of the quality payment program will impact overall physician reimbursement under the Medicare program.

Further, there has been heightened governmental scrutiny in the United States of pharmaceutical pricing practices in light of the rising cost of prescription drugs and biologics. Such scrutiny has resulted in several recent Congressional inquiries and proposed and enacted federal and state legislation designed to, among other things, bring more transparency to product pricing, review the relationship between pricing and manufacturer patient programs, and reform government program reimbursement methodologies for products. At the federal level, the Trump administration's budget proposal for fiscal year 2019 contains further drug price control measures that could be enacted during the 2019 budget process or in other future legislation, including, for example, measures to permit Medicare Part D plans to negotiate the price of certain drugs under Medicare Part B, to allow some states to negotiate drug prices under Medicaid, and to eliminate cost sharing for generic drugs for low-income patients. While any proposed measures will require authorization through additional legislation to become effective, Congress and the Trump administration have each indicated that it will continue to seek new legislative and/or administrative measures to control drug costs. At the state level, legislatures have increasingly enacted legislation and implemented regulations designed to control pharmaceutical and biological product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain product access and marketing cost disclosure and transparency measures, and, in some cases, designed to encourage importation from other countries and bulk purchasing. In addition, regional healthcare authorities and individual hospitals are increasingly using bidding procedures to determine what pharmaceutical products and which suppliers will be included in their prescription drug and other healthcare programs. These measures could reduce the ultimate demand for our products, once approved, or put pressure on our product pricing.

U.S. Foreign Corrupt Practices Act, U.K. Bribery Act and Other Laws

The Foreign Corrupt Practices Act, or the 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 United States 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. Activities that violate the FCPA, even if they occur wholly outside the United States, can result in criminal and civil fines, imprisonment, disgorgement, oversight, and debarment from government contracts.

Our operations are also subject to non-U.S. anti-corruption laws such as the U.K. Bribery Act 2010, or the Bribery Act. As with the FCPA, these laws generally prohibit us and our employees and intermediaries from authorizing, promising, offering, or providing, directly or indirectly, improper or prohibited payments, or anything else of value, to government officials or other persons to obtain or retain business or gain some other business advantage. Under the Bribery Act, we may also be liable for failing to prevent a person associated with us from committing a bribery offense.

We are also subject to other laws and regulations governing our international operations, including regulations administered by the governments of the United Kingdom and the United States and authorities in the European Union, including applicable export control regulations, economic sanctions and embargoes on certain countries and persons, anti-money laundering laws, import and customs requirements and currency exchange regulations, collectively referred to as trade control laws.

Failure to comply with the Bribery Act, the FCPA and other anti-corruption laws and trade control laws could subject us to criminal and civil penalties, disgorgement and other sanctions and remedial measures, and legal expenses.

Competition

The development and commercialization for new products to treat cancer, including the indications we are pursuing is highly competitive, and considerable competition exists from major pharmaceutical, biotechnology and specialty cancer companies. In addition, many of these companies have more experience in preclinical and clinical development, manufacturing, regulatory, and global commercialization. We are also competing with academic institutions, governmental agencies, and private organizations that are conducting research in the field of cancer. Competition for highly qualified employees and their retention is intense, particularly as companies adjust to the current economic environment.

The biopharmaceutical industry, and the rapidly evolving market for developing genetically engineered T-cells and NK cells, is characterized by intense competition and rapid innovation. Genetically engineering T-cells and NK cells faces significant competition in the CAR and TCR technology space from multiple companies and their collaborators. Two such companies have now commercialized autologous CAR+ T cells against CD19: Novartis (Kymriah™ for treatment of pediatric and young adult patients with relapsed/refractory B-cell precursor ALL) and Kite Pharma/Gilead (Yescarta™ for treatment of adult patients with relapsed/refractory DLBCL). Additional companies developing autologous CAR+ T targets include Juno Therapeutics/Celgene (CD19), bluebird bio, in collaboration with Celgene (BCMA), Nanjing Legend Biotech and Janssen Biotech, Inc., a subsidiary of Johnson & Johnson (BCMA), Kite Pharma/Gilead (BCMA), Bellicum Pharmaceuticals (PSCA), Juno Therapeutics (CD22, BCMA, WT1, MUC16, L1CAM, ROR1), Autolus Limited (BCMA and TACI), CARsgen (EGFRvIII, Claudin-18.1), Mustang Bio (CD123, IL-13Ralpha2) and Aurora BioPharma (HER2 and CMV).

At least one company, Cellectis is pursuing the development of allogeneic CAR+ T therapies (in collaboration with Pfizer) and CD123 which may compete with our product candidates.

In the TCR arena, we face competition from companies targeting shared antigens including Adaptimmune in collaboration with GlaxoSmithKline (NY ESO, MAGE-A10, MAGE-A4, AFP), Kite Pharma/Gilead (MAGE-A3/A6), Tmunity and others. Additional competitors are pursuing a vaccine platform to target neoantigens for solid tumors. This includes Advaxis/Amgen, BioNTech, Neon Therapeutics and Gritstone Oncology. Neon has also announced that they are developing a T-cell therapy against neoantigens using a technology which may compete with our product candidates.

Other companies are developing non-viral gene therapies including Poseida Therapeutics (*piggyBac*). The CRISPR technology is being developed by several competitors and is being adapted for stable integration; although this genetic approach for insertion of transgenes is not yet in the clinic.

We also face competition from non-cell based treatments offered by other companies such as Amgen, AstraZeneca, Bristol-Myers, Incyte, Merck, and Roche.

In addition, our gene therapy, immuno-oncology product Ad-RTS-hIL-12 + veledimex faces competition in glioblastoma. Immunotherapy is an attractive approach for the treatment of glioma, an aggressive cancer with few treatment options. IL-12 is among the most potent anti-cancer immune cytokines, yet carries equally significant potential for immune-mediated toxicities. Our ability to control IL-12 expression *e.g.*, on and off and up and down using an orally activated gene switch, particularly in the brain's immune privileged environment, is an advancement in the potential of this therapeutic approach. Delivery of Ad-RTS-hIL-12 is done at the time of surgery and takes approximately one minute to administer and then the patient takes an oral pill. We believe this is an important distinction between the Ziopharm immunotherapy and other immunotherapies.

Companies that sell marketed drugs for recurrent glioblastoma are Genentech and Roche with Avastin (bevacizumab), a vascular endothelial growth factor directed antibody indicated for the treatment of adults with

rGBM. Arbor Pharmaceuticals markets GLIADEL Wafer which is indicated in patients with newly diagnosed high-grade malignant glioma as an adjunct to surgery and radiation and is also indicated in patients with recurrent glioblastoma multiforme as an adjunct to surgery.

Four companies have product candidates in Phase 3 development for the treatment of glioblastoma. Immunocellular Therapeutics is developing ICT-107, a dendritic cell immunotherapy, for the treatment of newly diagnosed glioblastoma. Tocagen is conducting a Phase 2/3 randomized, open-label study of Toca 511, a retroviral replicating vector, combined with Toca FC in subjects undergoing planned resection for recurrent glioblastoma. VBL Therapeutics is developing VB-111, an anti-angiogenic non-replicating adenovirus, combined with bevacizumab vs. bevacizumab monotherapy in patients with recurrent glioblastoma. DelMar is developing VAL-083, dianhydrogalactitol a systemic alkylating agent, in patients with recurrent glioblastoma who have failed standard temozolomide/radiation therapy and bevacizumab.

Other competitors with product candidates currently in Phase 2 clinical trials include Abbvie's Depatus-M (ABT-414) and DNA-2401, a conditionally replicative adenovirus being evaluated in combination with pembrolizumab (KEYTRUDA®) for recurrent glioblastoma by DNATrix and Merck. Duke University is enrolling a randomized Phase 2 study of oncolytic polio/rhinovirus recombinant (PVSRIPO) alone or in combination with lomustine in recurrent WHO Grade IV malignant glioma patients. Also, MedImmune/Astra-Zeneca's durvalumab was evaluated in a Phase 2 trial in patients with rGBM.

In addition, OncoSec is advancing IL-12 for the treatment of melanoma and has generated Phase 2 data for ImmunoPulse® IL-12 in combination with pembrolizumab.

Employees

As of February 21, 2018, we had 46 full-time employees, 33 of whom were engaged in research and development activities and 13 of whom were engaged in business development, finance, information systems, facilities, human resources or administrative support. None of our employees are subject to a collective bargaining agreement.

Corporate Information

We originally incorporated in Colorado in September 1998 (under the name Net Escapes, Inc.) and later changed our name to "EasyWeb, Inc." in February 1999. We re-incorporated in Delaware on May 16, 2005 under the same name. On September 13, 2005, we completed a "reverse" acquisition of privately held Ziopharm, Inc., a Delaware corporation. To affect this transaction, we caused ZIO Acquisition Corp., our wholly-owned subsidiary, to merge with and into Ziopharm, Inc., with Ziopharm, Inc. surviving as our wholly owned subsidiary. In accordance with the terms of the merger, the outstanding common stock of Ziopharm, Inc. automatically converted into the right to receive an aggregate of approximately 97.3% of our outstanding common stock (after giving effect to the transaction). Following the merger, we caused Ziopharm, Inc. to merge with and into us and we changed our name to "Ziopharm Oncology, Inc." Although EasyWeb, Inc. was the legal acquirer in the transaction, we accounted for the transaction as a reverse acquisition under generally accepted accounting principles. As a result, Ziopharm, Inc. became the registrant with the Securities and Exchange Commission, or the SEC, and the historical financial statements of Ziopharm, Inc. became our historical financial statements.

Our principal executive offices are located at One First Avenue, Parris Building 34, Navy Yard Plaza, Boston, Massachusetts 02129, and our telephone number is (617) 259-1970.

Available Information

Our website address is www.ziopharm.com. Our website and information included in or linked to our website are not part of this Annual Report on Form 10-K. We file reports with the SEC, which we make available on our website free of charge. These reports include annual reports on Form 10-K, quarterly reports on Form 10-Q, current reports on Form 8-K and amendments to such reports, each of which is provided on our website as soon as reasonably practicable after we electronically file such materials with or furnish them to the SEC. You can also read and copy any materials we file with the SEC at the SEC's Public Reference Room at 100 F Street, N.E., Washington, DC 20549. You can obtain additional information about the operation of the Public Reference Room by calling the SEC at 1-800-SEC-0330. In addition, the SEC maintains a website (www.sec.gov) that contains reports, proxy and information statements, and other information regarding issuers, like us, that file electronically with the SEC, including us.

Item 1A. Risk Factors

An investment in our common stock is very risky. In addition to the other information in this Annual Report on Form 10-K, you should carefully consider the following risk factors in evaluating us and our business. If any of the events described in the following risk factors were to occur, our business, financial condition, results of operation and future growth prospects would likely be materially and adversely affected. In that event, the trading price of our common stock could decline, and you could lose all or a part of your investment in our common stock. Therefore, we urge you to carefully review this entire report and consider the risk factors discussed below. Moreover, the risks described below are not the only ones that we face. Additional risks not presently known to us or that we currently deem immaterial may also affect our business, financial condition, operating results or prospects.

RISKS RELATED TO OUR BUSINESS

Our plans to develop and commercialize non-viral and viral adoptive cellular therapies based on engineered cytokines and CAR T-cell or NK cell therapies as well as TCR therapies can be considered as new approaches to cancer treatment, the successful development of which is subject to significant challenges.

We intend to employ technologies such as the technology licensed from MD Anderson pursuant to the MD Anderson License described above, and from Precigen, pursuant to the Channel Agreement, to pursue the development and commercialization of non-viral and viral adoptive cellular therapies based on cytokines, T-cells, NK cells, CARs and TCRs, possibly under control of the RTS® and other switch technologies targeting both hematologic and solid tumor malignancies. Because this is a new approach to cancer immunotherapy and cancer treatment generally, developing and commercializing product candidates subjects us to a number of challenges, including:

- obtaining regulatory approval from the FDA and other regulatory authorities that have very limited experience with the commercial development of genetically modified and/or unmodified T-cell and NK-cell therapies for cancer;
- developing and deploying consistent and reliable processes for engineering a patient's and/or donor's T-cells or NK cells *ex vivo* and infusing the T-cells or NK cells back into the patient;
- possibly conditioning patients with chemotherapy in conjunction with delivering each of the potential products, which may increase the risk of adverse side effects of the potential products;
- educating medical personnel regarding the potential side effect profile of each of the potential products, such as the potential adverse side effects related to cytokine release;
- addressing any competing technological and market developments;
- developing processes for the safe administration of these potential products, including long-term follow-up for all patients who receive the potential products;
- sourcing additional clinical and, if approved, commercial supplies for the materials used to manufacture and process the potential products;
- developing a manufacturing process and distribution network with a cost of goods that allows for an attractive return on investment;
- establishing sales and marketing capabilities after obtaining any regulatory approval to gain market acceptance;
- developing therapies for types of cancers beyond those addressed by the current potential products;
- maintaining and defending the intellectual property rights relating to any products we develop; and
- not infringing the intellectual property rights, in particular, the patent rights, of third parties, including competitors, such as developing T-cell and/or NK-cell therapies.

We cannot be sure that immunotherapy technologies that we intend to develop in partnership with MD Anderson and Precigen will yield satisfactory products that are safe and effective, scalable, or profitable. Moreover, public perception of therapy safety issues, including adoption of new therapeutics or novel approaches to treatment, may adversely influence the willingness of subjects to participate in clinical trials, or if approved, of physicians to subscribe to the novel treatment mechanics. Physicians, hospitals and third-party payors often are slow to adopt new products, technologies and treatment practices that require additional upfront costs and training. Physicians may not be willing to undergo training to adopt this novel and personalized therapy, may decide the therapy is too complex to adopt without appropriate training and may choose not to administer the therapy. Based on these and other factors, hospitals and payors may decide that the benefits of this new therapy do not or will not outweigh its costs.

We cannot assure you that we will be able to successfully address these challenges, which could prevent us from achieving our research, development and commercialization goals.

Our current product candidates are based on novel technologies and are supported by limited clinical data and we cannot assure you that our current and planned clinical trials will produce data that supports regulatory approval of one or more of these product candidates.

Our Channel Agreement with Precigen described the terms of our use of Precigen's Controlled IL-12 platform technology. The immuno-oncology effector platform in which we have acquired rights represents early-stage technology in the field of human oncology biotherapeutics, with Ad-RTS-IL-12 + veledimex having completed trials, in melanoma and breast cancer. We are continuing to pursue intratumoral injection of Ad-RTS-IL-12 + veledimex in brain cancer. Although we plan to leverage Precigen's immuno-oncology platform for additional products targeting key pathways used by cancers to grow and metastasize, we may not be successful in developing and commercializing these products for a variety of reasons.

Similarly, our genetically modified and/or non-modified T-cell and/or NK cell product candidates are supported by limited clinical data, all of which has been generated through trials conducted by MD Anderson, not by us. We plan to assume control of the overall clinical and regulatory development of our T-cell and NK-cell product candidates, and any failure to obtain, or delays in obtaining, sponsorship of new INDs, or in filing INDs sponsored by us for these or any other product candidates we determine to advance could negatively affect the timing of our potential future clinical trials. Such an impact on timing could increase research and development costs and could delay or prevent obtaining regulatory approval for our product candidates, either of which could have a material adverse effect on our business. Further, we did not control the design or conduct of the previous trials. It is possible that the FDA will not accept these previous trials as providing adequate support for future clinical trials, whether controlled by us or third parties, for any of one or more reasons, including the safety, purity, and potency of the product candidate, the degree of product characterization, elements of the design or execution of the previous trials or safety concerns, or other trial results. We may also be subject to liabilities arising from any treatment-related injuries or adverse effects in patients enrolled in these previous trials. As a result, we may be subject to unforeseen third-party claims and delays in our potential future clinical trials. We may also be required to repeat in whole or in part clinical trials previously conducted by MD Anderson or other entities, which will be expensive and delay the submission and licensure or other regulatory approvals with respect to any of our product candidates.

In addition, the results of the limited clinical trials conducted by us, Precigen and MD Anderson to date may not be replicated in future clinical trials. Our Ad-RTS-IL-12 + veledimex and genetically modified and non-modified T-cell and NK-cell product candidates, as well as other product candidates, may fail to show the desired safety and efficacy in clinical development, and we cannot assure you that the results of any future trials will demonstrate the value and efficacy of our product candidates. Moreover, there are a number of regulatory requirements that we must satisfy before we can continue clinical trials of CAR^+ T or other cellular therapy product candidates in the United States. Satisfaction of these requirements will entail substantial time, effort and financial resources. Any time, effort and financial resources we expend on our Ad-RTS-IL-12 + veledimex and

genetically modified and non-modified T-cell and NK-cell product candidates and other early-stage product candidate development programs may adversely affect our ability to continue development and commercialization of our immuno-oncology product candidates.

We report interim data on certain of our clinical trials and we cannot assure you that interim data will be predictive of either future interim results or final study results.

As part of our business, we provide updates related to the development of our product candidates, which may include updates related to interim clinical trial data. To date, our clinical trials have involved small patient populations and because of the small sample size, the interim results of these clinical trials may be subject to substantial variability and may not be indicative of either future interim results or final results.

If we cannot compete successfully for market share against other biopharmaceutical companies, we may not achieve sufficient product revenues and our business will suffer.

The biopharmaceutical industry, and the rapidly evolving market for developing genetically engineered T-cells and NK cells in particular, is characterized by intense competition and rapid innovation. Genetically engineering T-cells and NK cells faces significant competition in the CAR and TCR technology space from multiple companies and their collaborators. Two such companies have now commercialized autologous CAR+ T-cells against CD19: Novartis and Kite Pharma. Additional companies developing autologous CAR+ T targets include Juno Therapeutics/Celgene, bluebird bio, in collaboration with Celgene, Nanjing Legend Biotech and Janssen Biotech, Inc., a subsidiary of Johnson & Johnson, Kite Pharma/Gilead, Bellicum Pharmaceuticals, Juno Therapeutics, Autolus Limited, CARsgen, Mustang Bio and Aurora BioPharma. At least one company, Cellectis is pursuing the development of allogeneic CAR+ T therapies (in collaboration with Pfizer) and CD123 which may compete with our product candidates. In the TCR arena, we face competition from companies targeting shared antigens including Adaptimmune in collaboration with GlaxoSmithKline, Kite Pharma/Gilead, Tmunity and others. Additional competitors are pursuing a vaccine platform to target neoantigens for solid tumors. This includes Advaxis/Amgen, BioNTech, Neon Therapeutics and Gritstone Oncology. Neon has also announced that they are developing a T-cell therapy against neoantigens using a technology which may compete with our product candidates.

Other companies are developing non-viral gene therapies including Poseida Therapeutics. We also face competition from non-cell based treatments offered by other companies such as Amgen, AstraZeneca, Bristol-Myers, Incyte, Merck, and Roche. Companies that sell marketed drugs for recurrent glioblastoma are Genentech and Roche with Avastin and Arbor Pharmaceuticals. Four companies have product candidates in Phase 3 development for the treatment of glioblastoma. Immunocellular Therapeutics, Tocagen, VBL Therapeutics, and DelMar. Other competitors with product candidates currently in Phase 2 clinical trials include Abbvie's Depatus-M (ABT-414) and DNA-2401, a conditionally replicative adenovirus being evaluated in combination with pembrolizumab (KEYTRUDA®) for recurrent glioblastoma by DNATrix and Merck. Duke University is enrolling a randomized Phase 2 study of oncolytic polio/rhinovirus recombinant (PVSRIPO) alone or in combination with lomustine in recurrent WHO Grade IV malignant glioma patients. Also, MedImmune/Astra-Zeneca's durvalumab was evaluated in a Phase 2 trial in patients with rGBM. In addition, OncoSec is advancing IL-12 for the treatment of melanoma and has generated Phase 2 data for ImmunoPulse® IL-12 in combination with pembrolizumab.

Even if we obtain regulatory approval of potential products, we may not be the first to market and that may affect the price or demand for our potential products. Existing or future competing products may provide greater therapeutic convenience or clinical or other benefits for a specific indication than our products, or may offer comparable performance at a lower cost. Additionally, the availability and price of our competitors' products could limit the demand and the price we are able to charge for our potential products. We may not be able to implement our business plan if the acceptance of our potential products is inhibited by price competition or the reluctance of physicians to switch from existing methods of treatment to our potential products, or if physicians

switch to other new drug or biologic products or choose to reserve our potential products. Additionally, a competitor could obtain orphan product exclusivity from the FDA with respect to such competitor's product. If such competitor product is determined to be the same product as one of our potential products, that may prevent us from obtaining approval from the FDA for such potential products for the same indication for seven years, except in limited circumstances. If our products fail to capture and maintain market share, we may not achieve sufficient product revenues and our business will suffer.

We compete against fully integrated pharmaceutical companies and smaller companies that are collaborating with larger pharmaceutical companies, academic institutions, government agencies and other public and private research organizations. Many of these competitors have products already approved or in development. In addition, many of these competitors, either alone or together with their collaborative partners, operate larger research and development programs or have substantially greater financial resources than we do, as well as significantly greater experience in:

- developing drugs and biopharmaceuticals;
- undertaking preclinical testing and human clinical trials;
- obtaining FDA and other regulatory approvals of drugs and biopharmaceuticals;
- formulating and manufacturing drugs and biopharmaceuticals; and
- launching, marketing, and selling drugs and biopharmaceuticals.

Our commercial opportunity could be reduced or eliminated if our competitors develop and commercialize products that are 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, our ability to compete may be affected in many cases by insurers or other third-party payors seeking to encourage the use of generic products.

Any termination of our licenses with Precigen or MD Anderson could result in the loss of significant rights and could harm our ability to develop and commercialize our product candidates.

We are dependent on patents, know-how, and proprietary technology that are licensed from others, particularly MD Anderson and Precigen. Any termination of these licenses could result in the loss of significant rights and could harm our ability to commercialize our product candidates. Disputes may also arise between us and these licensors regarding intellectual property subject to a license agreement, including those relating to:

- the scope of rights granted under the applicable license agreement and other interpretation-related issues;
- whether and the extent to which our technology and processes, and the technology and processes of Precigen, MD Anderson and our other licensors, infringe on intellectual property of the licensor that is not subject to the applicable license agreement;
- our right to sublicense patent and other rights to third parties pursuant to our relationships with our licensors and partners;
- whether we and/or Precigen are complying with our diligence obligations with respect to the use of the licensed technology in relation to our development and commercialization of our potential products under the MD Anderson License; and
- the allocation of ownership of inventions and know-how resulting from the joint creation or use of intellectual property by our licensors and by us.

If disputes over intellectual property that we have licensed prevent or impair our ability to maintain our current licensing arrangements, particularly with MD Anderson and Precigen, on acceptable terms, we may be unable to

successfully develop and commercialize the affected potential products. We are generally also subject to all of the same risks with respect to protection of intellectual property that we license as we are for intellectual property that we own. If we or our licensors fail to adequately protect this intellectual property, our ability to commercialize potential products under our applicable licenses could suffer.

There is a substantial amount of litigation involving patents and other intellectual property rights in the biotechnology and pharmaceutical industries, as well as administrative proceedings for challenging patents, including interference, derivation, and reexamination proceedings before the United States Patent and Trademark Office, or USPTO, or oppositions and other comparable proceedings in foreign jurisdictions. Recently, due to changes in U.S. law referred to as patent reform, new procedures including inter partes review and post-grant review have been implemented, which adds uncertainty to the possibility of challenge to our or our licensors' patents in the future.

We will require additional financial resources in order to continue ongoing development of our product candidates; if we are unable to obtain these additional resources, we may be forced to delay or discontinue clinical testing of our product candidates.

We have not generated significant revenue and have incurred significant net losses in each year since our inception. For the year ended December 31, 2017, we had a net loss of $54.3 million, and, as of December 31, 2017, we have incurred approximately $712.4 million of accumulated deficit since our inception in 2003. We expect to continue to incur significant operating expenditures and net losses. Further development of our product candidates, including product candidates that we may develop under our Channel Agreement with Precigen, pursuant to the MD Anderson License or pursuant to the Ares Trading Agreement, will likely require substantial increases in our expenses as we:

- continue to undertake clinical trials for product candidates;
- scale-up the formulation and manufacturing of our product candidates;
- seek regulatory approvals for product candidates;
- work with regulatory authorities to identify and address program-related inquiries;
- implement additional internal systems and infrastructure;
- hire additional personnel;
- begin to advance candidates pursuant to the MD Anderson License; and
- commence providing funding for certain research and development activities of MD Anderson pursuant to the terms of the MD Anderson License.

We continue to seek additional financial resources to fund the further development of our product candidates. If we are unable to obtain sufficient additional capital, one or more of these programs could be placed on hold. Because we are currently devoting a significant portion of our resources to the development of immuno-oncology, further progress with the development of our other candidates may be significantly delayed and may depend on the licensing of those compounds to third parties.

As of December 31, 2017, we have approximately $70.9 million of cash and cash equivalents. Given our development plans, we anticipate cash resources will be sufficient to fund our operations into the fourth quarter of 2018, and we have no committed sources of additional capital at this time. The forecast of cash resources is forward-looking information that involves risks and uncertainties, and the actual amount of our expenses could vary materially and adversely as a result of a number of factors. We have based our estimates on assumptions that may prove to be wrong, and our expenses could prove to be significantly higher than we currently anticipate. Management does not know whether additional financing will be on terms favorable or acceptable to us when needed, if at all. If adequate additional funds are not available when required, or if we are unsuccessful in

entering into partnership agreements for further development of our product candidates, management may need to curtail development efforts. Based on the forecast, management determined that there is substantial doubt regarding our ability to continue as a going concern. As a result, our independent registered public accounting firm has expressed substantial doubt as to our ability to continue as a going concern in their report dated March 1, 2018 included in this Annual Report on Form 10-K.

We need to raise additional capital to fund our operations. The manner in which we raise any additional funds may affect the value of your investment in our common stock.

As of December 31, 2017, we have incurred approximately $712.4 million of accumulated deficit and had approximately $70.9 million of cash and cash equivalents. Given our current development plans, we anticipate that our current cash resources will be sufficient to fund our operations into the fourth quarter of 2018. However, changes may occur that would consume our existing capital prior to then, including expansion of the scope of, and/or slower than expected progress of, our research and development efforts and changes in governmental regulation. Actual costs may ultimately vary from our current expectations, which could materially impact our use of capital and our forecast of the period of time through which our financial resources will be adequate to support our operations. Also our estimates include the advancement of our immuno-oncology product candidates in the clinic under our Channel Agreement with Precigen and our increased expenses as we begin to advance candidates pursuant to the MD Anderson License with MD Anderson and commence providing funding for certain research and development activities of MD Anderson pursuant to the terms of the MD Anderson License, and we expect that the costs associated with these and any additional product candidates we pursue will increase the level of our overall research and development expenses significantly going forward.

In addition to above factors, our actual cash requirements may vary materially from our current expectations for a number of other factors that may include, but are not limited to, changes in the focus and direction of our development programs, competitive and technical advances, costs associated with the development of our product candidates, our ability to secure partnering arrangements, and costs of filing, prosecuting, defending and enforcing our intellectual property rights. If we exhaust our capital reserves more quickly than anticipated, regardless of the reason, and we are unable to obtain additional financing on terms acceptable to us or at all, we will be unable to proceed with development of some or all of our product candidates on expected timelines and will be forced to prioritize among them.

The unpredictability of the capital markets may severely hinder our ability to raise capital within the time periods needed or on terms we consider acceptable, if at all. Moreover, if we fail to advance one or more of our current product candidates to later-stage clinical trials, successfully commercialize one or more of our product candidates, or acquire new product candidates for development, we may have difficulty attracting investors that might otherwise be a source of additional financing.

Our need for additional capital and limited capital resources may force us to accept financing terms that could be significantly dilutive to existing stockholders. To the extent that we raise additional capital by issuing equity securities, our stockholders may experience dilution. In addition, we may grant future investors rights superior to those of our existing stockholders. If we raise additional funds through collaborations and licensing arrangements, it may be necessary to relinquish some rights to our technologies, product candidates or products, or grant licenses on terms that are not favorable to us. If we raise additional funds by incurring debt, we could incur significant interest expense and become subject to covenants in the related transaction documentation that could affect the manner in which we conduct our business.

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

Human clinical trials are very expensive and difficult to design, initiate and implement, in part because they are subject to rigorous regulatory requirements. The clinical trial start-up and process itself is also time-consuming and results are inherently uncertain. We estimate that clinical trials of our product candidates will take at least

several years to complete. Furthermore, failure can occur at any stage of the trials, and we could encounter problems that cause us to delay the start of, abandon or repeat clinical trials. The commencement and completion of clinical trials may be delayed by several factors, including:

- Additional nonclinical data requests by regulatory agencies;
- Unforeseen safety issues;
- Determination of dosing issues;
- Lack of effectiveness during clinical trials;
- Slower than expected rates of patient recruitment and enrollment;
- Inability to monitor patients adequately during or after treatment;
- Inability or unwillingness of medical investigators to follow our clinical protocols; and
- Regulatory determinations to temporarily or permanently cease enrollment for other reasons not related to patient safety.

Success in preclinical testing and early clinical trials does not ensure that later clinical trials will be successful. In addition, we or the FDA may suspend our clinical trials at any time if it appears that we are exposing participants to unacceptable health risks or if the FDA finds deficiencies in our IND submission or in the conduct of these trials.

See also "Risks Related to the Clinical Testing, Regulatory Approval and Manufacturing of our Product Candidates—*Our product candidates are in various stages of clinical trials, which are very expensive and time-consuming. We cannot be certain when we will be able to submit a BLA, to the FDA and any failure or delay in completing clinical trials for our product candidates could harm our business.*"

We may not be able to obtain or maintain orphan drug exclusivity for our product candidates.

We have received orphan drug designation for Ad-RTS-IL-12 + veledimex for the treatment of malignant glioma in the United States, and we may be able to receive additional orphan drug designation from the FDA and the European Medicines Agency, or EMA, for our other product candidates. In the United States, orphan designation is available to drugs intended to treat, diagnose or prevent a rare disease or condition that affects fewer than 200,000 people in the United States at the time of application for orphan designation. Orphan designation qualifies the sponsor of the product for a tax credit and marketing incentives. The first sponsor to receive FDA marketing approval for a drug with an orphan designation is entitled to a seven-year exclusive marketing period in the United States for that product for that indication and, typically, a waiver of the prescription drug user fee for its marketing application. However, a drug that the FDA considers to be clinically superior to, or different from, the approved orphan drug, even though for the same indication, may also obtain approval in the United States during the seven-year exclusive marketing period. Orphan drug exclusive marketing rights may also be lost if the FDA later determines that the request for designation was materially defective or if the manufacturer is unable to assure sufficient quantity of the drug. There is no guarantee that any of our other product candidates will receive orphan drug designation or that, even if such product candidate is granted such status, the product candidate's clinical development and regulatory approval process will not be delayed or will be successful.

We may not be able to commercialize any products, generate significant revenues, or attain profitability.

To date, none of our product candidates have been approved for commercial sale in any country. The process to develop, obtain regulatory approval for, and commercialize potential product candidates is long, complex, and costly. Unless and until we receive approval from the FDA and/or other foreign regulatory authorities for our product candidates, we cannot sell our drugs and will not have product revenues. Even if we obtain regulatory approval for one or more of our product candidates, if we are unable to successfully commercialize our products, we may not be able to generate sufficient revenues to achieve or maintain profitability, or to continue our business without raising significant additional capital, which may not be available. Our failure to achieve or maintain profitability could negatively impact the trading price of our common stock.

Ethical, legal and social concerns about synthetic biologically engineered products could limit or prevent the use of our product candidates.

Our product candidates use an immuno-oncology platform. Public perception about the safety and environmental hazards of, and ethical concerns over, genetically engineered products could influence public acceptance of our product candidates. If we and our collaborators are not able to overcome the ethical, legal and social concerns relating to biological engineering, our product candidates may not be accepted. These concerns could result in increased expenses, regulatory scrutiny, delays or other impediments to the public acceptance and commercialization of our product candidates. Our ability to develop and commercialize products could be limited by public attitudes and governmental regulation.

The subject of genetically modified organisms has received negative publicity, which has aroused public debate. This adverse publicity could lead to greater regulation and trade restrictions on the development and commercialization of genetically altered products. Further, there is a risk that our product candidates could cause adverse health effects or other AEs, which could also lead to negative publicity.

The biological platform that we use may have significantly enhanced characteristics compared to those found in naturally occurring organisms, enzymes or microbes. While we believe we produce biological technologies only for use in a controlled laboratory and industrial environment, the release of such biological technologies into uncontrolled environments could have unintended consequences. Any adverse effect resulting from such a release could have a material adverse effect on our business and financial condition, and we may have exposure to liability for any resulting harm.

We will incur additional expenses in connection with our Channel Agreement with Precigen.

Under the Channel Agreement, and subject to certain exceptions, we are responsible for, among other things, the performance of the Cancer Program, including the development, commercialization and certain aspects of manufacturing of Ziopharm Products. Precigen is responsible for establishing manufacturing capabilities and facilities for the bulk manufacture of products developed under the Cancer Program, certain other aspects of manufacturing and costs of discovery-stage research with respect to platform improvements and costs of filing, prosecution and maintenance of Precigen's patents. We expect our overall research and development expenses will continue to increase as we move forward and particularly as we move into pivotal trials. Although all human clinical trials are expensive and difficult to design and implement, we believe that due to complexity, costs associated with clinical trials for immuno-oncology products are greater than the corresponding costs associated with clinical trials for small-molecule candidates. In addition to increased research and development costs, we may need to [continue to?] add headcount to support our Channel Agreement endeavors, which would add to our general and administrative expenses going forward.

Although our forecasts for expenses and the sufficiency of our capital resources take into account our plans to develop the products under the Cancer Program, the actual costs associated therewith may be significantly in excess of forecasted amounts. In addition to the amount and timing of expenses related to the clinical trials, our actual cash requirements may vary materially from our current expectations for a number of other factors that may include, but are not limited to, changes in the focus and direction of our development programs, competitive and technical advances, costs associated with the development of our product candidates and costs of filing, prosecuting, defending and enforcing our intellectual property rights. If we exhaust our capital reserves more quickly than anticipated, regardless of the reason, and we are unable to obtain additional financing on terms acceptable to us or at all, we will be unable to proceed with development of some or all of our product candidates on expected timelines and will be forced to prioritize among them.

Failing to pay any dividends on our Series 1 preferred stock issued to Precigen may have adverse consequences.

In June 2016, we amended our Channel Agreement and GvHD Agreement with Intrexon (now Precigen) in order to, among other things, reduce the royalty rate on operating profits payable by us to Precigen from 50% to 20%.

In consideration for these amendments, we issued to Intrexon shares of our Series 1 preferred stock, $0.001 par value per share, or Series 1 preferred stock, which include, among other things, a monthly dividend of 1% payable in additional shares of Series 1 preferred stock. If we fail to pay such dividends when due, it would affect our eligibility to file Registration Statements on Form S-3 and our status as a "well-known seasoned issuer," which may increase the expense and time associated with both the filing and effectiveness of future registration statements and the consummation of future financing transactions or other offerings of our securities.

Our common stockholders may experience additional dilution as a result of the Series 1 preferred stock issued to Intrexon.

The shares of our Series 1 preferred stock include a monthly dividend of 1% which shall accrue and be paid each month in the form of additional shares of Series 1 preferred stock. For the year ended December 31, 2017, we issued an aggregate of 13,460 shares, as dividends, of our Series 1 preferred stock to Intrexon, the holder of all the outstanding shares of our Series 1 preferred stock. As a result of the monthly dividend, the number of shares of outstanding Series 1 preferred stock will increase each month that they are outstanding. Since the number of shares of our common stock issuable upon conversion of the Series 1 preferred stock is based on the 20-day volume-weighted average price of our common stock immediately prior to the public announcement of the first approval in the United States of (i) a Ziopharm Product under the Channel Agreement, (ii) a Product under the GvHD Agreement or (iii) a Product under the Ares Trading Agreement, if, at the time of such public announcement, the 20-day volume-weighted average price of our common stock has not increased by more than the cumulative amount of the dividends on the shares of Series 1 preferred stock that we originally issued to Intrexon, then our common stockholders may experience additional dilution as a result of the conversion of the Series 1 preferred stock into shares of our common stock.

The holders of our Series 1 preferred stock are entitled to rights and preferences that are significantly greater than the rights and preferences of the holders of our common stock, including payments upon a liquidation event, as well as dividend and registration rights associated with their shares.

The shares of Series 1 preferred stock that we issued to Intrexon in June 2016 in consideration for amending the Channel Agreement and GvHD Agreement are entitled to a number of rights and preferences which our common stock do not and will not have. Among these rights and preferences is the right to receive a portion of all funds to be distributed in connection with a voluntary or involuntary liquidation, dissolution or winding up of the Company or Deemed Liquidation Event, as defined in our Amended and Restated Certificate of Designation, Preferences and Rights of Series 1 preferred stock, or the Certificate of Designation (which includes a change of control or the sale, lease transfer or exclusive license of all or substantially all of our assets), in proportion to the holders' proportionate share of our common stock on an as-converted to common stock basis. For purposes of determining the Series 1 preferred stock's proportionate share on an as-converted basis in such a transaction, it would be assumed that the Series 1 preferred stock is convertible into a number of shares of common stock equal to (i) the stated value of all outstanding shares of Series 1 preferred stock, divided by (ii) the volume weighted average price of our common stock for the 20-day period ending on the date of the public announcement of such voluntary or involuntary liquidation, dissolution or winding up of the Company or Deemed Liquidation Event, rounded down to the nearest whole share, unless such transaction occurred following the public announcement of the first approval in the United States of a Ziopharm Product under the Channel Agreement, a Product under the GvHD Agreement or a Product under the Ares Trading Agreement, in which case the stated value would be divided by the volume weighted average price of the Company's common stock for the 20-day period ending on the date of the public announcement such approval. We refer to this proportionate share allocated to the holders of Series 1 preferred stock as the Series 1 Liquidation Amount. In addition, the Company may elect to redeem the shares of Series 1 preferred stock in connection with or following a Deemed Liquidation Event at a price per share equal to the Series 1 Liquidation Amount. Since the conversion rate is based on the stated value of the shares of Series 1 preferred stock, which was initially $120 million and increases at a rate of 1% per month, the holders of shares of our Series 1 preferred stock could receive a disproportionate amount of the proceeds of any voluntary or involuntary liquidation, dissolution or winding up of the Company or Deemed Liquidation Event if

our stock price has not sufficiently increased prior to the time that their proportionate share is calculated. Further, pursuant to the terms of a Securities Issuance Agreement we entered into with Intrexon in connection with the issuance of the Series 1 preferred stock, we agreed that the holders of common stock issued upon the conversion of the shares of Series 1 preferred stock issued to Intrexon shall be entitled to piggy-back registration rights with respect to any common stock registered by us following such conversion.

The Series 1 preferred stock contains protective provisions that may limit our business flexibility.

For so long as any shares of Series 1 preferred stock are outstanding, we may not, without first obtaining the consent of the holders of at least a majority of the Series 1 preferred stock then outstanding, voting together as a single class:

- amend our certificate of incorporation or the Certificate of Designation of the Series 1 preferred stock, in each case in a manner that adversely affects the powers, preferences or rights of the Series 1 preferred stock in a manner that is more adverse than the effect on any other class or series of our capital stock;
- authorize, create, issue or obligate us to issue (by reclassification, merger or otherwise) any security (or any class or series thereof) that has any powers, preferences or rights senior to the Series 1 preferred stock with respect to the distribution of assets on the liquidation, dissolution or winding up of the Company, the payment of dividends or rights of redemption; or
- enter into any transaction (or series of related transactions) the effect of which would adversely affect the holders of the Series 1 preferred stock in a manner that is more adverse than the effect on any other class or series of our capital stock.

As a result, we will not be able to take any of these actions without first seeking and obtaining the approval of the holders of our Series 1 preferred stock. In addition, we may not be able to obtain such approval in a timely manner or at all, even if we think that taking the action for which we seek approval is in our best interests. Any failure to obtain such approval could harm our business and result in a decrease in the value of our common stock.

We may not be able to retain the exclusive rights licensed to us by Precigen to develop and commercialize products involving DNA administered to humans for expression of anti-cancer effectors for the purpose of treatment or prophylaxis of cancer.

Under the Channel Agreement, we use Precigen's technology directed towards in vivo expression of effectors in connection with the development of Ad-RTS-IL-12 + veledimex, our cell therapy programs and generally to research, develop and commercialize products, in each case in which DNA is administered to humans for expression of anti-cancer effectors for the purpose of treatment or prophylaxis of cancer, which we collectively refer to as the Cancer Program. The Channel Agreement grants us a worldwide license to use patents and other intellectual property of Precigen in connection with the research, development, use, importing, manufacture, sale, and offer for sale of products involving DNA administered to humans for expression of anti-cancer effectors for the purpose of treatment or prophylaxis of cancer, which we refer to collectively as the Ziopharm Products. Such license is exclusive with respect to any clinical development, selling, offering for sale or other commercialization of Ziopharm Products, and otherwise is non-exclusive. Subject to limited exceptions, we may not sublicense the rights described without Precigen's written consent. Under the Channel Agreement, and subject to certain exceptions, we are responsible for, among other things, the performance of the Cancer Program, including development, commercialization and certain aspects of manufacturing of Ziopharm Products.

Precigen may terminate the Channel Agreement if we fail to use diligent efforts to develop and commercialize Ziopharm Products or if we elect not to pursue the development of a Cancer Program identified by Precigen that is a "Superior Therapy" as defined in the Channel Agreement. We may voluntarily terminate the Channel

Agreement upon 90 days written notice to Precigen. Upon termination of the Channel Agreement, we may continue to develop and commercialize any Ziopharm Product that, at the time of commercialization:

- is being commercialized by us;
- has received regulatory approval;
- is a subject of an application for regulatory approval that is pending before the applicable regulatory authority; or
- is the subject of at least an ongoing Phase 2 clinical trial (in the case of a termination by Precigen due to an uncured breach or a voluntary termination by us), or an ongoing Phase 1 clinical trial in the field (in the case of a termination by us due to an uncured breach or a termination by Precigen following an unconsented assignment by us or our election not to pursue development of a Superior Therapy).

With respect to these "retained" Ziopharm Products, our obligation to pay 20% of net profits derived from the sale of Ziopharm Products and 50% of revenue derived from a sublicensor will survive termination of the Channel Agreement, as described further in Note 7 to our financial statements (Commitments and Contingencies), as well as additional disclosures in our Annual Report on Form 10-K under the heading "*Business—License Agreements, Intellectual Property and Other Agreements—Exclusive Channel Partner Agreement with Precigen for the Cancer Program*."

There can be no assurance that we will be able to successfully perform under the Channel Agreement and if the Channel Agreement is terminated it may prevent us from achieving our business objectives.

The technology on which our Channel Agreement with Precigen is based relies in part on early stage technology in the field of human oncologic and autoimmune therapeutics.

Our Channel Agreement with Precigen contemplates our use of Precigen's advanced transgene engineering platform for the controlled and precise cellular production of anti-cancer effectors. The synthetic immuno-oncology effector platform in which we have acquired rights represents early-stage technology in the field of human oncology biotherapeutic, with Ad-RTS-IL-12 + veledimex having completed two Phase 2 studies, in melanoma and breast cancer. We are continuing to pursue intratumoral injection of Ad-RTS-IL-12 + veledimex in brain cancer. Although we plan to leverage Precigen's synthetic immuno-oncology platform for additional products targeting key pathways used by cancers to grow and metastasize, we may not be successful in developing and commercializing these products for a variety of reasons. The risk factors set forth herein that apply to our small molecule drug candidates, which are in various stages of development, also apply to product candidates that we seek to develop under our Channel Agreement with Precigen.

We may not be able to retain the exclusive rights licensed to us by Precigen to develop and commercialize products involving DNA administered to humans for expression of anti-cancer effectors for the purpose of treatment or prophylaxis of cancer.

Under the Channel Agreement, we use Precigen's technology directed towards in vivo expression of effectors in connection with the development of Ad-RTS-IL-12+ veledimex and generally to research, develop and commercialize products, in each case in which DNA is administered to humans for expression of anti-cancer effectors for the purpose of treatment or prophylaxis of cancer, which we collectively refer to as the Cancer Program. The Channel Agreement grants us a worldwide license to use patents and other intellectual property of Precigen in connection with the research, development, use, importing, manufacture, sale, and offer for sale of products involving DNA administered to humans for expression of anti-cancer effectors for the purpose of treatment or prophylaxis of cancer, which we refer to collectively as the Ziopharm Products. Such license is exclusive with respect to any clinical development, selling, offering for sale or other commercialization of Ziopharm Products, and otherwise is non-exclusive. Subject to limited exceptions, we may not sublicense the rights described without Precigen's written consent. Under the Channel Agreement, and subject to certain

exceptions, we are responsible for, among other things, the performance of the Cancer Program, including development, commercialization and certain aspects of manufacturing of Ziopharm Products.

Precigen may terminate the Channel Agreement if we fail to use diligent efforts to develop and commercialize Ziopharm Products or if we elect not to pursue the development of a Cancer Program identified by Precigen that is a "Superior Therapy" as defined in the Channel Agreement. We may voluntarily terminate the Channel Agreement upon 90 days written notice to Precigen.

With respect to any "retained" Ziopharm Products, our obligation to pay 20% of net profits derived from the sale of Ziopharm Products and 50% of revenue derived from a sublicensor will survive termination of the Channel Agreement, as described further in our Annual Report on Form 10-K under the heading "*Business—License Agreements, Intellectual Property and Other Agreements—Exclusive Channel Partner Agreement with Precigen*".

There can be no assurance that we will be able to successfully perform under the Channel Agreement and if the Channel Agreement is terminated it may prevent us from achieving our business objectives.

We will incur additional expenses in connection with our License Agreement with M.D. Anderson

Pursuant to the MD Anderson License with MD Anderson, we, together with Precigen, obtained an exclusive, worldwide license to certain technologies owned and licensed by MD Anderson including technologies relating to novel CAR+ T cell, NK cell and TCR cell therapies arising from the laboratory of Laurence Cooper, M.D., Ph.D., who was then at MD Anderson, as well as either co-exclusive or non-exclusive licenses under certain related technologies. Pursuant to the MD Anderson License, MD Anderson agreed to transfer to us certain existing research programs described in the MD Anderson License and we, together with Precigen, entered into a research and development agreement with MD Anderson pursuant to which we agreed to provide funding for certain research and development activities of MD Anderson for a period of three years from the date of the MD Anderson License, in an amount between $15.0 and $20.0 million per year. We made the final payment in January 2018. In addition, we also expect to enter into additional collaboration and technology transfer agreements with MD Anderson and Precigen to accelerate technology and clinical development of these product candidates. We expect to increase the level of our overall research and development expenses significantly going forward as a result of each of these items.

Although our forecasts for expenses and the sufficiency of our capital resources takes into account our plans to develop the technology licensed from MD Anderson and our obligations under the MD Anderson License, the MD Anderson License is still only beginning to be implemented, therefore the actual costs associated therewith may be significantly in excess of forecasted amounts. In addition to the amount and timing of expenses related to our relationship with MD Anderson, our actual cash requirements may vary materially from our current expectations for a number of other factors that may include, but are not limited to, changes in the focus and direction of our development programs, competitive and technical advances, costs associated with the development of our product candidates and costs of filing, prosecuting, defending and enforcing our intellectual property rights. If we exhaust our capital reserves more quickly than anticipated, regardless of the reason, and we are unable to obtain additional financing on terms acceptable to us or at all, we will be unable to proceed with development of some or all of our product candidates on expected timelines and will be forced to prioritize among them.

We may not be able to retain the rights licensed to us and Precigen by M.D. Anderson to technologies relating to CAR, T-cell therapies and other related technologies.

Under the MD Anderson License, we, together with Precigen, received an exclusive, worldwide license to certain technologies owned and licensed by MD Anderson including technologies relating to novel CAR+ T cell, NK cell and TCR cell therapies arising from the laboratory of Laurence Cooper, M.D., Ph.D., who was then at MD Anderson, as well as either co-exclusive or non-exclusive licenses under certain related technologies. When

combined with Precigen's technology suite and Ziopharm's clinically tested RTS® interleukin-12 modules, the resulting proprietary methods and technologies may help realize the promise of genetically modified CAR+ T cell and other immune cells by controlling cell expansion and activation in the body, minimizing off-target and unwanted on-target effects and toxicity while maximizing therapeutic efficacy. The term of the MD Anderson License expires on the last to occur of (a) the expiration of all patents licensed thereunder, or (b) the twentieth anniversary of the date of the MD Anderson License; provided, however, that following the expiration of the term, the Company and Precigen shall then have a fully-paid up, royalty free, perpetual, irrevocable and sublicensable license to use the licensed intellectual property thereunder.

After 10 years from the date of the MD Anderson License and subject to a 90-day cure period, MD Anderson will have the right to convert the MD Anderson License into a non-exclusive license if we and Precigen are not using commercially reasonable efforts to commercialize the licensed intellectual property on a case-by-case basis. After five years from the date of the MD Anderson License and subject to a 180-day cure period, MD Anderson will have the right to terminate the MD Anderson License with respect to specific technology(ies) funded by the government or subject to a third-party contract if we and Precigen are not meeting the diligence requirements in such funding agreement or contract, as applicable. Subject to a 30-day cure period, MD Anderson has the right to terminate the MD Anderson License if we and Precigen fail to timely deliver the shares due in consideration for the MD Anderson License. MD Anderson may also terminate the agreement with written notice upon material breach by us or Precigen, if such breach has not been cured within 60 days of receiving such notice. In addition, the MD Anderson License will terminate upon the occurrence of certain insolvency events for both us or Precigen and may be terminated by the mutual written agreement of us, Precigen and MD Anderson.

There can be no assurance that we will be able to successfully perform under the MD Anderson License and if the MD Anderson License is terminated it may prevent us from achieving our business objectives.

We have a limited operating history upon which to base an investment decision.

We have not demonstrated an ability to perform the functions necessary for the successful commercialization of any product candidates. The successful commercialization of any product candidates will require us to perform a variety of functions, including:

- Continuing to undertake preclinical development and clinical trials;
- Participating in regulatory approval processes;
- Formulating and manufacturing products; and
- Conducting sales and marketing activities.

Our operations have been limited to organizing and staffing our company, acquiring, developing and securing our proprietary product candidates, and undertaking preclinical and clinical trials of our product candidates. These operations provide a limited basis for you to assess our ability to commercialize our product candidates and the advisability of investing in our securities.

Because we currently neither have nor intend to establish internal research capabilities, we are dependent upon pharmaceutical and biotechnology companies and academic and other researchers to sell or license us their product candidates and technology.

Proposing, negotiating, and implementing an economically viable product acquisition or license is a lengthy and complex process. We compete for partnering arrangements and license agreements with pharmaceutical, biopharmaceutical, and biotechnology companies, many of which have significantly more experience than we do and have significantly more financial resources. Our competitors may have stronger relationships with certain third parties including academic research institutions, with whom we are interested in collaborating and may have, therefore, a competitive advantage in entering into partnering arrangements with those third parties. We may not be able to acquire rights to additional product candidates on terms that we find acceptable, or at all.

We expect that any product candidate to which we acquire rights will require significant additional development and other efforts prior to commercial sale, including extensive clinical testing and approval by the FDA and applicable foreign regulatory authorities. All drug product candidates are subject to the risks of failure inherent in pharmaceutical product development, including the possibility that the product candidate will not be shown to be sufficiently safe or effective for approval by regulatory authorities. Even if our product candidates are approved, they may not be economically manufactured or produced, or be successfully commercialized.

We actively evaluate additional product candidates to acquire for development. Such additional product candidates, if any, could significantly increase our capital requirements and place further strain on the time of our existing personnel, which may delay or otherwise adversely affect the development of our existing product candidates. We must manage our development efforts and clinical trials effectively, and hire, train and integrate additional management, administrative, and sales and marketing personnel. We may not be able to accomplish these tasks, and our failure to accomplish any of them could prevent us from successfully growing.

We may not be able to successfully manage our growth.

In the future, if we are able to advance our product candidates to the point of, and thereafter through, clinical trials, we will need to expand our development, regulatory, manufacturing, marketing and sales capabilities or contract with third parties to provide for these capabilities. Any future growth will place a significant strain on our management and on our administrative, operational, and financial resources. Therefore, our future financial performance and our ability to commercialize our product candidates and to compete effectively will depend, in part, on our ability to manage any future growth effectively. To manage this growth, we must expand our facilities, augment our operational, financial and management systems, and hire and train additional qualified personnel. If we are unable to manage our growth effectively, our business may be harmed.

Our business will subject us to the risk of liability claims associated with the use of hazardous materials and chemicals.

Our contract research and development activities may involve the controlled use of hazardous materials and chemicals. Although we believe that our safety procedures for using, storing, handling and disposing of these materials comply with federal, state and local laws and regulations, we cannot completely eliminate the risk of accidental injury or contamination from these materials. In the event of such an accident, we could be held liable for any resulting damages and any liability could have a materially adverse effect on our business, financial condition, and results of operations. In addition, the federal, state and local laws and regulations governing the use, manufacture, storage, handling and disposal of hazardous or radioactive materials and waste products may require our contractors to incur substantial compliance costs that could materially adversely affect our business, financial condition, and results of operations.

We rely on key executive officers and scientific and medical advisors, and their knowledge of our business and technical expertise would be difficult to replace.

We are highly dependent on Dr. Laurence J.N. Cooper, our Chief Executive Officer; Dr. David Mauney, our Executive Vice President and Chief Business Officer and interim Chief Operating Officer; Dr. Francois Lebel, our Chief Medical Officer, and Executive Vice President of Research and Development and our principal scientific, regulatory, and medical advisors. Each of Drs. Cooper, Mauney, and Lebel may terminate their employment with us at any time, subject, however, to certain non-compete and non-solicitation covenants. The loss of the technical knowledge and management and industry expertise of each of Drs. Cooper, Mauney, Lebel, or any of our other key personnel, could result in delays in product development, loss of customers and sales, and diversion of management resources, which could adversely affect our operating results. We do not carry “key person” life insurance policies on any of our officers or key employees.

If we are unable to hire additional qualified personnel, our ability to grow our business may be harmed.

We will need to hire additional qualified personnel with expertise in preclinical and clinical research and testing, government regulation, formulation and manufacturing, and eventually, sales and marketing. We compete for qualified individuals with numerous biopharmaceutical companies, universities, and other research institutions. Competition for such individuals is intense and we cannot be certain that our search for such personnel will be successful. Attracting and retaining qualified personnel will be critical to our success. If we are unable to hire additional qualified personnel, our ability to grow our business may be harmed.

We may incur substantial liabilities and may be required to limit commercialization of our products in response to product liability lawsuits.

The testing and marketing of medical products entail an inherent risk of product liability. If we cannot successfully defend ourselves against product liability claims, we may incur substantial liabilities or be required to limit commercialization of our products, if approved. Even a successful defense would require significant financial and management resources. Regardless of the merit or eventual outcome, liability claims may result in:

- Decreased demand for our product candidates;
- Injury to our reputation;
- Withdrawal of clinical trial participants;
- Withdrawal of prior governmental approvals;
- Costs of related litigation;
- Substantial monetary awards to patients;
- Product recalls;
- Loss of revenue; and
- The inability to commercialize our product candidates.

We currently carry clinical trial insurance and product liability insurance. However, an inability to renew our policies or to obtain sufficient insurance at an acceptable cost could prevent or inhibit the commercialization of pharmaceutical products that we develop, alone or with collaborators.

Our business and operations would suffer in the event of system failures.

Despite the implementation of security measures, our internal computer systems and those of our current and future contractors and consultants are vulnerable to damage from computer viruses, unauthorized access, natural disasters, terrorism, war and telecommunication and electrical failures. While we are not aware of any such material system failure, accident or security breach to date, if such an event were to occur and cause interruptions in our operations, it could result in a material disruption of our development programs and our business operations. For example, the loss of clinical trial data from completed or future clinical trials could result in delays in our regulatory approval efforts and significantly increase our costs to recover or reproduce the data. Likewise, we rely on third parties to manufacture our product candidates and conduct clinical trials, and similar events relating to their computer systems could also have a material adverse effect on our business. To the extent that any disruption or security breach were to result in a loss of, or damage to, our data or applications, or inappropriate disclosure of confidential or proprietary information, we could incur liability and the further development and commercialization of our product candidates could be delayed.

RISKS RELATED TO THE CLINICAL TESTING, REGULATORY APPROVAL AND MANUFACTURING OF OUR PRODUCT CANDIDATES

If we are unable to obtain the necessary U.S. or worldwide regulatory approvals to commercialize any product candidate, our business will suffer.

We may not be able to obtain the approvals necessary to commercialize our product candidates, or any product candidate that we may acquire or develop in the future for commercial sale. We will need FDA approval to commercialize our product candidates in the United States and approvals from regulatory authorities in foreign jurisdictions equivalent to the FDA to commercialize our product candidates in those jurisdictions. In order to obtain FDA approval of any product candidate, we must submit to the FDA a Biologics License Application, or BLA, demonstrating that the product candidate is safe for humans and effective for its intended use. This demonstration requires significant research and animal tests, which are referred to as preclinical studies, as well as human tests, which are referred to as clinical trials. Satisfaction of the FDA's regulatory requirements typically takes many years, depending upon the type, complexity, and novelty of the product candidate, and will require substantial resources for research, development, and testing. We cannot predict whether our research, development, and clinical approaches will result in drugs that the FDA will consider safe for humans and effective for their intended uses. The FDA has substantial discretion in the drug approval process and may require us to conduct additional preclinical and clinical testing or to perform post-marketing studies. The approval process may also be delayed by changes in government regulation, future legislation, or administrative action or changes in FDA policy that occur prior to or during our regulatory review. Delays in obtaining regulatory approvals may:

- Delay commercialization of, and our ability to derive product revenues from, our product candidates;
- Impose costly procedures on us; and
- Diminish any competitive advantages that we may otherwise enjoy.

Even if we comply with all FDA requests, the FDA may ultimately reject one or more of our BLAs. We cannot be sure that we will ever obtain regulatory approval for any of our product candidates. Failure to obtain FDA approval for our product candidates will severely undermine our business by leaving us without a saleable product, and therefore without any potential revenue source, until another product candidate can be developed. There is no guarantee that we will ever be able to develop or acquire another product candidate or that we will obtain FDA approval if we are able to do so.

In foreign jurisdictions, we similarly must receive approval from applicable regulatory authorities before we can commercialize any drugs. Foreign regulatory approval processes generally include all of the risks associated with the FDA approval procedures described above.

Our product candidates are in various stages of clinical trials, which are very expensive and time-consuming. We cannot be certain when we will be able to submit a BLA to the FDA and any failure or delay in completing clinical trials for our product candidates could harm our business.

Our product candidates are in various stages of development and require extensive clinical testing. Notwithstanding our current clinical trial plans for each of our existing product candidates, we may not be able to commence additional trials or see results from these trials within our anticipated timelines. As such, we cannot predict with any certainty if or when we might submit a BLA for regulatory approval of our product candidates or whether such a BLA will be accepted. Because we do not anticipate generating revenues unless and until we submit one or more BLAs and thereafter obtain requisite FDA approvals, the timing of our BLA submissions and FDA determinations regarding approval thereof, will directly affect if and when we are able to generate revenues.

Our product candidates may cause undesirable side effects or have other properties that could delay or prevent their regulatory approval, limit the commercial profile of an approved label, or result in significant negative consequences following any potential marketing approval.

As with many pharmaceutical and biological products, treatment with our product candidates may produce undesirable side effects or adverse reactions or events, including potential adverse side effects related to cytokine release. If our product candidates or similar products or product candidates under development by third parties demonstrate unacceptable AEs, we may be required to halt or delay further clinical development of our product candidates. The FDA or other foreign regulatory authorities could order us to cease further development of or deny approval of our product candidates for any or all targeted indications.

The product-related side effects could affect patient recruitment or the ability of enrolled patients to complete the trial or result in potential product liability claims. In addition, these side effects may not be appropriately or timely recognized or managed by the treating medical staff, particularly outside of the institutions that collaborate with us, as toxicities resulting from our novel technologies may not be normally encountered in the general patient population and by medical personnel. We expect to have to train medical personnel using our product candidates to understand their side effect profiles, both for our planned clinical trials and upon any commercialization of any product candidates. Inadequate training in recognizing or managing the potential side effects of our product candidates could result in adverse effects to patients, including death.

Additionally, if one or more of our product candidates receives marketing approval, and we or others later identify undesirable side effects caused by such products, including during any long-term follow-up observation period recommended or required for patients who receive treatment using our products, a number of potentially significant negative consequences could result, including:

- regulatory authorities may withdraw approvals of such product;
- regulatory authorities may require additional warnings on the label;
- we may be required to create a risk evaluation and mitigation strategy plan, which could include a medication guide outlining the risks of such side effects for distribution to patients, a communication plan for healthcare providers, and/or other elements to assure safe use;
- we could be sued and held liable for harm caused to patients; and
- our reputation may suffer.

Any of the foregoing could prevent us from achieving or maintaining market acceptance of the particular product candidate, if approved. Furthermore, any of these occurrences may harm our business, financial condition and prospects significantly.

Our cell-based and gene therapy immuno-oncology products rely on the availability of reagents, specialized equipment, and other specialty materials and infrastructure, which may not be available to us on acceptable terms or at all. For some of these reagents, equipment, and materials, we rely or may rely on sole source vendors or a limited number of vendors, which could impair our ability to manufacture and supply our products.

Manufacturing our product candidates will require many reagents, which are substances used in our manufacturing processes to bring about chemical or biological reactions, and other specialty materials and equipment, some of which are manufactured or supplied by small companies with limited resources and experience to support commercial biologics production. We currently depend on a limited number of vendors for certain materials and equipment used in the manufacture of our product candidates. Some of these suppliers may not have the capacity to support commercial products manufactured under current good manufacturing practices by biopharmaceutical firms or may otherwise be ill-equipped to support our needs. We also do not have supply contracts with many of these suppliers and may not be able to obtain supply contracts with them on acceptable terms or at all. Accordingly, we may experience delays in receiving key materials and equipment to support clinical or commercial manufacturing.

For some of these reagents, equipment, infrastructure, and materials, we rely and may in the future rely on sole source vendors or a limited number of vendors. An inability to continue to source product from any of these suppliers, which could be due to regulatory actions or requirements affecting the supplier, adverse financial or other strategic developments experienced by a supplier, labor disputes or shortages, unexpected demands, or quality issues, could adversely affect our ability to satisfy demand for our product candidates, which could adversely and materially affect our product sales and operating results or our ability to conduct clinical trials, either of which could significantly harm our business.

As we continue to develop and scale our manufacturing process, we expect that we will need to obtain rights to and supplies of certain materials and equipment to be used as part of that process. We may not be able to obtain rights to such materials on commercially reasonable terms, or at all, and if we are unable to alter our process in a commercially viable manner to avoid the use of such materials or find a suitable substitute, it would have a material adverse effect on our business. Even if we are able to alter our process so as to use other materials or equipment, such a change may lead to a delay in our clinical development and/or commercialization plans. If such a change occurs for product candidate that is already in clinical testing, the change may require us to perform both ex vivo comparability studies and to collect additional data from patients prior to undertaking more advanced clinical trials.

The results of our clinical trials may not support our product candidate claims.

Even if our clinical trials are completed as planned, we cannot be certain that their results will support approval of our product candidates. The FDA normally expects two randomized, well-controlled Phase 3 pivotal trials in support of approval of a BLA. Success in preclinical testing and early clinical trials does not ensure that later clinical trials will be successful, and we cannot be certain that the results of later clinical trials will replicate the results of prior clinical trials and preclinical testing. The clinical trial process may fail to demonstrate that our product candidates are safe for humans and effective for the indicated uses. This failure would cause us to abandon a product candidate and may delay development of other product candidates. Any delay in, or termination of, our clinical trials will delay the submission of our BLAs with the FDA and, ultimately, our ability to commercialize our product candidates and generate product revenues. In addition, our clinical trials involve small patient populations. Because of the small sample size, the results of these clinical trials may not be indicative of future results.

Our synthetic immuno-oncology product candidates are based on a novel technology, which makes it difficult to predict the time and cost of product candidate development and subsequently obtaining regulatory approval. Currently, few gene therapy products have been approved in the United States and Europe.

We are currently focused on developing products in immuno-oncology that employ novel gene expression, control and cell technologies to deliver safe, effective and scalable cell- and viral-based therapies for the treatment of cancer. Due to the novelty of this medical technology, there can be no assurance that any development problems we experience in the future related to our immuno-oncology platform will not cause significant delays or unanticipated costs, or that such development problems can be solved. We may also experience unanticipated problems or delays in expanding our manufacturing capacity or transferring our manufacturing process to commercial partners, which may prevent us from completing our clinical trials or commercializing our immuno-oncology product candidates on a timely or profitable basis, if at all.

In addition, the clinical study requirements of the FDA, the EMA and other regulatory agencies and the criteria these regulators use to determine the safety and efficacy of a product candidate vary substantially according to the type, complexity, novelty and intended use and market of the potential products. The regulatory approval process for novel product candidates such as ours can be more expensive and take longer than for other, better known or extensively studied pharmaceutical or other product candidates. Currently, two gene therapy products, Glybera and Strimvelis, have received approval from the EMA. UniQure’s Glybera, received marketing authorization from the EMA in 2012 but has struggled commercially as a result of high cost and limited demand.

GlaxoSmithKline's Strimvelis was approved by the EMA in May 2016 and in March 2017 dosed its first patient. According to GlaxoSmithKline, delays in Strimvelis's commercialization were due to cross-border European reimbursement. These factors make it difficult to determine how long it will take or how much it will cost to obtain regulatory approvals for our product candidates in either the United States or Europe. Approvals by the EMA may not be indicative of what the FDA may require for approval. The FDA approved its first gene therapy, Luxturna, in December 2017.

Regulatory requirements governing gene and cell therapy products have changed frequently and may continue to change in the future. For example, the FDA has established the Office of Cellular, Tissue and Gene Therapies within its Center for Biologics Evaluation and Research, or CBER, to consolidate the review of gene therapy and related products, and the Cellular, Tissue and Gene Therapies Advisory Committee to advise CBER on its review. Gene therapy clinical trials conducted at institutions that receive funding for recombinant DNA research from the U.S. National Institutes of Health, or the NIH, are also subject to potential review by the NIH Office of Biotechnology Activities' Recombinant DNA Advisory Committee, or the RAC. Although the FDA decides whether individual gene therapy protocols may proceed, the RAC review process can impede the initiation of a clinical trial, even if the FDA has reviewed the trial and approved its initiation. Conversely, the FDA can put an IND on clinical hold even if the RAC has provided a favorable review. Also, before a clinical trial can begin at an NIH-funded institution, that institution's institutional review board, or IRB, and its Institutional Biosafety Committee will have to review the proposed clinical trial to assess the safety of the trial. In addition, adverse developments in clinical trials of gene therapy products conducted by others may cause the FDA or other regulatory bodies to change the requirements for approval of any of our product candidates.

These regulatory review committees and advisory groups and the new guidelines they promulgate may lengthen the regulatory review process, require us to perform additional studies, increase our development costs, lead to changes in regulatory positions and interpretations, delay or prevent approval and commercialization of these treatment candidates or lead to significant post-approval limitations or restrictions. As we advance our immuno-oncology product candidates, we will be required to consult with these regulatory and advisory groups, and comply with applicable guidelines. If we fail to do so, we may be required to delay or discontinue development of our product candidates. These additional processes may result in a review and approval process that is longer than we otherwise would have expected for oncology product candidates. Delay or failure to obtain, or unexpected costs in obtaining, the regulatory approval necessary to bring a potential product to market could decrease our ability to generate sufficient product revenue to maintain our business.

Because we are dependent upon clinical research institutions and other contractors for clinical testing and for research and development activities, the results of our clinical trials and such research activities are, to a certain extent, beyond our control.

We materially rely upon independent investigators and collaborators, such as universities and medical institutions, to conduct our preclinical and clinical trials under agreements with us. These collaborators are not our employees and we cannot control the amount or timing of resources that they devote to our programs. These investigators may not assign as great a priority to our programs or pursue them as diligently as we would if we were undertaking such programs ourselves. If outside collaborators fail to devote sufficient time and resources to our drug development programs, or if their performance is substandard, the approval of our FDA applications, if any, and our introduction of new products, if any, will be delayed. These collaborators may also have relationships with other commercial entities, some of whom may compete with us. If our collaborators assist our competitors to our detriment, our competitive position would be harmed.

Our reliance on third parties to formulate and manufacture our product candidates exposes us to a number of risks that may delay the development, regulatory approval and commercialization of our products or result in higher product costs.

We do not have experience in drug formulation or manufacturing of drugs or biologics and do not intend to establish our own manufacturing facilities. Although we will work closely with and rely upon Precigen on the

manufacturing and scale-up of Precigen product candidates, we lack the resources and expertise to formulate or manufacture our own product candidates. We currently are contracting for the manufacture of our product candidates. We intend to contract with one or more manufacturers to manufacture, supply, store, and distribute drug supplies for our clinical trials. If a product candidate we develop or acquire in the future receives FDA approval, we will rely on one or more third-party contractors or Precigen to manufacture our products. Our anticipated future reliance on a limited number of third-party manufacturers exposes us to the following risks:

- We may be unable to identify manufacturers on acceptable terms or at all because the number of potential manufacturers is limited and the FDA must approve any replacement contractor. This approval would require new testing and compliance inspections. In addition, a new manufacturer would have to be educated in, or develop substantially equivalent processes for, production of our products after receipt of FDA approval, if any.
- Our third-party manufacturers might be unable to formulate and manufacture our products in the volume and of the quality required to meet our clinical needs and commercial needs, if any.
- Our future contract manufacturers may not perform as agreed or may not remain in the contract manufacturing business for the time required to supply our clinical trials or to successfully produce, store, and distribute our products.
- Drug manufacturers are subject to ongoing periodic unannounced inspection by the FDA, the Drug Enforcement Administration and corresponding state and foreign agencies to ensure strict compliance with current good manufacturing practices, or cGMP, and other government regulations and corresponding foreign standards. We do not have control over third-party manufacturers' compliance with these regulations and standards.
- If any third-party manufacturer makes improvements in the manufacturing process for our products, we may not own, or may have to share, the intellectual property rights to the innovation.
- Our third-party manufacturers may not be able to comply with cGMP regulations or similar regulatory requirements outside the United States. Our failure, or the failure of our third-party manufacturers, to comply with applicable regulations could result in sanctions being imposed on us, including clinical holds, fines, injunctions, civil penalties, delays, suspension or withdrawal of approvals, license revocation, seizures or recalls of drug candidates or products, operating restrictions and criminal prosecutions, any of which could significantly and adversely affect supplies of our products.

Each of these risks could delay our clinical trials, the approval, if any, of our product candidates by the FDA or the commercialization of our product candidates or result in higher costs or deprive us of potential product revenues.

Any product candidate for which we obtain marketing approval could be subject to post-marketing restrictions or withdrawal from the market and we may be subject to penalties if we fail to comply with regulatory requirements or if we experience unanticipated problems with our products, when and if any of them are approved.

Any product candidate for which we obtain marketing approval, along with the manufacturing processes, post-approval clinical data, labeling, advertising and promotional activities for such product, will be subject to continual requirements of and review by the FDA and other regulatory authorities. These requirements include, among other things, submissions of safety and other post-marketing information and reports, registration and listing requirements, cGMP requirements relating to manufacturing, quality control, quality assurance and corresponding maintenance of records and documents, requirements regarding the distribution of samples to physicians and recordkeeping. Even if marketing approval of a product candidate is granted, the approval may be subject to limitations on the indicated uses for which the product may be marketed or to the conditions of approval, including the requirement to implement a risk evaluation and mitigation strategy, or REMS, which could include requirements for a restricted distribution system. If any of our product candidates receives marketing approval, the accompanying label may limit the approved uses, which could limit sales of the product.

The FDA may also impose requirements for costly post-marketing studies or clinical trials and surveillance to monitor the safety or efficacy of our approved products. The FDA closely regulates the post-approval marketing and promotion of products to ensure that they are marketed only for the approved indications and in accordance with the provisions of the approved labeling. The FDA imposes stringent restrictions on manufacturers' communications regarding off-label use and if we market our products outside of their approved indications, we may be subject to enforcement action for off-label marketing. Violations of the Federal Food, Drug and Cosmetic Act relating to the promotion of prescription drugs may lead to investigations alleging violations of federal and state health care fraud and abuse laws, as well as state consumer protection laws.

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

- Litigation involving patients taking our product;
- Restrictions on such products, manufacturers or manufacturing processes;
- Restrictions on the labeling or marketing of a product;
- Restrictions on product distribution or use;
- Requirements to conduct post-marketing studies or clinical trials;
- Warning letters;
- Withdrawal of the products from the market;
- Refusal to approve pending applications or supplements to approved applications that we submit;
- Recall of products;
- Fines, restitution or disgorgement of profits or revenues;
- Suspension or withdrawal of marketing approvals;
- Damage to relationships with existing and potential collaborators;
- Unfavorable press coverage and damage to our reputation;
- Refusal to permit the import or export of our products;
- Product seizure; or
- Injunctions or the imposition of civil or criminal penalties.

Noncompliance with similar EU requirements regarding safety monitoring or pharmacovigilance can also result in significant financial penalties. Similarly, failure to comply with U.S. and foreign regulatory requirements regarding the development of products for pediatric populations and the protection of personal health information can also lead to significant penalties and sanctions.

RISKS RELATED TO OUR ABILITY TO COMMERCIALIZE OUR PRODUCT CANDIDATES

If we are unable either to create sales, marketing and distribution capabilities or enter into agreements with third parties to perform these functions, we will be unable to commercialize our product candidates successfully.

We currently have no marketing, sales, or distribution capabilities. If and when we become reasonably certain that we will be able to commercialize our current or future product candidates, we anticipate allocating resources to the marketing, sales and distribution of our proposed products in North America and in certain other countries; however, we cannot assure that we will be able to market, sell, and distribute our products successfully. Our future success also may depend, in part, on our ability to enter into and maintain collaborative relationships for

such capabilities and to encourage the collaborator's strategic interest in the products under development, and such collaborator's ability to successfully market and sell any such products. Although we intend to pursue certain collaborative arrangements regarding the sale and marketing of certain of our product candidates, there are no assurances that we will be able to establish or maintain collaborative arrangements or, if we are able to do so, whether we would be able to conduct our own sales efforts. There can also be no assurance that we will be able to establish or maintain relationships with third-party collaborators or develop in-house sales and distribution capabilities. To the extent that we depend on third parties for marketing and distribution, any revenues we receive will depend upon the efforts of such third parties, and there can be no assurance that such efforts will be successful. In addition, there can also be no assurance that we will be able to market and sell our product candidates in the United States or overseas.

If we are not able to partner with a third party and are not successful in recruiting sales and marketing personnel or in building a sales and marketing infrastructure, we will have difficulty commercializing our product candidates, which would harm our business. If we rely on pharmaceutical or biotechnology companies with established distribution systems to market our products, we will need to establish and maintain partnership arrangements, and we may not be able to enter into these arrangements on acceptable terms or at all. To the extent that we enter into co-promotion or other arrangements, any revenues we receive will depend upon the efforts of third parties that may not be successful and that will be only partially in our control.

If we cannot compete successfully for market share against other biopharmaceutical companies, we may not achieve sufficient product revenues and our business will suffer.

The market for our product candidates is characterized by intense competition and rapid technological advances. If a product candidate receives FDA approval, it will compete with a number of existing and future products and therapies developed, manufactured and marketed by others. Existing or future competing products may provide greater therapeutic convenience or clinical or other benefits for a specific indication than our products, or may offer comparable performance at a lower cost. If our products fail to capture and maintain market share, we may not achieve sufficient product revenues and our business will suffer.

We will compete against fully integrated pharmaceutical companies and smaller companies that are collaborating with larger pharmaceutical companies, academic institutions, government agencies and other public and private research organizations. Many of these competitors have products already approved or in development. In addition, many of these competitors, either alone or together with their collaborative partners, operate larger research and development programs or have substantially greater financial resources than we do, as well as significantly greater experience in:

- Developing drugs and biopharmaceuticals;
- Undertaking preclinical testing and human clinical trials;
- Obtaining FDA and other regulatory approvals of drugs and biopharmaceuticals;
- Formulating and manufacturing drugs and biopharmaceuticals; and
- Launching, marketing, and selling drugs and biopharmaceuticals.

Our commercial opportunity could be reduced or eliminated if our competitors develop and commercialize products that are 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, our ability to compete may be affected in many cases by insurers or other third-party payors seeking to encourage the use of generic products.

If physicians and patients do not accept and use our product candidates, our ability to generate revenue from sales of our products will be materially impaired.

Even if the FDA and/or foreign equivalents thereof approve our product candidates, physicians and patients may not accept and use them. Acceptance and use of our products will depend upon a number of factors including:

- Perceptions by members of the healthcare community, including physicians, about the safety and effectiveness of our drugs;
- Pharmacological benefit and cost-effectiveness of our products relative to competing products;
- Availability of coverage and adequate reimbursement for our products from government or other healthcare payors;
- Effectiveness of marketing and distribution efforts by us and our licensees and distributors, if any; and
- The price at which we sell our products.

Because we expect sales of our current product candidates, if approved, to generate substantially all of our product revenues for the foreseeable future, the failure of a drug to find market acceptance would harm our business and could require us to seek additional financing in order to fund the development of future product candidates.

Our ability to generate product revenues will be diminished if our products do not obtain coverage or adequate reimbursement from payors.

Our ability to commercialize our product candidates, if approved, alone or with collaborators, will depend in part on the extent to which coverage and reimbursement will be available from government and health administration authorities, private health maintenance organizations and health insurers and other third-party payors.

Patients who are prescribed medicine for the treatment of their conditions generally rely on third-party payors to reimburse all or part of the costs associated with their prescription drugs. Adequate coverage and reimbursement from governmental healthcare programs, such as Medicare and Medicaid, and commercial payors is critical to new product acceptance. Coverage decisions may depend upon clinical and economic standards that disfavor new drug products when more established or lower cost therapeutic alternatives are already available or subsequently become available. Even if we obtain coverage for our product candidates, the resulting reimbursement payment rates might not be adequate or may require co-payments that patients find unacceptably high. Patients are unlikely to use our product candidates unless coverage is provided and reimbursement is adequate to cover a significant portion of the cost of our product candidates.

In addition, the market for our product candidates for which we may receive regulatory approval will depend significantly on access to third-party payors' drug formularies, or lists of medications for which third-party payors provide coverage and reimbursement, which might not include all of the FDA-approved drugs for a particular indication. The industry competition to be included in such formularies often leads to downward pricing pressures on pharmaceutical companies. Also, third-party payors may refuse to include a particular branded drug in their formularies or otherwise restrict patient access to a branded drug when a less costly generic equivalent or other alternative is available.

Third-party payors, whether foreign or domestic, or governmental or commercial, are developing increasingly sophisticated methods of controlling healthcare costs. In addition, in the United States, no uniform policy of coverage and reimbursement for drug products exists among third-party payors. Therefore, coverage and reimbursement for drug products can differ significantly from payor to payor. As a result, the coverage determination process is often a time-consuming and costly process that requires us to provide scientific and clinical support for the use of our products to each payor separately, with no assurance that approval will be obtained. If we are unable to obtain coverage of and adequate payment levels for our product candidates from third-party payors, physicians may limit how much or under what circumstances they will prescribe or administer our products and patients may decline to purchase them. This in turn could affect our ability to successfully

commercialize our products and impact our profitability, results of operations, financial condition, and future success.

In addition, in many foreign countries, particularly the countries of the EU, the pricing of prescription drugs is subject to government control. In some non-U.S. jurisdictions, the proposed pricing for a drug must be approved before it may be lawfully marketed. The requirements governing drug pricing vary widely from country to country. For example, the EU provides options for its member states to restrict the range of medicinal products for which their national health insurance systems provide reimbursement and to control the prices of medicinal products for human use. A member state may approve a specific price for the medicinal product or it may instead adopt a system of direct or indirect controls on the profitability of the company placing the medicinal product on the market. We may face competition for our product candidates from lower-priced products in foreign countries that have placed price controls on pharmaceutical products. In addition, there may be importation of foreign products that compete with our own products, which could negatively impact our profitability.

The market opportunities for our product candidates may be limited to those patients who are ineligible for or have failed prior treatments and may be small.

Cancer therapies are sometimes characterized as first line, second line, or third line, and the FDA often approves new therapies initially only for third line use. When cancer is detected early enough, first line therapy is sometimes adequate to cure the cancer or prolong life without a cure. Whenever first line therapy, usually chemotherapy, hormone therapy, surgery, or a combination of these, proves unsuccessful, second line therapy may be administered. Second line therapies often consist of more chemotherapy, radiation, antibody drugs, tumor targeted small molecules, or a combination of these. Third line therapies can include bone marrow transplantation, antibody and small molecule targeted therapies, more invasive forms of surgery, and new technologies. We expect to initially seek approval of our product candidates as a third line therapy for patients who have failed other approved treatments.

Subsequently, for those products that prove to be sufficiently beneficial, if any, we would expect to seek approval as a second line therapy and potentially as a first line therapy, but there is no guarantee that our product candidates, even if approved, would be approved for second line or first line therapy. In addition, we may have to conduct additional clinical trials prior to gaining approval for second line or first line therapy.

Our projections of both the number of people who have the cancers we are targeting, as well as the subset of people with these cancers in a position to receive third line therapy and who have the potential to benefit from treatment with our product candidates, are based on our beliefs and estimates. These estimates have been derived from a variety of sources, including scientific literature, surveys of clinics, patient foundations, or market research and may prove to be incorrect. Further, new studies may change the estimated incidence or prevalence of these cancers. The number of patients may turn out to be lower than expected. Additionally, the potentially addressable patient population for our product candidates may be limited or may not be amenable to treatment with our product candidates. Even if we obtain significant market share for our product candidates, because the potential target populations are small, we may never achieve profitability without obtaining regulatory approval for additional indications, including use as a first or second line therapy.

Our market opportunities may also be limited by competitor treatments that may enter the market. See also “Risks Related to Our Ability to Commercialize Our Product Candidates—*If we cannot compete successfully for market share against other biopharmaceutical companies, we may not achieve sufficient product revenues and our business will suffer*.”

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

In both the United States and certain foreign jurisdictions, there have been a number of legislative and regulatory enactments in recent years that change the healthcare system in ways that could impact our future ability to sell our product candidates profitably.

Furthermore, there have been and continue to be a number of initiatives at the federal and state level that seek to reduce healthcare costs. Most significantly, in March 2010, President Obama signed into law the Patient Protection and Affordable Health Care Act, as amended by the Health Care and Education Reconciliation Act, or collectively the ACA, which includes measures that significantly change the way healthcare is financed by both governmental and private insurers. Among the provisions of the ACA of importance to the pharmaceutical industry are the following:

- An annual, nondeductible fee on any entity that manufactures or imports certain branded prescription drugs and biologic agents, apportioned among these entities according to their market share in certain government healthcare programs;
- An increase in the statutory minimum rebates a manufacturer must pay under the Medicaid Drug Rebate Program to 23.1% and 13% of the average manufacturer price for most branded and generic drugs, respectively;
- A new Medicare Part D coverage gap discount program, in which manufacturers must agree to offer 50% point-of-sale discounts off negotiated prices of applicable brand drugs to eligible beneficiaries during their coverage gap period, as a condition for the manufacturer's outpatient drugs to be covered under Medicare Part D;
- An extension of manufacturers' Medicaid rebate liability to covered drugs dispensed to individuals who are enrolled in Medicaid managed care organizations;
- New methodologies by which rebates owed by manufacturers under the Medicaid Drug Rebate Program are calculated for drugs that are inhaled, infused, instilled, implanted or injected, and for drugs that are line extensions;
- 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 both the volume of sales and manufacturers' Medicaid rebate liability;
- Expansion of the entities eligible for discounts under the Public Health Service pharmaceutical pricing program;
- A new requirement to annually report drug samples that certain manufacturers and authorized distributors provide to physicians;
- Expansion of healthcare fraud and abuse laws, including the False Claims Act and the Anti-Kickback Statute, new government investigative powers, and enhanced penalties for noncompliance;
- A licensure framework for follow-on biologic products;
- A new Patient-Centered Outcomes Research Institute to oversee, identify priorities in, and conduct comparative clinical effectiveness research, along with funding for such research; and
- Establishment of a Center for Medicare & Medicaid Innovation at the Centers for Medicare & Medicaid Services, or CMS to test innovative payment and service delivery models to lower Medicare and Medicaid spending, potentially including prescription drug spending.

We cannot predict the full impact of the ACA, as many of the reforms require the promulgation of detailed regulations implementing the statutory provisions, some of which have not yet fully occurred. Further, since its enactment there have been judicial and Congressional challenges to certain aspects of the ACA. As a result, there have been delays in the implementation of, and action taken to repeal or replace, certain aspects of the ACA. In January 2017, President Trump signed an Executive Order directing federal agencies with authorities and responsibilities under the ACA to waive, defer, grant exemptions from, or delay the implementation of any provision of the ACA that would impose a fiscal or regulatory burden on states, individuals, healthcare providers, health insurers, or manufacturers of pharmaceuticals or medical devices. More recently, the U.S. House of

Representatives passed legislation known as the American Health Care Act of 2017, and Senate Republicans have released a draft bill known as the Better Care Reconciliation Act of 2017, each of which would repeal certain aspects of the ACA if ultimately enacted. The Senate Republicans also introduced legislation to repeal the ACA without companion legislation to replace it, and a "skinny" version of the Better Care Reconciliation Act of 2017. Each of these measures was rejected by the full Senate. The prospects for enactment of these legislative initiatives remain uncertain. Further, Congress will likely consider other legislation to replace elements of the ACA. We cannot know how efforts to repeal and replace the ACA or any future healthcare reform legislation will impact our business.

We expect that the ACA, as well as other healthcare reform measures that may be adopted in the future, may result in more rigorous coverage criteria and in additional downward pressure on the price that we receive for any approved product. Any reduction in reimbursement from Medicare or other government programs may result in a similar reduction in payments from private payors. The implementation of cost containment measures or other healthcare reforms may prevent us from being able to generate revenue, attain profitability, or commercialize our products.

In addition, other legislative changes have been proposed and adopted since the ACA was enacted. For example, in August 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 proposals in spending reductions to Congress. The Joint Select Committee on Deficit Reduction did not achieve its targeted deficit reduction of at least $1.2 trillion for the years 2013 through 2021, triggering the legislation's automatic reductions to several government programs. These reductions include aggregate 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. In January 2013, President Obama signed into law the American Taxpayer Relief Act of 2012, which, among other things, further reduced Medicare payments to several providers and increased the statute of limitations period for the government to recover overpayments to providers from three to five years. Further, there have been several recent U.S. 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, and reform government program reimbursement methodologies for drugs. The full impact of these new laws, as well as laws and other reform and cost containment measures that may be proposed and adopted in the future, remains uncertain, but may result in additional reductions in Medicare and other healthcare funding, which could have a material adverse effect on our future customers and accordingly, our ability to generate revenue, attain profitability, or commercialize our products.

If we fail to comply with federal and state healthcare laws, including fraud and abuse and health information privacy and security laws, we could face substantial penalties and our business, results of operations, financial condition and prospects could be adversely affected.

As a pharmaceutical company, even though we do not and will not control referrals of healthcare services or bill directly to Medicare, Medicaid or other third-party payors, certain federal and state healthcare laws and regulations pertaining to fraud and abuse and patients' rights are and will be applicable to our business. For example, we could be subject to healthcare fraud and abuse and patient privacy regulation by both the federal government and the states in which we conduct our business. The laws that may affect our ability to operate include, among others:

- The federal Anti-Kickback Statute, which regulates our business activities, including our marketing practices, educational programs, pricing policies, and relationships with healthcare providers or other entities, by prohibiting, among other things, soliciting, receiving, offering or paying remuneration, directly or indirectly, to induce, or in return for, either the referral of an individual or the purchase or recommendation of an item or service reimbursable under a federal healthcare program, such as the Medicare and Medicaid programs;

- Federal civil and criminal false claims laws and civil monetary penalty laws, which prohibit, among other things, individuals or entities from knowingly presenting, or causing to be presented, claims for payment from Medicare, Medicaid, or other third-party payors that are false or fraudulent;
- The federal Health Insurance Portability and Accountability Act of 1996, or HIPAA, which created new federal criminal statutes that prohibit, among other things, executing a scheme to defraud any healthcare benefit program or making false statements relating to healthcare matters;
- HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act of 2009, or HITECH, and its implementing regulations, which imposes certain requirements relating to the privacy, security and transmission of individually identifiable health information;
- Requirements to report annually to CMS certain financial arrangements with physicians and teaching hospitals, as defined in the ACA and its implementing regulations, including reporting any "transfer of value" made or distributed to teaching hospitals, prescribers, and other healthcare providers and reporting any ownership and investment interests held by physicians and their immediate family members and applicable group purchasing organizations during the preceding calendar year; and
- State and foreign law equivalents of each of the above federal laws, such as anti-kickback and false claims laws which may apply to items or services reimbursed by any third-party payor, including commercial insurers; state laws that require pharmaceutical companies to comply with the industry's voluntary compliance guidelines and the applicable compliance guidance promulgated by the federal government that otherwise restricts certain payments that may be made to healthcare providers and entities; state laws that require drug manufacturers to report information related to payments and other transfer of value to physicians and other healthcare providers and entities; and state and foreign laws governing the privacy and security of health information in certain circumstances, many of which differ from each other in significant ways and often are not preempted by HIPAA, thus complicating compliance efforts.

Because of the breadth of these laws and the narrowness of the statutory exceptions and safe harbors available, it is possible that some of our business activities, including our consulting agreements with physicians, some of whom receive stock or stock options as compensation for their services, could be subject to challenge under one or more of such laws. In addition, recent health care reform legislation has further strengthened these laws. For example, the ACA, among other things, amends the intent requirement of the federal anti-kickback statute and certain criminal healthcare fraud statutes. A person or entity no longer needs to have actual knowledge of this statute or specific intent to violate it. Moreover, the ACA provides that the government may assert that a claim including items or services resulting from a violation of the federal anti-kickback statute constitutes a false or fraudulent claim for purposes of the False Claims Act.

To the extent that any of our product candidates is ultimately sold in a foreign country, we may be subject to similar foreign laws and regulations.

If we or our operations are found to be in violation of any of the laws described above or any other governmental regulations that apply to us, we may be subject to penalties, including administrative, civil and criminal penalties, damages, fines, exclusion from participation in United States federal or state health care programs, such as Medicare and Medicaid, disgorgement, individual imprisonment and the curtailment or restructuring of our operations any of which could materially adversely affect our ability to operate our business and our financial results. Although compliance programs can mitigate the risk of investigation and prosecution for violations of these laws, the risks cannot be entirely eliminated. Any action against us for violation of these laws, even if we successfully defend against it, could cause us to incur significant legal expenses and divert our management's attention from the operation of our business. Moreover, achieving and sustaining compliance with applicable federal and state privacy, security and fraud laws may prove costly.

Our ability to use net operating loss carryforwards and research tax credits to reduce future tax payments may be limited or restricted.

We have generated significant net operating loss carryforwards, or NOLs, and research and development tax credits, or R&D credits, as a result of our incurrence of losses and our conduct of research activities since inception. We generally are able to carry NOLs and R&D credits forward to reduce our tax liability in future years. However, our ability to utilize the NOLs and R&D credits is subject to the rules of Sections 382 and 383 of the Internal Revenue Code of 1986, as amended, or the Code, respectively. Those sections generally restrict the use of NOLs and R&D credits after an "ownership change." An ownership change occurs if, among other things, the stockholders (or specified groups of stockholders) who own or have owned, directly or indirectly, 5% or more of a corporation's common stock or are otherwise treated as 5% stockholders under Section 382 of the code and the United States Treasury Department regulations promulgated thereunder increase their aggregate percentage ownership of that corporation's stock by more than 50 percentage points over the lowest percentage of the stock owned by these stockholders over the applicable testing period. In the event of an ownership change, Section 382 imposes an annual limitation on the amount of taxable income a corporation may offset with NOL carry forwards and Section 383 imposes an annual limitation on the amount of tax a corporation may offset with business credit (including the R&D credit) carry forwards. Any unused annual limitation may be carried over to later years until the applicable expiration date for the respective NOL or R&D credit carry forwards. We may have experienced an "ownership change" within the meaning of Section 382 in the past and there can be no assurance that we will not experience additional ownership changes in the future. As a result, our NOLs and business credits (including the R&D credit) may be subject to limitations and we may be required to pay taxes earlier and in larger amounts than would be the case if our NOLs or R&D credits were freely usable.

Our synthetic immuno-oncology product candidates may face competition in the future from biosimilars.

The Biologics Price Competition and Innovation Act of 2009, or BPCIA, provides an abbreviated pathway for the approval of follow-on biological products. Under the BPCIA, an application for a biosimilar product cannot be approved by the FDA until 12 years after the original branded product was approved under a BLA. However, there is a risk that the U.S. Congress could amend the BPCIA to significantly shorten this exclusivity period, potentially creating the opportunity for generic competition sooner than anticipated. Further, this data exclusivity does not prevent another company from developing a product that is highly similar to the original branded product, generating its own data and seeking approval. Data exclusivity only assures that another company cannot rely upon the data within the innovator's application to support the biosimilar product's approval.

RISKS RELATED TO OUR INTELLECTUAL PROPERTY

If we or our licensors fail to adequately protect or enforce our intellectual property rights or secure rights to patents of others, the value of our intellectual property rights would diminish and our ability to successfully commercialize our products may be impaired.

Our success, competitive position, and future revenues will depend in part on our ability and the abilities of our licensors to obtain and maintain patent protection for our products, methods, processes and other technologies, to preserve our trade secrets, to prevent third parties from infringing on our proprietary rights, and to operate without infringing the proprietary rights of third parties.

To date, we have exclusive rights to certain U.S. and foreign intellectual property with respect to the Precigen technology, including the existing Precigen product candidates, such as Ad-RTS-IL-12 + veledimex, and with respect to CAR$^+$ T, NK and TCR cell therapies arising from the laboratory of Laurence Cooper, M.D., Ph.D., who was then at MD Anderson. Under our Channel Agreement with Precigen, Precigen has the sole right to conduct and control the filings, prosecution and maintenance of the patents and patent applications licensed to us. Although under the agreement Precigen has agreed to consider in good faith and consult with us regarding any comments we may have regarding these patents and patent applications, we cannot guarantee that our comments will be solicited or followed. Under the MD Anderson License, future filings and applications require the

agreement of each of MD Anderson, Precigen and us, and MD Anderson has the right to control the preparation and filing of additional patent applications unless the parties agree that we or Precigen may prosecute the application directly. Although under the agreement MD Anderson has agreed to review and incorporate any reasonable comments that we or Precigen may have regarding these patents and patent applications, we cannot guarantee that our comments will be solicited or followed. Without direct control of the channel program patents and patent applications, we are dependent on Precigen or MD Anderson, as applicable, to keep us advised of prosecution, particularly in foreign jurisdictions where prosecution information may not be publicly available. We anticipate that we, Precigen and MD Anderson will file additional patent applications both in the United States and in other countries. However, we cannot predict or guarantee:

- The degree and range of protection any patents will afford us against competitors, including whether third parties will find ways to invalidate or otherwise circumvent our patents;
- If and when patents will be issued;
- Whether or not others will obtain patents claiming subject matter related to or relevant to our product candidates; or
- Whether we will need to initiate litigation or administrative proceedings that may be costly whether we win or lose.

The patent prosecution process is expensive and time-consuming, and we may not be able to file and prosecute all necessary or desirable patent applications at a reasonable cost, in a timely manner, or in all jurisdictions. It is also possible that we will fail to identify patentable aspects of our research and development output before it is too late to obtain patent protection. Moreover, in some circumstances, we do not have the right to control the preparation, filing and prosecution of patent applications, or to maintain the patents, covering technology that we license from third parties. We may also require the cooperation of our licensors in order to enforce the licensed patent rights, and such cooperation may not be provided. Therefore, these patents and applications may not be prosecuted and enforced in a manner consistent with the best interests of our business.

The patent position of biotechnology and pharmaceutical companies generally is highly uncertain, involves complex legal and factual questions and has in recent years been the subject of much litigation. In addition, the laws of foreign countries may not protect our rights to the same extent as the laws of the United States and we may fail to seek or obtain patent protection in all major markets. For example, European patent law restricts the patentability of methods of treatment of the human body more than United States law does. Publications of discoveries in the scientific literature often lag behind the actual discoveries, and patent applications in the United States and other jurisdictions are typically not published until 18 months after filing, or in some cases not at all.

Changes in patent laws or in interpretations of patent laws in the United States and other countries may diminish the value of our intellectual property or narrow the scope of our patent protection. In September 2011, the Leahy-Smith America Invents Act, or the Leahy-Smith Act, was signed into law, resulting in a number of significant changes to United States patent law. These changes include provisions that affect the way patent applications will be prosecuted and may also affect patent litigation. In addition, the United States Supreme Court has ruled on several patent cases in recent years, either narrowing the scope of patent protection available in certain circumstances or weakening the rights of patent owners in certain situations. This combination of events has created uncertainty with respect to the value of patents, once obtained, and with regard to our ability to obtain patents in the future. As the USPTO continues to implement the Leahy-Smith Act, and as the federal courts have the opportunity to interpret the Leahy-Smith Act, the laws and regulations governing patents, and the rules regarding patent procurement could change in unpredictable ways that would weaken our ability to obtain new patents or to enforce our existing patents and patents that we might obtain in the future.

Certain technologies utilized in our research and development programs are already in the public domain. Moreover, a number of our competitors have developed technologies, filed patent applications or obtained

patents on technologies, compositions and methods of use that are related to our business and may cover or conflict with our owned or licensed patent applications, technologies or product candidates. Such conflicts could limit the scope of the patents that we may be able to obtain or may result in the rejection of claims in our patent applications. Because patent applications in the United States and many foreign jurisdictions are typically not published until eighteen months after filing, or in some cases not at all, and because publications of discoveries in the scientific literature often lag behind actual discoveries, neither we nor our licensors can be certain that others have not filed or maintained patent applications for technology used by us or covered by our pending patent applications without our being aware of these applications. Therefore, we cannot know with certainty whether we were the first to make the inventions claimed in our owned patents or pending patent applications, or that we were the first to file for patent protection of such inventions, nor can we know whether those from whom we license patents were the first to make the inventions claimed or were the first to file. As a result, the issuance, scope, validity, enforceability and commercial value of our patent rights are highly uncertain. Our pending and future patent applications may not result in patents being issued which protect our technology or products, in whole or in part, or which effectively prevent others from commercializing competitive technologies and products. Changes in either the patent laws or interpretation of the patent laws in the United States and other countries may diminish the value of our patents or narrow the scope of our patent protection. In addition, our own earlier filed patents and applications or those of Precigen may limit the scope of later patents we obtain or may result in the rejection of claims in our later filed patent applications. If third parties filed patent applications or obtained patents on technologies, compositions and methods of use that are related to our business and that cover or conflict with our owned or licensed patent applications, technologies or product candidates, we may be required to challenge such protection, terminate or modify our programs impacted by such protection or obtain licenses from such third parties, which might not be available on acceptable terms, or at all.

Even if our owned and licensed patent applications issue as patents, they may not issue in a form that will provide us with any meaningful protection, prevent competitors from competing with us or otherwise provide us with any competitive advantage. Our competitors may be able to circumvent our owned or licensed patents by developing similar or alternative technologies or products in a non-infringing manner.

The issuance of a patent is not conclusive as to its inventorship, scope, validity or enforceability, and our owned and licensed patents may be challenged in the courts or patent offices in the United States and abroad. Such challenges may result in loss of exclusivity or freedom to operate or in patent claims being narrowed, invalidated or held unenforceable, in whole or in part, which could limit our ability to stop others from using or commercializing similar or identical technology and products, or limit the duration of the patent protection of our technology and products. Given the amount of time required for the development, testing and regulatory review of new product candidates, patents protecting such candidates might expire before or shortly after such candidates are commercialized. As a result, our owned and licensed patent portfolio may not provide us with sufficient rights to exclude others from commercializing products similar or identical to ours.

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

Our success also depends upon the skills, knowledge, and experience of our scientific and technical personnel, our consultants and advisors, as well as our licensors and contractors. To help protect our proprietary know-how and our inventions for which patents may be unobtainable or difficult to obtain, and to maintain our competitive position, we rely on trade secret protection and confidentiality agreements. To this end, it is our general policy to require our employees, consultants, advisors, and contractors to enter into agreements that prohibit the disclosure of confidential information and, where applicable, require disclosure and assignment to us of the ideas, developments, discoveries, and inventions important to our business. These agreements may not provide adequate protection for our trade secrets, know-how or other proprietary information in the event of any unauthorized use or disclosure or the lawful development by others of such information. Moreover, we may not be able to obtain adequate remedies for any breaches of these agreements. Our trade secrets may also be obtained by third parties by other means, such as breaches of our physical or computer security systems. Enforcing a claim

that a party illegally disclosed or misappropriated a trade secret is difficult, expensive and time-consuming, and the outcome is unpredictable. In addition, some courts inside and outside the United States are less willing or unwilling to protect trade secrets. If any of our trade secrets were to be lawfully obtained or independently developed by a competitor, we would have no right to prevent them, or those to whom they communicate it, from using that technology or information to compete with us. If any of our trade secrets, know-how or other proprietary information is disclosed, the value of our trade secrets, know-how and other proprietary rights would be significantly impaired and our business and competitive position would suffer.

Third-party claims of intellectual property infringement would require us to spend significant time and money and could prevent us from developing or commercializing our products.

In order to protect or enforce patent rights, we, or Precigen, may initiate patent infringement litigation against third parties. Similarly, we may be sued by others for patent infringement. We also may become subject to proceedings conducted in the United States Patent and Trademark Office, including interference proceedings to determine the priority or derivation of inventions, or post-grant review, inter partes review, or reexamination proceedings reviewing the patentability of our patented claims. In addition, any foreign patents that are granted may become subject to opposition, nullity, or revocation proceedings in foreign jurisdictions having such proceedings. The defense and prosecution, if necessary, of intellectual property actions are costly and divert technical and management personnel away from their normal responsibilities.

Our commercial success depends upon our ability, and the ability of our collaborators, to develop, manufacture, market and sell our product candidates without infringing the proprietary rights of third parties. There is considerable intellectual property litigation in the biotechnology and pharmaceutical industries. While no such litigation has been brought against us and we have not been held by any court to have infringed a third party's intellectual property rights, we cannot guarantee that our products or use of our products do not infringe third-party patents. It is also possible that we have failed to identify relevant third-party patents or applications. For example, applications filed before November 29, 2000 and certain applications filed after that date that will not be filed outside the United States remain confidential until patents issue. Patent applications in the United States and elsewhere are published approximately 18 months after the earliest filing, which is referred to as the priority date. Therefore, patent applications covering our products or technology could have been filed by others without our knowledge. Additionally, pending patent applications which have been published can, subject to certain limitations, be later amended in a manner that could cover our products or the use of our products.

Our research, development and commercialization activities, as well as any product candidates or products resulting from these activities, may infringe or be claimed to infringe patents or patent applications under which we do not hold licenses or other rights. Patents do not protect its owner from a claim of infringement of another owner's patent. Therefore, our patent position cannot and does not provide any assurance that we are not infringing the patent rights of another.

The patent landscape in the field of synthetic immuno-oncology, which we are pursuing under our Channel Agreement with Precigen, is particularly complex. We are aware of numerous United States and foreign patents and pending patent applications of third parties that cover compositions, methods of use and methods of manufacture of synthetic immuno-oncology, including biotherapeutics involving the in vivo expression of human IL-12. In addition, there may be patents and patent applications in the field of which we are not aware. The technology we license from Precigen is early-stage technology and we are in the process of designing and developing products using this technology. Although we will seek to avoid pursuing the development of products that may infringe any patent claims that we believe to be valid and enforceable, we may fail to do so. Moreover, given the breadth and number of claims in patents and pending patent applications in the field of synthetic immuno-oncology and the complexities and uncertainties associated with them, third parties may allege that we are infringing upon patent claims even if we do not believe such claims to be valid and enforceable.

If a claim for patent infringement is asserted, there can be no assurance that the resolution of the claim would permit us to continue marketing the relevant product on commercially reasonable terms, if at all. We may not

have sufficient resources to bring these actions to a successful conclusion. If we do not successfully defend any infringement actions to which we become a party or are unable to have infringed patents declared invalid or unenforceable, we may have to pay substantial monetary damages, which can be tripled if the infringement is deemed willful, or be required to discontinue or significantly delay commercialization and development of the affected products.

Any legal action against us or our collaborators claiming damages and seeking to enjoin developmental or marketing activities relating to affected products could, in addition to subjecting us to potential liability for damages, require us or our collaborators to obtain licenses to continue to develop, manufacture, or market the affected products. Such a license may not be available to us on commercially reasonable terms, if at all.
An adverse determination in a proceeding involving our owned or licensed intellectual property may allow entry of generic substitutes for our products.

Obtaining and maintaining our patent protection depends on compliance with various procedural, document submission, fee payment and other requirements imposed by governmental patent agencies, and our patent protection could be reduced or eliminated for noncompliance with these requirements.

Periodic maintenance fees on any issued patent are due to be paid to the USPTO and foreign patent agencies in several stages over the lifetime of the patent. The USPTO and various foreign governmental patent agencies require compliance with a number of procedural, documentary, fee payment and other similar provisions during the patent application process. While an inadvertent lapse can in many cases be cured by payment of a late fee or by other means in accordance with the applicable rules, there are situations in which noncompliance can result in abandonment or lapse of the patent or patent application, resulting in partial or complete loss of patent rights in the relevant jurisdiction. Noncompliance events that could result in abandonment or lapse of a patent or patent application include, but are not limited to, failure to respond to official actions within prescribed time limits, non-payment of fees and failure to properly legalize and submit formal documents. In such an event, our competitors might be able to enter the market, which would have a material adverse effect on our business.

If we breach any of the agreements under which we license rights to products or technology from others, we could lose license rights that are material to our business or be subject to claims by our licensors.

We license rights to products and technology that are important to our business, and we expect to enter into additional licenses in the future. For instance, we have exclusively licensed patents and patent applications under our Channel Agreement, and the ECP with Precigen as well as under the MD Anderson License. Under these agreements, we are subject to a range of commercialization and development, sublicensing, royalty, patent prosecution and maintenance, insurance and other obligations.

Any failure by us to comply with any of these obligations or any other breach by us of our license agreements could give the licensor the right to terminate the license in whole, terminate the exclusive nature of the license or bring a claim against us for damages. Any such termination or claim could have a material adverse effect on our financial condition, results of operations, liquidity or business. Even if we contest any such termination or claim and are ultimately successful, such dispute could lead to delays in the development or commercialization of potential products and result in time-consuming and expensive litigation or arbitration. On termination we may be required to license to the licensor any related intellectual property that we developed.

In addition, in certain cases, the rights licensed to us are rights of a third party licensed to our licensor. In such instances, if our licensors do not comply with their obligations under such licenses, our rights under our license agreements with our licensor may be adversely affected.

We may be subject to claims by third parties asserting that our employees or we have misappropriated their intellectual property, or claiming ownership of what we regard as our own intellectual property.

Many of our employees were previously employed at universities or other biotechnology or pharmaceutical companies, including our competitors or potential competitors. Although we try to ensure that our employees do

not use the proprietary information or know-how of others in their work for us, we may be subject to claims that these employees or we have used or disclosed intellectual property, including trade secrets or other proprietary information, of any such employee's former employer. Litigation may be necessary to defend against these claims.

In addition, while it is our policy to require our employees and contractors who may be involved in the development of intellectual property to execute agreements assigning such intellectual property to us, we may be unsuccessful in executing such an agreement with each party who in fact develops intellectual property that we regard as our own. Our and their assignment agreements may not be self-executing or may be breached, and we may be forced to bring claims against third parties, or defend claims they may bring against us, to determine the ownership of what we regard as our intellectual property.

If we fail in prosecuting or defending any such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights or personnel. Even if we are successful in prosecuting or defending against such claims, litigation could result in substantial costs and be a distraction to management.

OTHER RISKS RELATED TO OUR COMPANY

Our stock price has been, and may continue to be, volatile.

The market price for our common stock is volatile and may fluctuate significantly in response to a number of factors, most of which we cannot control, including:

- Price and volume fluctuations in the overall stock market;
- Market conditions or trends in our industry or the economy as a whole;
- Laboratory or clinical trial results;
- Public concern as to the safety of drugs developed by us or others;
- Changes in operating results and performance and stock market valuations of other biopharmaceutical companies generally, or those that develop and commercialize cancer drugs in particular;
- The financial or operational projections we may provide to the public, any changes in these projections or our failure to meet these projections;
- Comments by securities analysts or changes in financial estimates or ratings by any securities analysts who follow our common stock, our failure to meet these estimates or failure of those analysts to initiate or maintain coverage of our common stock;
- The public's response to press releases or other public announcements by us or third parties, including our filings with the Securities Exchange Commission, or the SEC, and announcements of the status of development of our products, announcements of technological innovations or new therapeutic products by us or our competitors, announcements regarding collaborative agreements and other announcements relating to product development, litigation and intellectual property impacting us or our business;
- Government regulation;
- FDA determinations on the approval of a product candidate BLA submission;
- The sustainability of an active trading market for our common stock;
- Future sales of our common stock by our executive officers, directors and significant stockholders;
- Announcements of mergers or acquisition transactions;
- Our inclusion or deletion from certain stock indices;
- Developments in patent or other proprietary rights;

- Changes in reimbursement policies;
- Announcements of medical innovations or new products by our competitors;
- Announcements of changes in our senior management;
- Other events or factors, including those resulting from war, incidents of terrorism, natural disasters or responses to these events; and
- Changes in accounting principles.

In addition, the stock market from time to time experiences significant price and volume fluctuations unrelated to the operating performance of particular companies. The stock markets, and in particular the Nasdaq Capital Market, have experienced extreme price and volume fluctuations that have affected and continue to affect the market prices of equity securities of many biopharmaceutical companies. Stock prices of many biopharmaceutical companies have fluctuated in a manner unrelated or disproportionate to the operating performance of those companies. In the past, stockholders have instituted securities class action litigation following periods of market volatility. If we were involved in securities litigation, we could incur substantial costs and our resources and the attention of management could be diverted from our business.

Anti-takeover provisions in our charter documents and under Delaware law may make an acquisition of us, which may be beneficial to our stockholders, more difficult.

Provisions of our amended and restated certificate of incorporation and bylaws, as well as provisions of Delaware law, could make it more difficult for a third party to acquire us, even if doing so would benefit our stockholders. These provisions authorize the issuance of “blank check” preferred stock that could be issued by our board of directors to increase the number of outstanding shares and hinder a takeover attempt, and limit who may call a special meeting of stockholders. In addition, Section 203 of the Delaware General Corporation Law generally prohibits a publicly-held Delaware corporation from engaging in a business combination with a party that owns at least 15% of its common stock unless the business combination is approved by the company’s board of directors before the person acquires the 15% ownership stake or later by its board of directors and two-thirds of its stockholders. Section 203 could have the effect of delaying, deferring or preventing a change in control that our stockholders might consider to be in their best interests.

In connection with our January 2011 issuance of shares of common stock to Intrexon in a private placement transaction, our board of directors waived the Section 203 prohibition with respect to a future business combination with Intrexon.

Because we do not expect to pay dividends, you will not realize any income from an investment in our common stock unless and until you sell your shares at profit.

We have never paid dividends on our common stock and we do not anticipate that we will pay any dividends for the foreseeable future. Accordingly, any return on an investment in us will be realized, if at all, only when you sell shares of our common stock.

If securities and/or industry analysts fail to continue publishing research about our business, if they change their recommendations adversely or if our results of operations do not meet their expectations, our stock price and trading volume could decline.

The trading market for our common stock will be influenced by the research and reports that industry or securities analysts publish about us or our business. If one or more of these analysts cease coverage of our company or fail to publish reports on us regularly, we could lose visibility in the financial markets, which in turn could cause our stock price or trading volume to decline. In addition, it is likely that in some future period our operating results will be below the expectations of securities analysts or investors. If one or more of the analysts who cover us downgrade our stock, or if our results of operations do not meet their expectations, our stock price could decline.

Our principal stockholders, executive officers and directors have substantial control over the company, which may prevent you and other stockholders from influencing significant corporate decisions and may harm the market price of our common stock.

As of December 31, 2017, our executive officers, directors and holders of five percent or more of our outstanding common stock, beneficially owned, in the aggregate, 21.8% of our outstanding common stock. These stockholders may have interests that conflict with our other stockholders and, if acting together, have the ability to influence the outcome of matters submitted to our stockholders for approval, including the election and removal of directors and any merger, consolidation or sale of all or substantially all of our assets. Accordingly, this concentration of ownership may harm the market price of our common stock by:

- Delaying, deferring or preventing a change in control;
- Impeding a merger, consolidation, takeover or other business combination involving us; or
- Discouraging a potential acquirer from making a tender offer or otherwise attempting to obtain control of us.

The recently passed comprehensive tax reform bill could adversely affect our business and financial condition.

On December 22, 2017, President Trump signed into law new legislation that significantly revises the Code. The newly enacted federal income tax law, among other things, contains significant changes to corporate taxation, including reduction of the corporate tax rate from a top marginal rate of 35% to a flat rate of 21%, limitation of the tax deduction for interest expense to 30% of adjusted earnings (except for certain small businesses), limitation of the deduction for NOLs to 80% of current year taxable income and elimination of NOL carrybacks, one time taxation of offshore earnings at reduced rates regardless of whether they are repatriated, elimination of U.S. tax on foreign earnings (subject to certain important exceptions), immediate deductions for certain new investments instead of deductions for depreciation expense over time, and modifying or repealing many business deductions and credits. Notwithstanding the reduction in the corporate income tax rate, the overall impact of the new federal tax law is uncertain and our business and financial condition could be adversely affected. In addition, it is uncertain if and to what extent various states will conform to the newly enacted federal tax law. The impact of this tax reform on holders of our common stock is also uncertain and could be adverse. We urge our stockholders to consult with their legal and tax advisors with respect to this legislation and the potential tax consequences of investing in or holding our common stock.

The SEC staff issued Staff Accounting Bulletin (SAB 118) to address the application of US GAAP in situations when a registrant does not have the necessary information available, prepared or analyzed in reasonable detail to complete the accounting for certain income tax effects of the Tax Act and allows the registrant to record provisional amounts during the measurement period. We are in the process of analyzing the impact of the various provisions of the Tax Act. We expect to complete our analysis within the measurement period in accordance with SAB 118.

Item 1B. Unresolved Staff Comments

None.

Item 2. Properties

Our corporate office is located at One First Avenue, Parris Building #34, Navy Yard Plaza, Boston, Massachusetts 02129. The Boston office is leased pursuant to a lease agreement that expires in August 2021. On May 22, 2015, we subleased vacant office space in our Boston office for approximately $105 thousand in total rent for the period of June 2015 through August 2016. On December 21, 2015, we renewed a portion of the lease for Boston office through August 31, 2021 for $427 thousand, annually. We believe that our existing facilities are adequate to meet our current needs.

We also lease office space in New York and at MD Anderson in Houston, Texas. Our New York office was leased pursuant to a lease agreement that expires in October 2018. Under the terms of our New York lease agreement, we lease approximately seven thousand square feet and are required to make rental payments at an average monthly rate of approximately $41 thousand. On October 17, 2013, we entered into a sublease agreement to lease all of our New York office space to a subtenant. We remain primarily liable to pay rent on the original lease. Under the sublease agreement, we receive sublease payments at an average monthly rate of approximately $28 thousand through the remainder of the term of the lease. In accordance with the sublease agreement, the subtenant provided us with a security deposit of an irrevocable standby letter of credit for approximately $167 thousand.

Our leased office space at MD Anderson in Houston is pursuant to a lease agreement that expires in April 2021. Under the terms of the Houston lease agreement, we lease approximately two hundred and ten square feet and are required to make rental payments at an average monthly rate of approximately $1 thousand. The monthly rent expense will be deducted from our prepayment at MD Anderson. See Note 7 to the accompanying financial statements.

Item 3. Legal Proceedings

In the ordinary course of business, we may periodically become subject to legal proceedings and claims arising in connection with ongoing business activities. The results of litigation and claims cannot be predicted with certainty, and unfavorable resolutions are possible and could materially affect our results of operations, cash flows or financial position. In addition, regardless of the outcome, litigation could have an adverse impact on us because of defense costs, diversion of management resources and other factors.

There are no matters, as of December 31, 2017, that, in the opinion of management, might have a material adverse effect on our financial position, results of operation or cash flows.

Item 4. Mine Safety Disclosures

Not applicable.

PART II

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

Market for Common Stock

Our common stock trades on the Nasdaq Capital Market under the symbol "ZIOP." The following table sets forth the high and low sale prices for our common stock during each quarter within the two most recently completed fiscal years as reported by the Nasdaq Capital Market.

	2017		2016	
Quarter Ended	High	Low	High	Low
March 31	$6.91	$5.41	$9.59	$4.89
June 30	$7.51	$5.37	$8.92	$5.31
September 30	$6.57	$4.99	$6.04	$4.49
December 31	$6.54	$4.00	$7.60	$4.88

Record Holders

As of February 21, 2018, we had approximately 335 holders of record of our common stock, one of which was Cede & Co., a nominee for Depository Trust Company, or DTC. Shares of common stock that are held by financial institutions as nominees for beneficial owners are deposited into participant accounts at DTC, and are considered to be held of record by Cede & Co. as one stockholder. As of February 21, 2018, we had approximately 32,332 beneficial holders of our common stock.

Dividends

We have never declared or paid a cash dividend on our common stock and do not anticipate paying any cash dividends in the foreseeable future.

Recent Sales of Unregistered Securities

In June 2016, we amended our Channel Agreement and GvHD Agreement with Intrexon (now Precigen) in order to, among other things, reduce the royalty rate on operating profits payable by us to Precigen from 50% to 20%. In consideration for these amendments, we issued to Intrexon shares of our Series 1 preferred stock, which include, among other things, a monthly dividend of 1% payable in additional shares of Series 1 preferred stock. For the three months ended December 31, 2017, we issued an aggregate of 3,517 shares of Series 1 preferred stock to Intrexon, the holder of all of the outstanding shares of our Series 1 preferred stock, as dividends, representing monthly dividends due from October 1, 2017 through December 31, 2017 to Intrexon. The issuances of the dividend shares were exempt from registration under Section 4(a)(2) of the Securities Act of 1933, as amended.

Issuer Purchases of Equity Securities

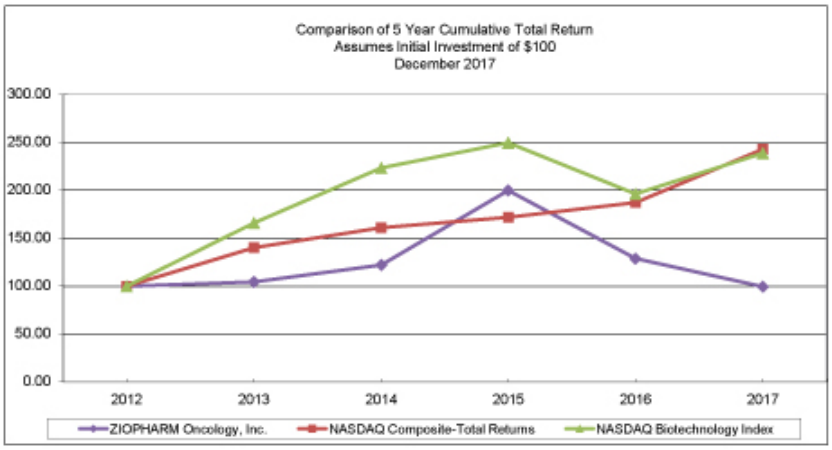
During the three months ended December 31, 2017, we purchased an aggregate of 245,602 shares of restricted stock from certain employees and members of our board of directors to cover the applicable withholding taxes due from them for the shares of restricted stock at the time that the applicable forfeiture restrictions lapsed. The following table provides information about these purchases of restricted shares for the three months ended December 31, 2017:

Period	Total Number of Shares Purchased	Average Price Paid Per Share
October 1 to 31, 2017	—	$ —
November 1 to 30, 2017	—	—
December 1 to 31, 2017	245,602	4.14
Total	245,602	

Stockholder Return Comparison

The information included in this section is not deemed to be "soliciting material" or to be "filed" with the SEC or subject to Regulation 14A or 14C under the Exchange Act or to the liabilities of Section 18 of the Exchange Act, and will not be deemed to be incorporated by reference into any filing under the Securities Act or the Exchange Act, except to the extent we specifically incorporate it by reference into such a filing.

The graph below matches the cumulative 5-year total return of holders of our common stock with the cumulative total returns of the Nasdaq Composite index and the Nasdaq Biotechnology index. The graph assumes that the value of the investment in our common stock and in each of the indexes (including reinvestment of dividends) was $100 on December 31, 2012 and tracks it through December 31, 2017.



Item 6. Selected Financial Data

The selected financial data presented below has been derived from our financial statements. This data may not be indicative of our future financial condition or results of operations and should be read in conjunction with "Management's Discussion and Analysis of Financial Condition and Results of Operations" and our financial statements and accompanying notes included elsewhere herein.

	Year Ended December 31, (in thousands, except share data and per share amounts)				
	2017	2016	2015	2014	2013
Statements of Operations Data:					
Collaboration revenue	$ 6,389	$ 6,861	$ 4,332	$ 1,373	$ 800
Total operating expenses	59,882	172,168	124,432	44,872	58,513
Loss from operations	(53,493)	(165,307)	(120,100)	(43,499)	(57,713)
Other income (expense), net	465	134	12	(5)	(579)
Change in fair value of warrants	—	—	—	11,723	1,185
Change in fair value of derivative liabilities	(1,295)	(124)	—	—	—
Net loss	(54,323)	(165,297)	(120,088)	(31,781)	(57,107)
Preferred stock dividends	(18,938)	(7,123)	—	—	—
Not loss applicable to common stockholders	(73,261)	(172,420)	(120,088)	(31,781)	(57,107)
Basic and diluted net loss per share	$ (0.53)	$ (1.32)	$ (0.96)	$ (0.31)	$ (0.66)
Weighted average number of common shares outstanding: basic and diluted	136,938,264	130,391,463	125,416,084	101,130,710	85,943,175

	Year Ended December 31, (in thousands)				
	2017	2016	2015	2014	2013
Balance Sheet Data:					
Cash and cash equivalents	$ 70,946	$ 81,053	$140,717	$42,803	$68,204
Total assets	105,606	106,348	153,724	45,237	71,754
Warrant liabilities	—	—	—	—	11,776
Derivative liabilities	2,424	862	—	—	—
Total liabilities	58,420	58,325	66,353	11,396	22,371
Series 1 Preferred Stock	143,992	125,321	—	—	—
Stockholders' equity (deficit)	(96,806)	(77,298)	87,371	33,841	49,383

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

The following discussion and analysis of our financial condition and results of operations should be read in conjunction with our consolidated financial statements and related notes appearing elsewhere in this Annual Report on Form 10-K. In addition to historical financial information, the following discussion contains forward-looking statements that reflect our plans, estimates and beliefs. Our actual results could differ materially from those contained in or implied by any forward-looking statements. Factors that could cause or contribute to these differences include those under "Risk Factors" included in Part I, Item 1A and under "Special Note Regarding Forward-Looking Statements" or in other parts of this Annual Report on Form 10-K.

Business Overview

Ziopharm Oncology, Inc. is a biopharmaceutical company focused on discovering, acquiring, developing and commercializing next generation immunotherapy platforms that leverage gene- and cell-based therapies to treat patients with cancer on its own and with partners. We are developing two immuno-oncology platform technologies designed to utilize the patient's immune system by employing novel, controlled gene expression and innovative cell engineering technologies to deliver safe, effective, and scalable cell- and viral-based therapies for the treatment of multiple cancer types.

Recent Developments

In January 2018, we provided updates on the continued development of our Controlled IL-12 platform and development programs for the treatment of brain cancer [at JPM?]. We announced the initiation of a Phase I clinical trial to evaluate Ad-RTS-hIL-12 plus veledimex in combination with OPDIVO® (nivolumab), an immune checkpoint, or PD-1 inhibitor, in adult patients with rGBM. We also updated guidance on our planned pivotal trial of Ad-RTS-hIL-12 plus veledimex and announced that we currently anticipate initiation in the second half of 2018, subject to regulatory approval. We have designed a Phase 3 randomized control trial to evaluate Controlled IL-12 for the treatment of patients with rGBM and following meetings with U.S. and European regulators, we are completing execution of Chemistry Manufacturing and Control (CMC) technical requirements.

In November 2017, during the 22nd Annual Meeting and Education Day of the Society for Neuro-Oncology (SNO) in San Francisco, we made multiple presentations on controlled IL-12. New data presented included sustained median overall survival (mOS) of 12.5 months for patients treated with Ad-RTS-hIL-12 plus 20mg of veledimex (n=15) at a longer mean follow-up time of 11.1 months as of October 18, 2017, which compares favorably to the 5- to 8-months overall survival data of approved therapies. Additional data relative to an influx of cytotoxic T-cells, increased expression levels of PD-1 and PD-L1, peripheral biomarkers and the impact of low-dose steroids on survival were presented.

In October 2017, we announced the first patient dosed in a Phase 1 trial of Ad-RTS-hIL-12 + veledimex for the treatment of pediatric brain tumors.

In December 2017, we delivered multiple presentations on our adoptive cell therapy programs and application of the SB technology at the 59th American Society of Hematology (ASH) Annual Meeting and Exposition in Atlanta. We presented on the advancement of our SB platform towards point-of-care (P-O-C) for very rapid manufacturing of genetically modified CAR^+ T cells. Data presented from first- and second-generation SB clinical trials demonstrate tolerability, disease response, long-term survival and persistence of infused CD19-specific CAR^+ T cells. Preclinical studies presented at ASH and at the Keystone Symposia in February 2018 showed that P-O-C CAR^+ T cells co-expressing membrane-bound interleukin-15 (mbIL15) and a control switch manufactured within two days do not require activation or propagation in tissue culture to achieve anti-tumor effects and prolonged T-cell survival in mice. Building on these data, we plan to initiate an investigator-led first P-O-C clinical trial in the second half of 2018 at MD Anderson.

The Company also updated guidance on the anticipated start of the National Cancer Institute (NCI)-led Phase 1 trial to evaluate adoptive cell transfer (ACT)-based immunotherapies genetically modified using the SB transposon/transposase system to express TCRs for the treatment of solid tumors. We, Precigen and NCI last year entered into a Cooperative Research and Development Agreement (CRADA) to develop and evaluate ACT for patients with advanced cancers using autologous peripheral blood lymphocytes genetically modified using the non-viral SB system to express TCRs that recognize specific immunogenic mutations, or neoantigens, expressed within a patient's cancer. We expect this phase 1 trial, which is being led by and conducted at the NCI, to be initiated in the second half of this year.

Lastly, as a result of an in-depth review of our research and development portfolio, we determined that the pursuit of GvHD as an indication was not a material part of our corporate strategy and therefore have decided to

stop pursuing the development of engineered cell therapy strategies, used either separately or in combination, for targeted treatment of GvHD. We have reverted our rights under the GvHD program back to Precigen [and are in the process of winding down the related activities]. We made this decision to focus our efforts and resources on the development of our Controlled IL-12 and Sleeping Beauty platforms for the treatment of oncology indications.

Financial Overview

Overview of Results of Operations

Collaboration Revenue

We recognize research and development funding revenue over the estimated period of performance. We have not generated product revenues since our inception. Unless and until we receive approval from the FDA and/or other regulatory authorities for our product candidates, we cannot sell our products and will not have product revenues.

Research and Development Expenses

Our research and development expense consists primarily of salaries and related expenses for personnel, costs of contract manufacturing services, costs of facilities and equipment, fees paid to professional service providers in conjunction with our clinical trials, fees paid to contract research organizations in conjunction with preclinical animal studies, costs of materials used in research and development, consulting, license and milestone payments and sponsored research fees paid to third parties.

We have not accumulated and tracked our internal historical research and development costs or our personnel and personnel-related costs on a program-by-program basis. Our employee and infrastructure resources are allocated across several projects, and many of our costs are directed to broadly applicable research endeavors. As a result, we cannot state the costs incurred for each of our oncology programs on a program-by-program basis.

For the twelve months ended December 31, 2017, our clinical stage projects included a Phase 1 trial with Ad-RTS-IL-12 + veledimex in progressive glioblastoma; a Phase 1b/2 trial with Ad-RTS-IL-12 + veledimex in metastatic breast cancer; an investigator-led Phase 1 trial infusing our 2nd generation CD19-specific CAR$^+$ T cells in patients with advanced lymphoid malignancies; an investigator-led Phase 1 trial infusing our CD33-specific CAR$^+$ T therapy for relapsed or refractory acute myeloid leukemia; and a Phase 1 trial of Ad-RTS-hIL-12 with veledimex for the treatment of pediatric brain tumors. The expenses incurred by us to third parties for our Phase 1 trial with Ad-RTS-IL-12 + veledimex in progressive glioblastoma were $0.8 million for the three months ended December 31, 2017, and $4.4 million from the project's inception in June 2015 through December 31, 2017. There were no expenses incurred by us to third parties for our Phase 1b/2 trial with Ad-RTS-IL-12 + veledimex in metastatic breast cancer for the three months ended December 31, 2017, and expenses from the project's inception in April 2015 through December 31, 2017 were $0.8 million. The expenses incurred by us to third parties for our investigator-led Phase 1 trial infusing our 2nd generation CD19-specific CAR$^+$ T cells in patients with advanced lymphoid malignancies were $0.2 million for the three months ended December 31, 2017 and $2.8 million from the project's inception in December 2015 through December 31, 2017. The expenses incurred by us to third parties for our investigator-led Phase 1 trial infusing our CD33-specific CAR$^+$ T therapy for relapsed or refractory acute myeloid leukemia were $0.9 million for the three months ended December 31, 2017 and $1.4 million from the project's inception in September 2017 through December 31, 2017. The expenses incurred by us to third parties for our investigator-led Phase 1 trial of Ad-RTS-hIL-12 with veledimex for the treatment of pediatric brain tumors were $0.6 million for the three months ended December 31, 2017 and the projects inception in October 2017.

Our future research and development expenses in support of our current and future programs will be subject to numerous uncertainties in timing and cost to completion. We test potential products in numerous preclinical studies for safety, toxicology and efficacy. We may conduct multiple clinical trials for each product. As we obtain results from trials, we may elect to discontinue or delay clinical trials for certain products in order to focus our resources on more promising products or indications. Completion of clinical trials may take several years or more, and the length of time generally varies substantially according to the type, complexity, novelty and intended use of a product. It is not unusual for preclinical and clinical development of each of these types of products to require the expenditure of substantial resources.

We estimate that clinical trials of the type generally needed to secure new drug approval are typically completed over the following timelines:

Clinical Phase	Estimated Completion Period
Phase 1	1 - 2 years
Phase 2	2 - 3 years
Phase 3	2 - 4 years

The duration and the cost of clinical trials may vary significantly over the life of a project as a result of differences arising during clinical development, including, among others, the following:

- The number of clinical sites included in the trials;
- The length of time required to enroll suitable patents;
- The number of patients that ultimately participate in the trials;
- The duration of patient follow-up to ensure the absence of long-term product-related adverse events; and
- The efficacy and safety profile of the product.

As a result of the uncertainties discussed above, we are unable to determine the duration and completion costs of our programs or when and to what extent we will receive cash inflows from the commercialization and sale of a product. Our inability to complete our programs in a timely manner or our failure to enter into appropriate collaborative agreements could significantly increase our capital requirements and could adversely impact our liquidity. These uncertainties could force us to seek additional, external sources of financing from time-to-time in order to continue with our product development strategy. Our inability to raise additional capital, or to do so on terms reasonably acceptable to us, would jeopardize the future success of our business.

General and Administrative Expenses

General and administrative expenses consist primarily of salaries, benefits and stock-based compensation, consulting and professional fees, including patent related costs, general corporate costs and facility costs not otherwise included in research and development expenses or cost of product revenue.

Other Income (Expense)

Other income (expense) consists primarily of changes in the fair value of Series 1 Preferred Stock.

Results of Operations for the Fiscal Year ended December 31, 2017 versus December 31, 2016

Collaboration Revenues

Revenues for the years ended December 31, 2017 and 2016 were as follows:

	Year ended December 31,			
	2017	2016	Change	
($ in thousands)				
Collaboration revenue	$ 6,389	$ 6,861	$(472)	-7%

Revenue for the year ended December 31, 2017 decreased by $472 thousand in comparison to revenue for the year ended December 31, 2016. During each of the years ended December 31, 2017 and 2016, we recognized revenue of $6.4 million under the Ares Trading Agreement. During the year ended December 31, 2016, we recognized $272 thousand from our agreement with Solasia and $200 thousand from our agreement with Predictive Therapeutics. We recognized no revenue from our agreements with Solasia and Predictive Therapeutics during the year ended December 31, 2017.

Research and Development Expenses

Research and development expenses during the years ended December 31, 2017 and 2016 were as follows:

($ in thousands)	Year ended December 31, 2017	2016	Change	
Research and development	$ 45,084	$ 157,791	$(112,707)	-71%

Research and development expenses for the year ended December 31, 2017 decreased by $112.7 million when compared to the year ended December 31, 2016. During the year ended December 31, 2016, we incurred a noncash charge of $119.0 million related to Series 1 preferred stock issued to Intrexon under our 2016 ECP Amendment and 2016 GvHD Amendment and related dividends. Excluding the noncash charge of $119.0 in the prior year, research and development expenses would have been higher by $6.3 million for the year ended December 31, 2017 compared to the year ended December 31, 2016. The increase in expenses during the year ended December 31, 2017 was due to an increase of $2.8 million for salary and employee related expense due to increased headcount, $1.6 million in cell therapy expenses to support our ongoing trials at MD Anderson, $1.2 million to support our ongoing gene therapy programs, and $0.7 million in other operating expense.

General and Administrative Expenses

General and administrative expenses during the years ended December 31, 2017 and 2016 were as follows:

($ in thousands)	Year ended December 31, 2017	2016	Change	
General and administrative	$14,798	$14,377	$421	3%

General and administrative expenses for the year ended December 31, 2017 increased by $421 thousand as compared to the prior year. The change was primarily due to increased salary and employee related expenses as a result of headcount additions during the year ended December 31, 2017.

Other Income (Expense)

Other income (expense) during the years ended December 31, 2017 and 2016 were as follows:

($ in thousands)	Year ended December 31, 2017	2016	Change	
Other income (expense), net	$ 465	$ 134	$ 331	247%
Change in fair value of derivative liabilities	(1,295)	(124)	(1,171)	944%
Total	$ (830)	$ 10	$ (840)	

During the year ended December 31, 2017 and 2016, we recorded a loss on the change in fair value of the derivative liabilities of $1.3 million and $124 thousand, respectively (see Note 10 to the accompanying financial statements). These changes are derived from the number of outstanding shares of preferred stock and their respective valuations. Additionally, we recorded $465 thousand in other income for the year ended December 31, 2017, compared to $134 thousand earned in the prior year, due to increases in the fair value of our cash equivalent accounts (see Note 3 to the accompanying financial statements).

Results of Operations for the Fiscal Year ended December 31, 2016 versus December 31, 2015

Collaboration Revenues

Revenues for the years ended December 31, 2016 and 2015 were as follows:

	Year ended December 31,		Change	
	2016	2015		
($ in thousands)				
Collaboration revenue	$6,861	$4,332	$2,529	58%

Revenue for the year ended December 31, 2016 increased by $2.5 million compared to revenue for the year ended December 31, 2015. During the year ended December 31, 2016, we recognized revenue of $6.4 million under the Ares Trading Agreement, $272 thousand recognized from our agreement with Solasia, and $200 thousand recognized from our agreement with Predictive Therapeutics. During the year ended December 31, 2015, we recognized revenue of $3.2 million under the Ares Trading Agreement, $1.1 million from our agreement with Solasia, and $50 thousand from our agreement with Predictive Therapeutics.

Research and Development Expenses

Research and development expenses during the years ended December 31, 2016 and 2015 were as follows:

	Year ended December 31,		Change	
	2016	2015		
($ in thousands)				
Research and development	$157,791	$106,785	$51,006	48%

Research and development expenses for the year ended December 31, 2016 increased by $51.0 million when compared to the year ended December 31, 2015. During the year ended December 31, 2016, the company incurred a noncash charge of $126.2 million related to Series 1 preferred stock issued to Intrexon under our 2016 ECP Amendment and 2016 GvHD Amendment and related dividends. In 2015, we issued $67.3 million of common shares to MD Anderson in consideration for the MD Anderson agreement and a $10.0 million charge for in process research and development with Intrexon (see Note 7 to the accompanying financial statements) for costs related to our GvHD program. The remaining $2.1 million in increased spending for 2016 relates primarily to increased research and development expenses for cell therapy programs.

General and Administrative Expenses

General and administrative expenses during the years ended December 31, 2016 and 2015 were as follows:

	Year ended December 31,		Change	
	2016	2015		
($ in thousands)				
General and administrative	$14,377	$17,647	$(3,270)	-19%

General and administrative expenses for the year ended December 31, 2016 decreased by $3.3 million when compared to the year ended December 31, 2015. The change was primarily due to decreases in employee related and stock compensation expense, as a result of business development costs incurred in the prior year related to the MD Anderson License.

Other Income (Expense)

Other income (expense) during the years ended December 31, 2016 and 2015 were as follows:

	Year ended December 31,		Change	
	2016	2015		
($ in thousands)				
Other income (expense), net	$ 134	$ 12	$ 122	1017%
Change in fair value of derivative liabilities	(124)	—	(124)	100%
Total	$ 10	$ 12	$ (2)	

The increase in other income (expense) from year ended December 31, 2016 as compared to year ended December 31, 2015 was due primarily to interest received on our cash balance. The change in derivative liabilities was not applicable in 2015.

Liquidity and Capital Resources

As of December 31, 2017, we have approximately $70.9 million of cash and cash equivalents. Given our development plans, we anticipate our cash resources will be sufficient to fund our operations into the fourth quarter of 2018 and currently have no committed sources of additional capital. The forecast of cash resources is forward-looking information that involves risks and uncertainties, and the actual amount of our expenses could vary materially and adversely as a result of a number of factors. We have based our estimates on assumptions that may prove to be wrong, and our expenses could prove to be significantly higher than we currently anticipate. Management does not know whether additional financing will be on terms favorable or acceptable to us when needed, if at all. If adequate additional funds are not available when required, or if we are unsuccessful in entering into partnership agreements for further development of our products, management may need to curtail development efforts. Based on the forecast, management determined that there is substantial doubt regarding our ability to continue as a going concern. As a result, our independent registered accounting firm has expressed substantial doubt as to our ability to continue as a going concern in their report dated March 1, 2018 included in this Annual Report on the Form 10-K.

In addition to these factors, our actual cash requirements may vary materially from our current expectations for a number of other factors that may include, but are not limited to, changes in the focus and direction of our development programs, competitive and technical advances, costs associated with the development of our product candidates, our ability to secure partnering arrangements, and the costs of filing, prosecuting, defending and enforcing our intellectual property rights. If we exhaust our capital reserves more quickly than anticipated, regardless of the reason, and we are unable to obtain additional financing on terms acceptable to us or at all, we will be unable to proceed with development of some or all of our product candidates on expected timelines and will be forced to prioritize among them.

We expect that we will need additional financing to support our long-term plans for clinical trials and new product development. We expect to finance our cash needs through the sale of equity securities, strategic collaborations and/or debt financings, or through other sources that may be dilutive to existing stockholders. There can be no assurance that we will be able to obtain funding from any of these sources or, if obtained, what the terms of such funding(s) may be, or that any amount that we are able to obtain will be adequate to support our working capital requirements until we achieve profitable operations. We have no current committed sources of additional capital. Recently, capital markets have experienced a period of instability that may severely hinder our ability to raise capital within the time periods needed or on terms we consider acceptable, if at all. If we are unable to raise additional funds when needed, we may not be able to continue development and regulatory approval of our products, or we could be required to delay, scale back or eliminate some or all our research and development programs.

Recent Financing Transactions

February 2015 Public Offering

On February 3, 2015, we entered into an underwriting agreement with J.P. Morgan Securities LLC, as representative of the several underwriters named therein, relating to the issuance and sale of 10,000,000 shares of our common stock. The price to the public in the offering was $8.75 per share, and the underwriters agreed to purchase the shares from us pursuant to the underwriting agreement at a purchase price of $8.225 per share. Under the terms of the underwriting agreement, we also granted the underwriters an option, exercisable for 30 days, to purchase up to an additional 1,500,000 shares of common stock at a purchase price of $8.225 per share. The offering was made pursuant to our registration statement on Form S-3 (SEC File No. 333-201826) previously filed with the SEC, and a prospectus supplement thereunder. The underwriters purchased the 10,000,000 shares and the additional 1,500,000 shares on February 9 and February 17, 2015, respectively. The net proceeds from the offering were approximately $94.3 million after deducting underwriting discounts and estimated offering expenses paid by us.

May 2017 Public Offering

On May 11, 2017, we sold in an underwritten public offering an aggregate of 9,708,738 shares of our common stock to a single institutional investor in an underwritten offering. The price to the investor in the offering was $5.15 per share, and the underwriters agreed to purchase the shares from us pursuant to the underwriting agreement at a purchase price of $4.893 per share. The offering was made pursuant to a registration statement on Form S-3ASR previously filed with the SEC, and a prospectus supplement thereunder. The net proceeds from the offering were approximately $47.3 million after deducting underwriting commissions and estimated offering expenses payable by us.

Cash Increases and (Decreases)

The following table summarizes our net increase (decrease) in cash and cash equivalents for the years ended December 31, 2017, 2016 and 2015:

	Year ended December 31,		
($ in thousands)	**2017**	**2016**	**2015**
Net cash provided by (used in):			
Operating activities	$(54,669)	$(58,325)	$ (10)
Investing activities	(737)	(551)	(412)
Financing activities	45,299	(788)	98,336
Net increase (decrease) in cash and cash equivalents	$(10,107)	$(59,664)	$97,914

Cash flows from operating activities represent the cash receipts and disbursements related to all of our activities other than investing and financing activities. Operating cash flow is derived by adjusting our net loss for:

- Non-cash operating items such as depreciation and amortization, stock-based compensation and common and preferred stock issued in exchange for license agreements;
- Changes in operating assets and liabilities which reflect timing differences between the receipt and payment of cash associated with transactions and when they are recognized in results of operations; and
- Changes associated with the fair value of our derivative liabilities.

Net cash used in operating activities for the twelve months ended December 31, 2017 was $54.7 million, as compared to net cash used in operating activities of $58.3 million and $10 thousand for the years ended December 31, 2016 and 2015, respectively. The net cash used in operating activities for the twelve months ended

December 31, 2017 was primarily a result of our net loss of $54.3 million, offset by the decrease in prepaid expenses of $4.0 million, an increase in other noncurrent assets of $13.0 million, and an increase in accounts payable and accrued expenses of $5.1 million. The net cash used in operating activities for the twelve months ended December 31, 2016 was primarily a result of our net loss of $165.3 million, an increase of $12.5 million in charges related to prepayments for cell therapy programs under our license agreements, a decrease in deferred revenue of $6.9 million, a decrease in accounts payable and accrued expenses of $1.6 million and an increase in stock compensation of $0.4 million.

Net cash used in investing activities was $737 thousand for the twelve months ended December 31, 2017 compared to $551 thousand and $412 thousand for the years ended December 31, 2016 and December 31, 2015, respectively. The change was due primarily to equipment purchases under our agreement with MD Anderson to support our ongoing clinical trials in Houston, Texas.

Net cash provided by financing activities was $45.3 million for the twelve months ended December 31, 2017 compared to $788 thousand used in financing activities and $98.3 million provided by financing activities for the years ended December 31, 2016 and 2015, respectively. The $45.3 million provided by financing activities during the twelve months ended December 31, 2017 is a result of our May 2017 offering which is described in Note 2 to the accompanying financial statements. The $99.1 million decrease in cash provided by financing activities for the year ended December 31, 2016 is primarily attributable to proceeds of approximately $94.3 million associated with our February 2015 public offering and $4.6 million from stock option exercises, compared to $712 thousand in stock option exercises for the year ended December 31, 2015.

Operating Capital and Capital Expenditure Requirements

We anticipate that losses will continue for the foreseeable future. At December 31, 2017, our accumulated deficit was approximately $712.4 million. Our actual cash requirements may vary materially from those planned because of a number of factors including:

- Changes in the focus, direction and pace of our development programs;
- Competitive and technical advances;
- Costs associated with the development of our product candidates;
- Our ability to secure partnering arrangements;
- Costs of filing, prosecuting, defending and enforcing any patent claims and any other intellectual property rights, or other developments; and
- Other matters identified under Part I – Item 1A. “Risk Factors.”

Working capital as of December 31, 2017 was $69.9 million, consisting of $90.8 million in current assets and $20.9 million in current liabilities. Working capital as of December 31, 2016 was $89.1 million, consisting of $104.9 million in current assets and $15.8 million in current liabilities.

Contractual Obligations

The following table summarizes our outstanding obligations as of December 31, 2017, and subsequent events, and the effect those obligations are expected to have on our liquidity and cash flows in future periods:

($ in thousands)	Total	Less than 1 year	2 - 3 years	4 - 5 years	More than 5 years
Operating leases	$ 3,075	$ 1,129	$ 1,458	$ 488	$ —
CRADAs	$ 5,000	2,500	2,500	—	—
Royalty and license fees	$ 2,729	2,729	—	—	—
Total	$10,804	$ 6,358	$ 3,958	$ 488	$ —

Our commitments for operating leases relate to the lease for our corporate headquarters in Boston, Massachusetts, and office space in New York, New York and Houston, Texas. On December 21, 2015 and April 15, 2016, we renewed the sublease for our corporate headquarters in Boston, MA through August 31, 2021. Included in the above table are obligations for the subleased portion of our New York and Houston office space (see Note 7 to the accompanying financial statements). We expect to receive a total of $278 thousand in the next year from our subtenants in the New York office.

On January 13, 2015, we entered into the MD Anderson License (see Note 6 to the accompanying financial statements). The agreement includes minimum quarterly payments of $3.8 million less approved deductions included in the above table within "Royalty and License Fees." Our obligations related to this agreement includes our final quarterly payment of $2.7 million in the column "Less than 1 Year."

On January 10, 2017, we announced the signing of a CRADA with the NCI for the development of ACT-based immunotherapies genetically modified using the *Sleeping Beauty* transposon/transposase system for the treatment of solid tumors. Our obligation for the CRADA is reflected above with $2.5 million in the column "Less than 1 Year" and $2.5 million in the column "2 – 3 Years."

Critical Accounting Policies and Significant Estimates

Our Management's Discussion and Analysis of our financial condition and results of operations is based upon our financial statements, which have been prepared in accordance with accounting principles generally accepted in the United States. The preparation of these financial statements requires us to make estimates and assumptions that affect the reported amounts of assets and liabilities and the disclosure of contingent assets and liabilities at the date of the financial statements as well as the reported expenses during the reporting periods. We evaluate our estimates and judgments on an ongoing basis. Actual results may differ materially from these estimates under different assumptions or conditions.

We believe the following are our more significant estimates and judgments used in the preparation of our financial statements:

- Clinical trial expenses;
- Collaboration agreements;
- Fair value measurements of stock-based compensation and Series 1 preferred stock (and related dividends); and
- Income taxes.

Clinical Trial Expenses

Clinical trial expenses include expenses associated with clinical research organizations, or CROs. The invoicing from CROs for services rendered can lag several months. We accrue the cost of services rendered in connection with CRO activities based on our estimate of site management, monitoring costs, and project management costs. We maintain regular communication with our CROs to gauge the reasonableness of our estimates. Differences between actual clinical trial expenses and estimated clinical trial expenses recorded have not been material and are adjusted for in the period in which they become known.

Revenue Recognition from Collaboration Agreements

The Company has primarily generated revenue through collaboration arrangements with strategic partners for the development and commercialization of product candidates. The Company recognizes revenue for each unit of accounting when evidence of an arrangement exists, delivery has occurred, or services have been rendered, the seller's price to the buyer is fixed or determinable and collectability is reasonably assured.

The Company's collaboration agreements may provide for various types of payments, including upfront payments, funding of research and development, milestone payments, licensing fees and product royalties. The specifics of the Company's significant agreements are detailed in Note 7 to the accompanying financial statements.

The Company considers a variety of factors in determining the appropriate method of accounting for its collaboration agreements, including whether multiple deliverables can be separated and accounted for individually as separate units of accounting. Pursuant to the guidance in FASB Accounting Standards Codification (ASC) 605-25, *Multiple-Element Arrangements* (ASC 605-25), the Company evaluates multiple-element arrangements to determine whether the individual deliverables represent separate units of accounting or whether they must be accounted for as a combined unit of accounting. This evaluation involves subjective determinations and requires management to make judgments about the individual deliverables and whether such deliverables are separable from the other aspects of the contractual relationship. Deliverables are considered separate units of accounting provided that: (i) the delivered item(s) has value to the customer on a standalone basis and (ii) if the arrangement includes a general right of return relative to the delivered item(s), delivery or performance of the undelivered item(s) is considered probable and substantially in the control of the Company. In assessing whether an item has standalone value, the Company considers factors such as the research, manufacturing and commercialization capabilities of the collaboration partner and the availability of the associated expertise in the general marketplace. In addition, the Company considers whether the collaboration partner can use the other deliverable(s) for their intended purpose without the receipt of the remaining element(s), whether the value of the deliverable is dependent on the undelivered item(s) and whether there are other vendors that can provide the undelivered element(s). The Company's collaboration arrangements do not contain a general right of return relative to the delivered item(s).

Where there are multiple deliverables within a collaboration agreement that cannot be separated and therefore are combined into a single unit of accounting, revenues are deferred and recognized over the estimated period of performance, which is typically the development term. If the deliverables can be separated, the Company applies the relevant revenue recognition guidance to each individual unit of accounting. The specific methodology for the recognition of the underlying revenue is determined on a case-by-case basis according to the facts and circumstances applicable to each agreement. Generally, the Company has accounted for its collaboration agreements as a single unit of accounting.

At the inception of an arrangement that includes milestone payments, the Company evaluates whether each milestone is substantive and at risk to both parties on the basis of the contingent nature of the milestone. This evaluation includes an assessment of whether: (i) the consideration is commensurate with either the Company's performance to achieve the milestone or the enhancement of the value of the delivered item(s) as a result of a specific outcome resulting from the Company's performance to achieve the milestone, (ii) the consideration relates solely to past performance and (iii) the consideration is reasonable relative to all of the deliverables and payment terms within the arrangement. The Company evaluates factors such as the scientific, clinical, regulatory, commercial and other risks that must be overcome to achieve the respective milestone and the level of effort and investment required to achieve the respective milestone in making this assessment. There is considerable judgement involved in determining whether a milestone satisfies all of the criteria required to conclude that a milestone is substantive. In accordance with FASB ASC 605-28, *Milestone Method* (ASC 605-28), revenue from substantive milestone payments is recognized in its entirety in the period in which the milestone is achieved, assuming all other revenue recognition criteria are met. Payments from milestones that are not considered substantive payment is deferred and recognized as revenue over the estimated remaining period of performance under the contract as the Company completes its performance obligations assuming all other revenue recognition criteria are met. Revenue from commercial milestone payments is accounted for as royalties and recorded as revenue upon achievement of the milestone, assuming all other revenue recognition criteria are met. Royalties are recognized as earned in accordance with the terms of various research and collaboration agreements.

Fair Value Measurements of Stock Based Compensation and Series 1 Preferred Stock (including related dividends)

Accounting standards define fair value, establish a framework for measuring fair value under generally accepted accounting principles and enhance disclosures about fair value measurements. Fair value is defined as the exchange price that would be received for an asset or paid to transfer a liability (an exit price) in the principal or most advantageous market for the asset or liability in an orderly transaction between market participants on the measurement date. Valuation techniques used to measure fair value must maximize the use of observable inputs and minimize the use of unobservable inputs. The standard describes a fair value hierarchy based on three levels of inputs, of which the first two are considered observable and the last unobservable, that may be used to measure fair value which are the following:

- Level 1—Quoted prices in active markets for identical assets or liabilities.
- Level 2—Inputs other than Level 1 that are observable, either directly or indirectly, such as quoted prices for similar assets or liabilities; quoted prices in markets that are not active; or other inputs that are observable or can be corroborated by observable market data for substantially the full term of the assets or liabilities.
- Level 3—Unobservable inputs that are supported by little or no market activity and that are significant to the fair value of the assets or liabilities.

We make certain assumptions in order to value and expense our share-based compensation awards and Series 1 preferred stock (including related dividends). In connection with valuing stock options and use the Black-Scholes, which require us to estimate certain subjective assumptions. The key assumptions we make are: the expected volatility of our stock; the expected term of the award; and the forfeiture rate related to share based awards. In connection with our restricted stock programs, we make assumptions principally related to the forfeiture rate. The key assumptions used to estimate fair value for our warrants include current and expected stock prices, volatility, dividends, forward yield curves and discount rates.

We review our valuation assumptions periodically and, as a result, we may change our valuation assumptions used to value share-based awards granted in future periods and Series 1 preferred stock. Such changes may lead to a significant change in the expense we recognize in connection with share-based payments.

Income Taxes

In preparing our financial statements, we estimate our income tax liability in each of the jurisdictions in which we operate by estimating our actual current tax expense together with assessing temporary differences resulting from differing treatment of items for tax and financial reporting purposes. These differences result in deferred tax assets and liabilities, which, prior to the consideration for the need for a valuation allowance, are included on the balance sheet. Significant management judgment is required in assessing the realizability of our deferred tax assets. In performing this assessment, we consider whether it is more likely than not that some portion or all of the deferred tax assets will not be realized. The ultimate realization of deferred tax assets is dependent upon the generation of future taxable income during the periods in which those temporary differences become deductible. In making this determination, under the applicable financial accounting standards, we are allowed to consider the scheduled reversal of deferred tax liabilities, projected future taxable income, and the effects of tax planning strategies. Our estimates of future taxable income include, among other items, our estimates of future income tax deductions related to the exercise of stock options. In the event that actual results differ from our estimates, we adjust our estimates in future periods and we may need to establish a valuation allowance, which could materially impact our financial position and results of operations.

We account for uncertain tax positions using a “more-likely-than-not” threshold for recognizing and resolving uncertain tax positions. The evaluation of uncertain tax positions is based on factors that include, but are not limited to, changes in tax law, the measurement of tax positions taken or expected to be taken in tax returns, the

effective settlement of matters subject to audit, new audit activity and changes in facts or circumstances related to a tax position. We evaluate uncertain tax positions on an annual basis and adjust the level of the liability to reflect any subsequent changes in the relevant facts surrounding the uncertain positions. Our liabilities for uncertain tax positions can be relieved only if the contingency becomes legally extinguished through either payment to the taxing authority or the expiration of the statute of limitations, the recognition of the benefits associated with the position meet the "more-likely-than-not" threshold or the liability becomes effectively settled through the examination process. We consider matters to be effectively settled once the taxing authority has completed all of its required or expected examination procedures, including all appeals and administrative reviews; we have no plans to appeal or litigate any aspect of the tax position; and we believe that it is highly unlikely that the taxing authority would examine or re-examine the related tax position. We also accrue for potential interest and penalties, related to unrecognized tax benefits in income tax expense.

Recent Accounting Pronouncements

For a discussion of new accounting standards, please read Note 3 to the accompanying financial statements, *Summary of Significant Accounting Principles* included in this report.

Off-Balance Sheet Arrangements

We have not entered into, nor do we currently have any special purpose entities or off-balance sheet financing arrangements as defined under SEC rules.

Item 7A. Quantitative and Qualitative Disclosures About Market Risk

Our exposure to market risk is limited to our cash. The goals of our investment policy are preservation of capital, fulfillment of liquidity needs and fiduciary control of cash and investments. We also seek to maximize income from our investments without assuming significant risk. To achieve our goals, we maintain our cash in interest-bearing cash accounts. As all of our investments are cash deposits in a global bank, it is subject to minimal interest rate risk.

Effect of Currency Exchange Rates and Exchange Rate Risk Management

We conduct a number of clinical trials outside of the United States, primarily in Western Europe. These business operations are not material at this time, and therefore we do not anticipate that currency fluctuations will have a material impact on our financial position, results of operations or cash flows at this time.

Item 8. Financial Statements and Supplementary Data

The information required by this Item 8 is contained on pages F-1 through F-40 of this Annual Report on Form 10-K and is incorporated herein by reference.

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

None.

Item 9A. Controls and Procedures

Evaluation of Disclosure Controls and Procedures.

Under the supervision and with the participation of our management, including our Chief Executive Officer and Chief Accounting Officer, we have evaluated the effectiveness of our disclosure controls and procedures, as such term is defined under Rule 13a-15(e) or 15d-15(e) promulgated under the Exchange Act, as of December 31, 2017. Based on that evaluation, our Chief Executive Officer and Chief Accounting Officer have concluded that as of such date, our disclosure controls and procedures were effective.

Management's Report on Internal Control over Financial Reporting

Our management is responsible for establishing and maintaining adequate internal control over financial reporting for us. Internal control over financial reporting (as defined in Rule 13a-15(f) of the Exchange Act) is a process to provide reasonable assurance regarding the reliability of our financial reporting for external purposes in accordance with accounting principles generally accepted in the United States of America. Internal control over financial reporting includes maintaining records that in reasonable detail accurately and fairly reflect our transactions; providing reasonable assurance that transactions are recorded as necessary for preparation of our financial statements; providing reasonable assurance that receipts and expenditures of company assets are made in accordance with management authorization; and providing reasonable assurance that unauthorized acquisition, use or disposition of company assets that could have a material effect on our financial statements would be prevented or detected on a timely basis. Because of its inherent limitations, internal control over financial reporting is not intended to provide absolute assurance that a misstatement of our financial statements would be prevented or detected.

Management conducted an evaluation of the effectiveness, as of December 31, 2017, of our internal control over financial reporting based on the framework in *Internal Control—Integrated Framework* issued by the Committee of Sponsoring Organizations of the Treadway Commission in 2013. Based on this evaluation, management concluded that our internal control over financial reporting was effective as of December 31, 2017.

RSM US LLP, an independent registered public accounting firm, has issued an attestation report on our internal control over financial reporting as of December 31, 2017. That report is included in this Annual Report on Form 10-K.

Changes in Internal Controls over Financial Reporting

There were no changes in our internal control over financial reporting during the year ended December 31, 2017 that have materially affected, or are reasonably likely to materially affect, our internal control over financial reporting.

Item 9B. Other Information

None.

PART III

Item 10. Directors, Executive Officers and Corporate Governance

Information in response to this Item is incorporated herein by reference to the information from our definitive proxy statement to be filed pursuant to Regulation 14A within 120 days after the end of the fiscal year covered by this Annual Report on Form 10-K under the sections titled *Proposals—Election of Directors, Executive Officers, Information Regarding the Board of Directors and Corporate Governance* and *Stock Ownership*.

Item 11. Executive Compensation

Information in response to this Item is incorporated herein by reference to the information from our definitive proxy statement to be filed pursuant to Regulation 14A within 120 days after the end of the fiscal year covered by this Annual Report on Form 10-K under the section entitled *Executive Compensation*.

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

Securities Authorized for Issuance under Equity Compensation Plans

Our Amended and Restated 2003 Stock Option Plan, or the 2003 Plan, and our 2012 Stock Option Plan, or the 2012 Plan, are our only equity compensation plans approved by our stockholders. The following table sets forth certain information as of December 31, 2017 with respect to the 2003 and 2012 Plans:

Plan Category	Number of Securities to be Issued Upon Exercise of Outstanding Options (A)	Weighted-Average Exercise Price of Outstanding Options (B)	Number of Securities Remaining Available for Future Issuance Under Equity Compensation Plans (Excluding Securities Reflected in Column (A)) (C)
Equity compensation plans approved by stockholders:			
2003 Stock Option Plan	674,167	$ 4.31	—
2012 Stock Option Plan	3,177,968	5.30	303,928
Total:	3,852,135	$ 5.12	303,928
Equity compensation plans not approved by stockholders:			
Inducement Award	500,000	6.19	—
Total:	500,000	$ 6.19	—

Additional information in response to this Item is incorporated herein by reference to the information from our definitive proxy statement to be filed pursuant to Regulation 14A within 120 days after the end of the fiscal year covered by this Annual Report on Form 10-K under the section titled *Stock Ownership*.

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

Information in response to this Item is incorporated herein by reference to the information from our definitive proxy statement to be filed pursuant to Regulation 14A within 120 days after the end of the fiscal year covered by this Annual Report on Form 10-K under the section titled *Certain Relationships and Related Transactions and Information Regarding the Board of Directors and Corporate Governance*.

Item 14. Principal Accountant Fees and Services

Information in response to this Item is incorporated herein by reference to the information from our definitive proxy statement to be filed pursuant to Regulation 14A within 120 days after the end of the fiscal year covered by this Annual Report on Form 10-K under the section titled *Independent Registered Public Accounting Firm Fees and Other Matters*.

PART IV

Item 15. Exhibits, Financial Statement Schedules

(1) Financial Statements:

The Financial Statements required to be filed by Item 8 of this Annual Report on Form 10-K, and filed in this Item 15, are as follows:

(2) Financial Statement Schedules:

Schedules are omitted because they are not applicable, or are not required, or because the information is included in the financial statements and notes thereto.

(3) Exhibits:

Exhibit No.	Description of Document
2.1	Agreement and Plan of Merger among the Registrant (formerly "EasyWeb, Inc."), ZIO Acquisition Corp. and ZIOPHARM, Inc., dated August 3, 2005 (incorporated by reference to Exhibit 10.1 to the Registrant's Form 8-K, SEC File No. 000-32353, filed August 9, 2005).
3.1	Amended and Restated Certificate of Incorporation, as filed with the Delaware Secretary of State on April 26, 2006 (incorporated by reference to Exhibit 3.1 to the Registrant's Current Report on Form 8-K, SEC File No. 000-32353, filed April 26, 2006).
3.2	Certificate of Merger dated September 13, 2005, relating to the merger of ZIO Acquisition Corp. with and into ZIOPHARM, Inc. (incorporated by reference to Exhibit 3.1 to the Registrant's Form 8-K, SEC File No. 000-32353, filed September 19, 2005).
3.3	Certificate of Ownership of the Registrant (formerly "EasyWeb, Inc.") dated as of September 14, 2005, relating the merger of ZIOPHARM, Inc. with and into the Registrant, and changing the Registrant's corporate name from EasyWeb, Inc. to ZIOPHARM Oncology, Inc. (incorporated by reference to Exhibit 3.2 to the Registrant's Form 8-K, SEC File No. 000-32353, filed September 19, 2005).
3.4	Amended and Restated Certificate of Designation, Preferences and Rights of Series 1 Preferred Stock, as filed with the Delaware Secretary of State on July 1, 2016 (incorporated by reference to Exhibit 3.1 to the Registrant's Current Report on Form 8-K/A, SEC File No. 001-33038, filed July 1, 2016).
3.5	Bylaws, as amended to date (incorporated by reference to Exhibit 3.3 to the Registrant's Form 8-K, SEC File No. 000-32353, filed September 19, 2005).
4.1	Specimen common stock certificate (incorporated by reference to Exhibit 4.1 to the Registrant's Registration Statement on Form SB-2, SEC File No. 333-129020, filed October 14, 2005).
4.2	Form of Indenture between the registrant and one or more trustees to be named (incorporated by reference to Exhibit 4.4 to the Registrant's Registration Statement on Form S-3ASR, SEC File No. 333-201826, filed February 2, 2015).

Exhibit No.	Description of Document
4.3	Form of Common Stock Warrant Agreement and Warrant Certificate (incorporated by reference to Exhibit 4.5 to the Registrant's Registration Statement on Form S-3ASR, SEC File No. 333-201826, filed February 2, 2015).
4.4	Form of Preferred Stock Warrant Agreement and Warrant Certificate (incorporated by reference to Exhibit 4.6 to the Registrant's Registration Statement on Form S-3ASR, SEC File No. 333-201826, filed February 2, 2015).
4.5	Form of Debt Securities Warrant Agreement and Warrant Certificate (incorporated by reference to Exhibit 4.7 to the Registrant's Registration Statement on Form S-3ASR, SEC File No. 333-201826, filed February 2, 2015).
4.6	Form of Option for the Purchase of Shares of common stock dated August 30, 2004 and issued to The University of Texas M. D. Anderson Cancer Center (incorporated by reference to Exhibit 4.6 to the Registrant's Annual Report on Form 10-KSB, SEC File No. 000-32353, filed March 20, 2006).
4.7	Schedule identifying Material Terms of Options for the Purchase of Shares of Common Stock (incorporated by reference to Exhibit 4.7 to the Registrant's Annual Report on Form 10-KSB, SEC File No. 000-32353, filed March 20, 2006).
10.1	ZIOPHARM Oncology, Inc. Amended and Restated 2003 Stock Incentive Plan (incorporated by reference to Exhibit 10.1 to the Registrant's Annual Report on Form 10-K SEC File No. 001-33038 filed March 1, 2011).
10.2	Form of Incentive Stock Option Agreement granted under the Registrant's 2003 Stock Option Plan (incorporated by reference to Exhibit 10.8 to the Registrant's Annual Report on Form 10-KSB, SEC File No. 000-32353, filed March 20, 2006).
10.3	Form of Employee Non-Qualified Stock Option Agreement granted under the Registrant's 2003 Stock Option Plan (incorporated by reference to Exhibit 10.9 to the Registrant's Annual Report on Form 10-KSB, SEC File No. 000-32353, filed March 20, 2006).
10.4	Form of Director Non-Qualified Stock Option Agreement granted under the Registrant's 2003 Stock Option Plan (incorporated by reference to Exhibit 10.10 to the Registrant's Annual Report on Form 10-KSB, SEC File No. 000-32353, filed March 20, 2006).
10.5	Form of Restricted Stock Agreement granted under the Registrant's 2003 Stock Option Plan (incorporated by reference to Exhibit 10.1 to the Registrant's Current Report on Form 8-K SEC File No. 001-33038 filed December 18, 2007).
10.6	ZIOPHARM Oncology, Inc. 2012 Equity Incentive Plan (incorporated by reference to Exhibit 10.1 to the Registrant's Current Report on Form 8-K SEC File No. 001-33038 filed June 26, 2012).
10.7	Form of Restricted Stock Agreement Granted Under the ZIOPHARM Oncology, Inc. 2012 Equity Incentive Plan (incorporated by reference to Exhibit 10.2 to the Registrant's Current Report on Form 8-K SEC File No. 001-33038 filed June 26, 2012).
10.8	Form of Option Agreement Granted Under the ZIOPHARM Oncology, Inc. 2012 Equity Incentive Plan (incorporated by reference to Exhibit 10.3 to the Registrant's Current Report on Form 8-K SEC File No. 001-33038 filed June 26, 2012).
10.11+	Patent and Technology License Agreement dated August 24, 2004, among ZIOPHARM, Inc. (predecessor to the Registrant), the Board of Regents of the University of Texas System on behalf of the University of Texas M.D. Anderson Cancer Center and the Texas A&M University System (incorporated by reference to Exhibit 10.5 to the Registrant's Registration Statement on Form SB-2, SEC File No. 333-129020, filed October 14, 2005).

Exhibit No.	Description of Document
10.12+	Asset Purchase Agreement dated November 3, 2006 by and among Baxter Healthcare S.A., Baxter International, Inc., Baxter Oncology GmbH and the Registrant (incorporated by reference to Exhibit 10.1 to the Registrant's Quarterly Report on Form 10-QSB, SEC File No. 001-33038, filed November 13, 2006).
10.13+	License Agreement dated November 3, 2006 by and among Baxter Healthcare S.A., Baxter International, Inc. and the Registrant (incorporated by reference to Exhibit 10.1 to the Registrant's Quarterly Report on Form 10-QSB, SEC File No. 001-33038, filed November 13, 2006).
10.14	Amendment to License Agreement dated September 24, 2009 by and among Baxter Healthcare S.A., Baxter International, Inc. and the Registrant (incorporated by reference to Exhibit 10.16 to the Registrant's Annual Report on Form 10-K, SEC File No. 001-33038, filed March 17, 2010).
10.15+	Exclusive Channel Partner Agreement by and between the Registrant and Intrexon Corporation dated as of January 6, 2011 (incorporated by reference to Exhibit 10.1 to the Registrant's Current Report on Form 8-K, SEC File No. 001-33038, filed January 12, 2011).
10.16	First Amendment to Exclusive Channel Partner Agreement dated September 13, 2011 by and between the Registrant and Intrexon Corporation (incorporated by reference to Exhibit 10.1 to the Registrant's Quarterly Report on Form 10-Q, SEC File No. 001-33038, filed May 3, 2012)
10.17	Stock Purchase Agreement by and between the Registrant and Intrexon Corporation dated as of January 6, 2011 (incorporated by reference to Exhibit 10.2 to the Registrant's Current Report on Form 8-K, SEC File No. 001-33038, filed January 12, 2011).
10.18	Amendment to Stock Purchase Agreement by and between the Registrant and Intrexon Corporation dated as of February 1, 2011 (incorporated by reference to Exhibit 10.1 to the Registrant's Current Report on Form 8-K, SEC File No. 001-33038, filed February 7, 2011).
10.19	Registration Rights Agreement dated January 12, 2011 by and between the Registrant and Intrexon Corporation (incorporated by reference to Exhibit 10.24 to the Registrant's Annual Report on Form 10-K, SEC File No. 001-33038, filed March 1, 2011).
10.20	Form of Indemnity Agreement for directors and executive officers (incorporated by reference to Exhibit 99.1 to the Registrant's Current Report on Form 8-K, SEC File No. 001-33038, filed January 31, 2013).
10.21	Letter Agreement by and among the Registrant, Intrexon Corporation and The University of Texas System Board of Regents on behalf of The University of Texas M.D. Anderson Cancer Center dated as of January 9, 2015 (incorporated by reference to Exhibit 10.1 to the Registrant's Current Report on Form 8-K, SEC File No. 001-33038, filed January 14, 2015).
10.22	Securities Issuance Agreement by and between the Registrant and The University of Texas System Board of Regents on behalf of The University of Texas M.D. Anderson Cancer Center dated as of January 13, 2015 (incorporated by reference to Exhibit 10.2 to the Registrant's Current Report on Form 8-K, SEC File No. 001-33038, filed January 14, 2015).
10.23	Securities Issuance Agreement by and between the Registrant and The University of Texas System Board of Regents on behalf of The University of Texas M.D. Anderson Cancer Center dated as of January 13, 2015 (incorporated by reference to Exhibit 10.3 to the Registrant's Current Report on Form 8-K, SEC File No. 001-33038, filed January 14, 2015).
10.24	Registration Rights Agreement by and between the Registrant and The University of Texas System Board of Regents on behalf of The University of Texas M.D. Anderson Cancer Center dated as of January 13, 2015 (incorporated by reference to Exhibit 10.4 to the Registrant's Current Report on Form 8-K, SEC File No. 001-33038, filed January 14, 2015).

Exhibit No.	Description of Document
10.25	License Agreement by and among the Registrant, Intrexon Corporation and The University of Texas System Board of Regents on behalf of The University of Texas M.D. Anderson Cancer Center dated as of January 13, 2015 (incorporated by reference to Exhibit 10.5 to the Registrant's Current Report on Form 8-K, SEC File No. 001-33038, filed January 28, 2015).
10.26+	License and Collaboration Agreement by and among the Registrant, Intrexon Corporation and ARES TRADING Trading S.A. dated as of March 27, 2015 (incorporated by reference to Exhibit 10.1 to the Registrant's Current Report on Form 8-K, SEC File No. 001-33038, filed April 2, 2015).
10.27	Second Amendment to Exclusive Channel Partner Agreement by and between the Registrant and Intrexon Corporation dated as of March 27, 2015 (incorporated by reference to Exhibit 10.2 to the Registrant's Current Report on Form 8-K, SEC File No. 001-33038, filed April 2, 2015).
10.28	Employment Agreement by and between the Registrant and Laurence James Neil Cooper, M.D., Ph.D. dated as of May 5, 2015 (incorporated by reference to Exhibit 10.1 to the Registrant's Current Report on Form 8-K, SEC File No. 001-33038, filed May 7, 2015).
10.29	Amended and Restated Employment Agreement by and between the Registrant and Caesar J. Belbel dated as of June 1, 2015 (incorporated by reference to Exhibit 10.1 to the Registrant's Current Report on Form 8-K, SEC File No. 001-33038, filed June 2, 2015).
10.30	Research and Development Agreement by and among the Registrant, Intrexon Corporation and The University of Texas M.D. Anderson Cancer Center dated as of August 17, 2015 (incorporated by reference to Exhibit 10.1 to the Registrant's Current Report on Form 8-K, SEC File No. 001-33038, filed August 21, 2015).
10.31	Exclusive Channel Collaboration Agreement by and between the Registrant and Intrexon Corporation dated September 28, 2015 (incorporated by reference to Exhibit 10.1 to the Registrant's Current Report on Form 8-K, SEC File No. 001-33038, filed October 1, 2015).
10.32	Third Amendment to Exclusive Channel Partner Agreement by and between the Registrant and Intrexon Corporation dated as of June 29, 2016 (incorporated by reference to Exhibit 10.1 to the Registrant's Current Report on Form 8-K, SEC File No. 001-33038, filed June 30, 2016).
10.33	Amendment to Exclusive Channel Collaboration Agreement by and between the Registrant and Intrexon Corporation dated as of June 29, 2016 (incorporated by reference to Exhibit 10.2 to the Registrant's Current Report on Form 8-K, SEC File No. 001-33038, filed June 30, 2016).
10.34	Securities Issuance Agreement by and between the Registrant and Intrexon Corporation dated as of June 29, 2016 (incorporated by reference to Exhibit 10.3 to the Registrant's Current Report on Form 8-K, SEC File No. 001-33038, filed June 30, 2016).
10.35	Offer Letter by and between the Registrant and David Mauney, M.D., dated as of September 26, 2017 (incorporated by reference to Exhibit 10.1 to the Registrant's Current Report on Form 8-K, SEC File No. 001-33038, filed September 28, 2017).
10.36	Severance Agreement by and between the Registrant and David Mauney, M.D., dated as of September 28, 2017 (incorporated by reference to Exhibit 10.2 to the Registrant's Current Report on Form 8-K, SEC File No. 001-33038, filed September 28, 2017).
23.1	Consent of Independent Registered Public Accounting Firm
24.1	Power of Attorney (incorporated by reference to the signature page of this Annual Report on Form 10-K).
31.1	Certification of Chief Executive Officer pursuant to Exchange Act Rule 13a-14(a) or 15(d)-14(a), as adopted pursuant to Section 302 of the Sarbanes-Oxley Act of 2002. Certification of Chief Executive Officer pursuant to Exchange Act Rule 13a-14(a) or 15(d)-14(a), as adopted pursuant to Section 302 of the Sarbanes-Oxley Act of 2002.

Exhibit No.	Description of Document
31.2	Certification of Chief Accounting Officer pursuant to Exchange Act Rule 13a-14(a) or 15(d)-14(a), as adopted pursuant to Section 302 of the Sarbanes-Oxley Act of 2002.
32.1	Certification of Chief Executive Officer pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002.
32.2	Certification of Chief Accounting Officer pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002.
101.INS	XBRL Instance Document
101.SCH	XBRL Taxonomy Extension Schema Document
101.CAL	XBRL Taxonomy Extension Calculation Linkbase Document
101.DEF	XBRL Taxonomy Extension Definition Linkbase Document
101.LAB	XBRL Taxonomy Extension Label Linkbase Document
101.PRE	XBRL Taxonomy Extension Presentation Linkbase Document

Item 16. Form 10-K Summary

Not applicable.

SIGNATURES

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

ZIOPHARM ONCOLOGY, INC.

Date: March 1, 2018

By: /s/ Laurence J.N. Cooper
Laurence J.N. Cooper, M.D., Ph.D.
Chief Executive Officer
(Principal Executive Officer)

Date: March 1, 2018

By: /s/ Kevin G. Lafond
Kevin G. Lafond
Senior Vice President, Chief Accounting Officer and Treasurer (Principal Financial and Accounting Officer)

KNOW ALL PERSONS BY THESE PRESENTS, that each person whose signature appears below constitutes and appoints Laurence J.N. Cooper and Kevin G. Lafond, jointly and severally, as his or her true and lawful attorneys-in-fact and agents, with full power of substitution and resubstitution, for him or her, and in his or her name, place and stead, in any and all capacities, to sign any and all amendments to this report, and to file the same, with all exhibits thereto, and other documents in connection therewith, with the Securities and Exchange Commission, granting unto said attorneys-in-fact and agents full power and authority to do and perform each and every act and thing requisite or necessary to be done in and about the premises hereby ratifying and confirming all that said attorneys-in-fact and agents, or his substitute or substitutes, may lawfully do or cause to be done by virtue hereof.

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

Signature	Title	Date
/s/ Laurence J.N. Cooper Laurence J.N. Cooper, M.D., Ph.D.	Chief Executive Officer (Principal Executive Officer)	March 1, 2018
/s/ Kevin G. Lafond Kevin G. Lafond	Senior Vice President, Chief Accounting Officer and Treasurer (Principal Financial and Accounting Officer)	March 1, 2018
/s/ Murray Brennan Murray Brennan	Director	March 1, 2018
/s/ James Cannon James Cannon	Director	March 1, 2018
/s/ Wyche Fowler, Jr. Wyche Fowler, Jr.	Director	March 1, 2018
/s/ Randal J. Kirk Randal J. Kirk	Director	March 1, 2018

Signature	Title	Date
/s/ Scott Tariff Scott Tariff	Director	March 1, 2018
/s/ Michael Weiser Michael Weiser	Director	March 1, 2018

Table of Contents

ZIOPHARM Oncology, Inc.

INDEX TO FINANCIAL STATEMENTS

REPORT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

To the Stockholders and the Board of Directors of
ZIOPHARM Oncology, Inc.
Boston, MA

Opinions on the Financial Statements and Internal Control Over Financial Reporting

We have audited the accompanying balance sheets of ZIOPHARM Oncology, Inc. (the Company) as of December 31, 2017 and 2016, and the related statements of operations, stockholders' equity (deficit) and cash flows for each of the three years in the period ended December 31, 2017, and the related notes (collectively, the financial statements). We also have audited the Company's internal control over financial reporting as of December 31, 2017, based on criteria established in *Internal Control—Integrated Framework* issued by the Committee of Sponsoring Organizations of the Treadway Commission in 2013.

In our opinion, the financial statements referred to above present fairly, in all material respects, the financial position of the Company as of December 31, 2017 and 2016, and the results of its operations and its cash flows for each of the three years in the period ended December 31, 2017, in conformity with accounting principles generally accepted in the United States of America. Also in our opinion, the Company maintained, in all material respects, effective internal control over financial reporting as of December 31, 2017, based on criteria established in *Internal Control—Integrated Framework* issued by the Committee of Sponsoring Organizations of the Treadway Commission in 2013.

Emphasis of Matter

The accompanying financial statements have been prepared assuming that the Company will continue as a going concern. As discussed in Note 1 to the financial statements, the Company has suffered recurring losses from operations. This raises substantial doubt about the Company's ability to continue as a going concern. Management's plans in regard to these matters also are described in Note 1. The financial statements do not include any adjustments that might result from the outcome of this uncertainty.

Basis for Opinions

The Company's management is responsible for these financial statements, for maintaining effective internal control over financial reporting, and for its assessment of the effectiveness of internal control over financial reporting, included in the accompanying Management's Annual Report on Internal Control over Financial Reporting. Our responsibility is to express an opinion on the Company's financial statements and an opinion on the Company's internal control over financial reporting based on our audits. We are a public accounting firm registered with the Public Company Accounting Oversight Board (United States) (PCAOB) and are required to be independent with respect to the Company in accordance with U.S. federal securities laws and the applicable rules and regulations of the Securities and Exchange Commission and the PCAOB.

We conducted our audits in accordance with the standards of the PCAOB. Those standards require that we plan and perform the audits to obtain reasonable assurance about whether the financial statements are free of material misstatement, whether due to error or fraud, and whether effective internal control over financial reporting was maintained in all material respects.

Our audits of the financial statements included performing procedures to assess the risks of material misstatement of the financial statements, whether due to error or fraud, and performing procedures that respond to those risks. Such procedures included examining, on a test basis, evidence regarding the amounts and disclosures in the financial statements. Our audits also included evaluating the accounting principles used and significant estimates made by management, as well as evaluating the overall presentation of the financial

statements. Our audit of internal control over financial reporting included obtaining an understanding of internal control over financial reporting, assessing the risk that a material weakness exists, and testing and evaluating the design and operating effectiveness of internal control based on the assessed risk. Our audits also included performing such other procedures as we considered necessary in the circumstances. We believe that our audits provide a reasonable basis for our opinions.

Definition and Limitations of Internal Control Over Financial Reporting

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

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

/s/ RSM US LLP

We or our predecessor firms have served as the Company's auditor since 2005.

Boston, Massachusetts

March 1, 2018

ZIOPHARM Oncology, Inc.

BALANCE SHEETS

(in thousands, except share and per share data)

	December 31, 2017	December 31, 2016
ASSETS		
Current assets:		
Cash and cash equivalents	$ 70,946	$ 81,053
Receivables	19	21
Prepaid expenses and other current assets	19,818	23,810
Total current assets	90,783	104,884
Property and equipment, net	1,211	843
Deposits	128	128
Other non-current assets	13,484	493
Total assets	$ 105,606	$ 106,348
LIABILITIES, PREFERRED STOCK AND STOCKHOLDERS' DEFICIT		
Current liabilities:		
Accounts payable	$ 4,417	$ 156
Accrued expenses	9,909	9,109
Deferred revenue - current portion	6,389	6,389
Deferred rent - current portion	141	155
Total current liabilities	20,856	15,809
Deferred revenue, net of current portion	35,139	41,528
Deferred rent, net of current portion	1	126
Derivative liabilities	2,424	862
Total liabilities	58,420	58,325
Commitments and contingencies (Note 7)		
Preferred stock, $0.001 par value, 30,000,000 shares authorized		
Series 1 preferred stock, $1,200 stated value; 250,000 designated; 119,644 and 106,184 shares issued and outstanding at December 31, 2017 and respectively; liquidation value of $143.6 million and $127.4 million at December 31, 2017 and 2016, respectively	143,992	125,321
Stockholders' deficit:		
Common stock, $0.001 par value; 250,000,000 shares authorized; 142,658,037 and 132,376,670 shares issued and outstanding at December 31, 2017 and 2016, respectively	143	132
Additional paid-in capital - common stock	615,493	580,567
Accumulated deficit	(712,442)	(657,997)
Total stockholders' deficit	(96,806)	(77,298)
Total liabilities and stockholders' deficit	$ 105,606	$ 106,348

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

ZIOPHARM Oncology, Inc.

STATEMENTS OF OPERATIONS

(in thousands, except share and per share data)

	For the Year Ended December 31,		
	2017	2016	2015
Collaboration revenue	$ 6,389	$ 6,861	$ 4,332
Operating expenses:			
Research and development	45,084	157,791	106,785
General and administrative	14,798	14,377	17,647
Total operating expenses	59,882	172,168	124,432
Loss from operations	(53,493)	(165,307)	(120,100)
Other income (expense), net	465	134	12
Change in fair value of derivative liabilities	(1,295)	(124)	—
Net loss	$ (54,323)	$ (165,297)	$ (120,088)
Preferred stock dividends	$ (18,938)	$ (7,123)	$ —
Net loss applicable to common stockholders	$ (73,261)	$ (172,420)	$ (120,088)
Basic and diluted net loss per share	$ (0.53)	$ (1.32)	$ (0.96)
Weighted average common shares outstanding used to compute basic and diluted net loss per share	136,938,264	130,391,463	125,416,084

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

ZIOPHARM Oncology, Inc.

STATEMENTS OF CHANGES IN PREFERRED STOCK AND STOCKHOLDERS' EQUITY (DEFICIT)

(in thousands, except share and per share data)

	Series 1 Preferred Stock-Mezzanine		Common Stock		Additional Paid-in Capital Common Stock	Accumulated Deficit	Total Stockholders' Equity (Deficit)
	Shares	Amount	Shares	Amount			
Balance at December 31, 2014	—	$ —	104,452,105	$ 104	$406,349	$ (372,612)	$ 33,841
Stock-based compensation	—	—	—	—	7,997	—	7,997
Exercise of employee stock options	—	—	2,519,267	3	4,566	—	4,568
Issuance of restricted common stock	—	—	1,590,574	2	(2)	—	—
Repurchase of shares of restricted common stock	—	—	(61,819)	—	(518)	—	(518)
Repurchase of common stock	—	—	(3,711)	—	(34)	—	(34)
Issuance of common stock, net of commissions and expenses of $6,305	—	—	11,500,000	12	94,309	—	94,320
Issuance of common stock in licensing agreement	—	—	11,722,163	12	67,273	—	67,285
Net loss	—	—	—	—	—	(120,088)	(120,088)
Balance at December 31, 2015	—	$ —	131,718,579	$ 132	$579,939	$ (492,700)	$ 87,371

ZIOPHARM Oncology, Inc.

STATEMENTS OF CHANGES IN PREFERRED STOCK AND STOCKHOLDERS' EQUITY (DEFICIT) (Cont.)

(in thousands, except share and per share data)

	Series 1 Preferred Stock-Mezzanine		Common Stock		Additional Paid In Capital Common Stock	Accumulated Deficit	Total Stockholders' Equity (Deficit)
	Shares	Amount	Shares	Amount			
Exercise of employee stock options	—	—	189,696	2	712	—	714
Stock-based compensation	—	—	—	—	8,452	—	8,452
Issuance of restricted common stock			711,770	712	(712)	—	—
Issuance of common stock in a license agreement			—	—	87	—	87
Repurchase of common stock	—	—	(243,207)	(2)	(1,498)	—	(1,500)
Stock buy-back	—	—	(168)	—	(2)	—	(2)
Issuance of Series 1 Preferred Stock in a license agreement with Intrexon, net of issuance costs of $109	100,000	118,242	—	—	—	—	—
Preferred stock dividends	6,184	7,079	—	—	(7,123)	—	(7,123)
Net loss	—	—	—	—	—	(165,297)	(165,297)
Balance at December 31, 2016	106,184	$125,321	132,376,670	$ 132	$580,567	$ (657,997)	$ (77,298)

ZIOPHARM Oncology, Inc.

STATEMENTS OF CHANGES IN PREFERRED STOCK AND STOCKHOLDERS' EQUITY (DEFICIT) (Cont.)

(in thousands, except share and per share data)

	Series 1 Preferred Stock-Mezzanine		Common Stock		Additional Paid In Capital Common Stock	Accumulated Deficit	Total Stockholders' Equity (Deficit)
	Shares	Amount	Shares	Amount			
Cumulative effect adjustment (Note 3)	—	—	—	—	122	(122)	—
Exercise of stock options	—	—	59,864	1	87	—	88
Stock-based compensation	—	—	—	—	8,454	—	8,454
Issuance of restricted common stock	—	—	907,032	1	(1)	—	—
Repurchase of common stock	—	—	(394,267)	(1)	(2,058)	—	(2,059)
Issuance of common stock, net of commissions and expenses of $2.7 million	—	—	9,708,738	10	47,260	—	47,270
Preferred stock dividends	13,460	18,672	—	—	(18,938)	—	(18,938)
Net loss	—	—	—	—	—	(54,323)	(54,323)
Balance at December 31, 2017	119,644	$143,993	142,658,037	$ 143	$615,493	$ (712,442)	$ (96,806)

ZIOPHARM Oncology, Inc.

STATEMENTS OF CASH FLOWS

(in thousands)

	For the Year Ended December 31,		
	2017	**2016**	**2015**
Cash flows from operating activities:			
Net loss	$ (54,323)	$(165,297)	$(120,088)
Adjustments to reconcile net loss to net cash used in operating activities:			
Depreciation	369	290	357
Stock-based compensation	8,454	8,452	7,997
Common stock issued in exchange for license agreement	—	—	67,285
Preferred stock issued in exchange for 2016 ECP amendment	—	118,936	—
Change in fair value of derivative liabilities	1,295	124	
Issuance of common stock in a license agreement	—	87	—
Change in operating assets and liabilities:			
(Increase) decrease in:			
Receivables	2	425	(301)
Prepaid expenses and other current assets	3,992	(12,452)	(10,214)
Other noncurrent assets	(12,991)	—	(3)
Increase (decrease) in:			
Accounts payable	4,261	(1,852)	4
Accrued expenses	800	203	1,724
Deferred revenue	(6,389)	(6,861)	53,418
Deferred rent	(139)	(380)	(189)
Net cash used in operating activities	(54,669)	(58,325)	(10)
Cash flows from investing activities:			
Purchases of property and equipment	(737)	(551)	(412)
Net cash used in investing activities	(737)	(551)	(412)
Cash flows from financing activities:			
Proceeds from exercise of stock options	88	714	4,568
Issuance of restricted common stock	(2,059)	(1,500)	(518)
Repurchase of common stock	—	(2)	(34)
Proceeds from issuance of common stock, net	47,270	—	94,320
Net cash provided by (used in) financing activities	45,299	(788)	98,336
Net decrease in cash and cash equivalents	(10,107)	(59,664)	97,914
Cash and cash equivalents, beginning of period	81,053	140,717	42,803
Cash and cash equivalents, end of period	$ 70,946	$ 81,053	$ 140,717
Supplementary disclosure of cash flow information:			
Cash paid for interest	$ —	$ —	$ —
Cash paid for income taxes	$ —	$ —	$ —
Supplementary disclosure of noncash investing and financing activities:			
Issuance of common stock in license agreement	$ —	$ —	$ 67,285
Series 1 preferred stock issued as consideration for a license agreement	$ —	$ 119,045	$ —
Payment of Series 1 preferred stock dividends in preferred stock	$ 18,938	$ 7,123	$ —

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

ZIOPHARM Oncology, Inc.

NOTES TO FINANCIAL STATEMENTS

1. Organization and Going Concern

ZIOPHARM Oncology, Inc., which is referred to herein as "ZIOPHARM," the "Company," or "we", is a biopharmaceutical company seeking to develop, acquire, and commercialize, on its own or with partners, a diverse portfolio of immuno-oncology therapies.

The Company's operations to date have consisted primarily of raising capital and conducting research and development. The Company's fiscal year ends on December 31.

The Company has operated at a loss since its inception in 2003 and has minimal revenues. The Company anticipates that losses will continue for the foreseeable future. At December 31, 2017, the Company's accumulated deficit was approximately $712.4 million. Given its current development plans, the Company anticipates cash resources will be sufficient to fund operations into the fourth quarter of 2018. The Company's ability to continue operations after its current cash resources are exhausted depends on its ability to obtain additional financing or to achieve profitable operations, as to which no assurances can be given. Cash requirements may vary materially from those now planned because of changes in the Company's focus and direction of its research and development programs, competitive and technical advances, patent developments, regulatory changes or other developments. Additional financing will be required to continue operations after the Company exhausts its current cash resources and to continue its long-term plans for clinical trials and new product development (Note 3).

As of December 31, 2017, the Company had approximately $70.9 million of cash and cash equivalents. Given its development plans, the Company anticipates cash resources will be sufficient to fund its operations into the fourth quarter of 2018 and the Company has no committed sources of additional capital. The forecast of cash resources is forward-looking information that involves risks and uncertainties, and the actual amount of the Company's expenses could vary materially and adversely as a result of a number of factors. The Company has based its estimates on assumptions that may prove to be wrong, and the Company's expenses could prove to be significantly higher than currently anticipated. Management does not know whether additional financing will be on terms favorable or acceptable to the Company when needed, if at all. If adequate additional funds are not available when required, or if the Company is unsuccessful in entering into partnership agreements for further development of its products, management may need to curtail development efforts. Based on the forecast, management determined that there is substantial doubt regarding our ability to continue as a going concern.

2. Financings

On February 3, 2015, the Company entered into an underwriting agreement with J.P. Morgan Securities LLC, as representative of the several underwriters named therein, relating to the issuance and sale of 10,000,000 shares of its common stock. The price to the public in the offering was $8.75 per share, and the underwriters agreed to purchase the shares from the Company pursuant to the underwriting agreement at a purchase price of $8.225 per share. Under the terms of the underwriting agreement, the Company also granted the underwriters an option, exercisable for 30 days, to purchase up to an additional 1,500,000 shares of common stock at a purchase price of $8.225 per share. The offering was made pursuant to the Company's registration statement on Form S-3 (SEC File No. 333-201826) previously filed with the SEC, and a prospectus supplement thereunder. The underwriters purchased the 10,000,000 shares and the additional 1,500,000 shares on February 9 and February 17, 2015, respectively. The net proceeds from the offering were approximately $94.3 million after deducting underwriting discounts and estimated offering expenses paid by the Company.

On May 11, 2017, the Company sold in an underwritten offering an aggregate of 9,708,738 shares of its common stock to a single investor. The price to the investor in the offering was $5.15 per share, and the underwriters

ZIOPHARM Oncology, Inc.

NOTES TO FINANCIAL STATEMENTS

2. Financings (Continued)

agreed to purchase the shares from the Company pursuant to the underwriting agreement at a purchase price of $4.893 per share. The offering was made pursuant to the Company's registration statement on Form S-3ASR (File No. 333-201826) previously filed with the SEC, and a prospectus supplement thereunder. The net proceeds from the offering were approximately $47.3 million after deducting underwriting commissions and estimated offering expenses payable by the Company.

3. Summary of Significant Accounting Policies

Basis of Presentation

The accompanying financial statements have been prepared in accordance with accounting principles generally accepted in the United States of America or U.S. GAAP.

Use of Estimates

The preparation of financial statements in conformity with accounting principles generally accepted in the United States of America requires management to make estimates and assumptions that affect the reported amounts of assets and liabilities and the disclosure of contingent assets and liabilities at the date of the financial statements and the reported amounts of revenues and expenses during the reporting period. Although the Company regularly assesses these estimates, actual results could differ from those estimates. Changes in estimates are recorded in the period in which they become known.

The Company's most significant estimates and judgments used in the preparation of our financial statements are:

- Clinical trial expenses;
- Collaboration agreements;
- Fair value measurements of stock-based compensation and Series 1 preferred stock (and related dividends); and
- Income taxes.

Subsequent Events

The Company evaluated all events and transactions that occurred after the balance sheet date through the date of this filing. During this period, the Company did not have any material subsequent events that impacted its financial statements or disclosures.

Cash and Cash Equivalents

Cash equivalents consist primarily of demand deposit accounts and deposits in short-term U.S. treasury money market mutual funds. Cash equivalents are stated at cost, which approximates fair market value.

Concentrations of Credit Risk

Financial instruments which potentially subject the Company to concentrations of credit risk consist principally of cash and cash equivalents. The Company maintains cash accounts in commercial banks, which may, at times, exceed federally insured limits. The Company has not experienced any losses in such accounts. The Company believes it is not exposed to any significant credit risk on cash and cash equivalents.

ZIOPHARM Oncology, Inc.

NOTES TO FINANCIAL STATEMENTS

3. Summary of Significant Accounting Policies (Continued)

Property and Equipment

Property and equipment are recorded at cost. Expenditures for maintenance and repairs are charged to expense while the costs of significant improvements are capitalized. Depreciation is provided using the straight-line method over the following estimated useful lives of the related assets, which is between three and five years. Upon retirement or sale, the cost of the assets disposed of and the related accumulated depreciation are eliminated from the balance sheets and related gains or losses are reflected in the statements of operations.

Restricted Cash

Restricted cash consists of $388 thousand, which is restricted as collateral for the Company's facility leases and included in current assets, and $104 thousand, which is restricted as collateral for a line of credit and is included in other assets.

Long-Lived Assets

The Company reviews the carrying values of its long-lived assets for possible impairment whenever events or changes in circumstances indicate that the carrying amounts of the assets may not be recoverable. Any long-lived assets held for disposal are reported at the lower of their carrying amounts or fair values less costs to sell.

Operating Segments

Operating segments are identified as components of an enterprise about which separate discrete financial information is available for evaluation by the chief operating decision maker, the Company's Chief Executive Officer, in making decisions regarding resource allocation and assessing performance. The Company views its operations and manages its business in one operating segment and does not track expenses on a program-by-program basis.

Fair Value Measurements

The Company has certain financial assets and liabilities recorded at fair value which have been classified as Level 1, 2 or 3 within the fair value hierarchy as described in the accounting standards for fair value measurements.

- Level 1—Quoted prices in active markets for identical assets or liabilities.
- Level 2—Inputs other than Level 1 that are observable, either directly or indirectly, such as quoted prices for similar assets or liabilities; quoted prices in markets that are not active; or other inputs that are observable or can be corroborated by observable market data for substantially the full term of the assets or liabilities.
- Level 3—Unobservable inputs that are supported by little or no market activity and that are significant to the fair value of the assets or liabilities.

ZIOPHARM Oncology, Inc.

NOTES TO FINANCIAL STATEMENTS

3. Summary of Significant Accounting Policies (Continued)

Assets and liabilities measured at fair value on a recurring basis as of December 31, 2017 and 2016 are as follows:

($ in thousands)		Fair Value Measurements at Reporting Date Using		
Description	Balance as of December 31, 2017	Quoted Prices in Active Markets for Identical Assets/Liabilities (Level 1)	Significant Other Observable Inputs (Level 2)	Significant Unobservable Inputs (Level 3)
Cash equivalents	$ 66,156	$ 66,156	$ —	$ —
Derivative liabilities	$ (2,424)	$ —	$ —	$ (2,424)

($ in thousands)		Fair Value Measurements at Reporting Date Using		
Description	Balance as of December 31, 2016	Quoted Prices in Active Markets for Identical Assets/Liabilities (Level 1)	Significant Other Observable Inputs (Level 2)	Significant Unobservable Inputs (Level 3)
Cash equivalents	$ 77,120	$ 77,120	$ —	$ —
Derivative liabilities	$ (862)	$ —	$ —	$ (862)

The cash equivalents represent deposits in a short term United States treasury money market mutual fund quoted in an active market and classified as a Level 1 asset.

As discussed further in Notes 7 and 9, the Company issued Intrexon 100,000 shares of the Company's Series 1 preferred stock, a new class of preferred stock authorized by the Company's board of directors, in consideration of the parties entering into a Third Amendment to Exclusive Channel Partner Agreement, or the 2016 ECP Amendment, amending their existing Exclusive Channel Partner Agreement, effective January 6, 2011 and as amended to date, which the Company refers to as the Channel Agreement, and an Amendment to Exclusive Channel Collaboration Agreement, or the 2016 GvHD Amendment, amending their existing Exclusive Channel Collaboration Agreement, effective September 28, 2015, which the Company refers to as the GvHD Agreement.

At June 30, 2016, the Company's Series 1 preferred stock was valued using a probability-weighted approach and a Monte Carlo simulation model. Additionally, the monthly dividends issued on the outstanding Series 1 preferred stock are valued using the same probability-weighted approach and a Monte Carlo simulation model. However, there is no adjustment or further revaluation after the initial valuation on the Series 1 preferred stock.

The Company's Level 3 financial liabilities consist of a conversion option and a redemption feature associated with the Company's Series 1 preferred stock issued to Intrexon that has been bifurcated from the Series 1 preferred stock and are accounted for as derivative liabilities at fair value. The preferred stock derivative liabilities were valued using a probability-weighted approach and a Monte Carlo simulation model. The fair value of the embedded derivatives was estimated using the "with" and "without" method where the preferred stock was first valued with all of its features ("with" scenario) and then without derivatives subject to the valuation analysis ("without" scenario). The fair value of the derivatives was then estimated as the difference between the fair value of the preferred stock in the "with" scenario and the preferred stock in the "without" scenario. See Note 7 for additional disclosures on the 2016 ECP Amendment and 2016 GvHD Amendment and Note 9 for additional disclosure on the rights and preferences of the Series 1 preferred stock and valuation methodology.

ZIOPHARM Oncology, Inc.

NOTES TO FINANCIAL STATEMENTS

3. Summary of Significant Accounting Policies (Continued)

Revenue Recognition from Collaboration Agreements

The Company has primarily generated revenue through collaboration arrangements with strategic partners for the development and commercialization of product candidates. The Company recognizes revenue for each unit of accounting when evidence of an arrangement exists, delivery has occurred or services have been rendered, the seller's price to the buyer is fixed or determinable and collectability is reasonably assured.

The Company's collaboration agreements may provide for various types of payments, including upfront payments, funding of research and development, milestone payments, licensing fees and product royalties. The specifics of the Company's significant agreements are detailed in Note 7.

The Company considers a variety of factors in determining the appropriate method of accounting for its collaboration agreements, including whether multiple deliverables can be separated and accounted for individually as separate units of accounting. Pursuant to the guidance in FASB Accounting Standards Codification (ASC) 605-25, *Multiple-Element Arrangements* (ASC 605-25), the Company evaluates multiple-element arrangements to determine whether the individual deliverables represent separate units of accounting or whether they must be accounted for as a combined unit of accounting. This evaluation involves subjective determinations and requires management to make judgments about the individual deliverables and whether such deliverables are separable from the other aspects of the contractual relationship. Deliverables are considered separate units of accounting provided that: (i) the delivered item(s) has value to the customer on a standalone basis and (ii) if the arrangement includes a general right of return relative to the delivered item(s), delivery or performance of the undelivered item(s) is considered probable and substantially in the control of the Company. In assessing whether an item has standalone value, the Company considers factors such as the research, manufacturing and commercialization capabilities of the collaboration partner and the availability of the associated expertise in the general marketplace. In addition, the Company considers whether the collaboration partner can use the other deliverable(s) for their intended purpose without the receipt of the remaining element(s), whether the value of the deliverable is dependent on the undelivered item(s) and whether there are other vendors that can provide the undelivered element(s). The Company's collaboration arrangements do not contain a general right of return relative to the delivered item(s).

Where there are multiple deliverables within a collaboration agreement that cannot be separated and therefore are combined into a single unit of accounting, revenues are deferred and recognized over the estimated period of performance, which is typically the development term. If the deliverables can be separated, the Company applies the relevant revenue recognition guidance to each individual unit of accounting. The specific methodology for the recognition of the underlying revenue is determined on a case-by-case basis according to the facts and circumstances applicable to each agreement. Generally, the Company has accounted for its collaboration agreements as a single unit of accounting.

At the inception of an arrangement that includes milestone payments, the Company evaluates whether each milestone is substantive and at risk to both parties on the basis of the contingent nature of the milestone. This evaluation includes an assessment of whether: (i) the consideration is commensurate with either the Company's performance to achieve the milestone or the enhancement of the value of the delivered item(s) as a result of a specific outcome resulting from the Company's performance to achieve the milestone, (ii) the consideration relates solely to past performance and (iii) the consideration is reasonable relative to all of the deliverables and payment terms within the arrangement. The Company evaluates factors such as the scientific, clinical, regulatory, commercial and other risks that must be overcome to achieve the respective milestone and the level of effort and investment required to achieve the respective milestone in making this assessment. There is considerable

ZIOPHARM Oncology, Inc.

NOTES TO FINANCIAL STATEMENTS

3. Summary of Significant Accounting Policies (Continued)

judgement involved in determining whether a milestone satisfies all of the criteria required to conclude that a milestone is substantive. In accordance with FASB ASC 605-28, *Milestone Method* (ASC 605-28), revenue from substantive milestone payments is recognized in its entirety in the period in which the milestone is achieved, assuming all other revenue recognition criteria are met. Payments from milestones that are not considered substantive payment is deferred and recognized as revenue over the estimated remaining period of performance under the contract as the Company completes its performance obligations assuming all other revenue recognition criteria are met. Revenue from commercial milestone payments is accounted for as royalties and recorded as revenue upon achievement of the milestone, assuming all other revenue recognition criteria are met. Royalties are recognized as earned in accordance with the terms of various research and collaboration agreements.

Research and Development Costs

Research and development expenditures are charged to the statement of operations as incurred. Such costs include proprietary research and development activities, purchased research and development, and expenses associated with research and development contracts, whether performed by the Company or contracted with independent third parties.

Income Taxes

Income taxes are accounted for under the liability method. Deferred tax assets and liabilities are recognized for the estimated future tax consequences of temporary differences between the financial statement carrying amounts and their respective tax bases. Deferred tax assets and liabilities are measured using enacted tax rates expected to apply to taxable income in the year in which the temporary differences are expected to be recovered or settled. The Company evaluates the realizability of its deferred tax assets and establishes a valuation allowance when it is more likely than not that all or a portion of deferred tax assets will not be realized.

The Company accounts for uncertain tax positions using a “more-likely-than-not” threshold for recognizing and resolving uncertain tax positions. The evaluation of uncertain tax positions is based on factors including, but not limited to, changes in tax law, the measurement of tax positions taken or expected to be taken in tax returns, the effective settlement of matters subject to audit, new audit activity and changes in facts or circumstances related to a tax position. The Company evaluates this tax position on an annual basis. The Company also accrues for potential interest and penalties, related to unrecognized tax benefits in income tax expense (see Note 8).

Accounting for Stock-Based Compensation

Stock-based compensation cost is measured at the grant date, based on the estimated fair value of the award, and is recognized as expense over the employee’s requisite service period. Stock-based compensation expense is based on the number of awards ultimately expected to vest and is therefore reduced for an estimate of the awards that are expected to be forfeited prior to vesting. Consistent with prior years, the Company uses the Black-Scholes option pricing model which requires estimates of the expected term option holders will retain their options before exercising them and the estimated volatility of the Company’s common stock price over the expected term.

The Company recognizes the full impact of its share-based employee payment plans in the statements of operations for each of the years ended December 31, 2017, 2016, and 2015 and did not capitalize any such costs on the balance sheets. The Company recognized $2.5 million, $3.0 million, and $5.3 million of compensation

ZIOPHARM Oncology, Inc.

NOTES TO FINANCIAL STATEMENTS

3. Summary of Significant Accounting Policies (Continued)

expense related to vesting of stock options during the years ended December 31, 2017, 2016, and 2015, respectively. In the years ended December 31, 2017, 2016, and 2015, the Company recognized $6.0 million, $5.5 million, and $2.7 million of compensation expense, respectively, related to vesting of restricted stock (see Note 11). The total compensation expense relating to vesting of stock options and restricted stock awards for the years ended December 31, 2017, 2016, and 2015 was $8.5 million, $8.5 million, and $8.0 million, respectively. The following table presents share-based compensation expense included in the Company's Statements of Operations:

	Year ended December 31,		
(in thousands)	2017	2016	2015
Research and development	$2,401	$2,077	$1,403
General and administrative	6,053	6,375	6,594
Share based employee compensation expense before tax	8,454	8,452	7,997
Income tax benefit	—	—	—
Net share based employee compensation expense	$8,454	$8,452	$7,997

The fair value of each stock option is estimated at the date of grant using the Black-Scholes option pricing model. The estimated weighted-average fair value of stock options granted to employees in 2017, 2016, and 2015 was approximately $3.94, $4.43, and $10.47 per share, respectively. Assumptions regarding volatility, expected term, dividend yield and risk-free interest rate are required for the Black-Scholes model. The volatility assumption is based on the Company's historical experience. The risk-free interest rate is based on a U.S. treasury note with a maturity similar to the option award's expected life. The expected life represents the average period of time that options granted are expected to be outstanding. The Company calculated expected term using the simplified method described in SEC Staff Accounting Bulletin, or SAB, No. 107 and No. 110 as it continues to meet the requirements promulgated in SAB No. 110. The assumptions for volatility, expected life, dividend yield and risk-free interest rate are presented in the table below:

	2017	2016	2015
Weighted average risk-free interest rate	1.85 - 2.27%	1.27 - 2.09%	1.46 - 1.93%
Expected life in years	6	6	6
Expected volatility	80.31 - 81.03%	79.15 - 82.95%	79.13 - 86.81%
Expected dividend yield	0	0	0

Net Loss Per Share

Basic net loss per share is computed by dividing net loss by the weighted average number of common shares outstanding for the period. The Company's potentially dilutive shares, which include outstanding common stock options, unvested restricted stock and preferred stock, have not been included in the computation of diluted net loss per share for any of the periods presented as the result would be antidilutive. Such potential common shares at December 31, 2017, 2016, and 2015 consist of the following:

	December 31,		
	2017	2016	2015
Stock options	4,352,135	3,465,335	3,481,468
Unvested restricted stock	1,808,559	1,680,492	1,586,388
Preferred stock	34,134,524	20,465,067	—
	40,295,218	25,610,894	5,067,856

ZIOPHARM Oncology, Inc.

NOTES TO FINANCIAL STATEMENTS

3. Summary of Significant Accounting Policies (Continued)

The Series 1 preferred stock automatically converts into shares of common stock upon the date the first approval in the United States of (i) a ZIOPHARM Product, as defined in and developed under the Exclusive Channel Partner Agreement dated as of January 6, 2011 and as amended from time to time, by and between the Company and Intrexon (now Precigen), or (ii) a Product, as defined in and developed under the Exclusive Channel Collaboration Agreement dated September 28, 2015 and as amended from time to time, by and between the Company and Intrexon (now Precigen), or (iii) a Product as defined in and developed under the License and Collaboration Agreement dated March 27, 2015 and as amended from time to time, by and among Intrexon (now Precigen), ARES TRADING, S.A. and the Company, is publicly announced. Assuming a conversion event date of December 31, 2017, the Series 1 preferred stock would convert into 34,134,524 shares of common stock using the greater of (i) the volume weighted average closing price of the Company's Common Stock as reported by the Nasdaq Stock Market, LLC over previous the 20 trading days ending on the conversion event date or (ii) $1.00 per share. See Note 7 and Note 9 for additional disclosure regarding the 2016 ECP Amendment and 2016 GvHD Amendment, valuation methodology and significant assumptions.

New Accounting Pronouncements

In May 2014, the FASB issued ASU No. 2014-09, *Revenue from Contracts with Customers* ("ASU 2014-09") to provide updated guidance on revenue recognition. ASU 2014-09 requires a company to recognize revenue when it transfers promised goods or services to customers in an amount that reflects the consideration to which the company expects to be entitled in exchange for those goods or services. In doing so, companies may need to use more judgment and make more estimates than under today's guidance. These may include identifying performance obligations in the contract, estimating the amount of variable consideration to include in the transaction price, and allocating the transaction price to each separate performance obligation. In August 2015, the FASB issued ASU 2015-14, *Revenue from Contracts with Customers (Topic 606): Deferral of the Effective Date*, which deferred the effective date of ASU 2014-09 by one year. Accordingly, ASU 2014-09 is effective for public business entities for annual reporting periods beginning after December 15, 2017, including interim reporting periods within each annual reporting period. In March 2016, the FASB issued ASU No. 2016-08, *Revenue from Contracts with Customers (Topic 606): Principal versus Agent Considerations (Reporting Revenue Gross Versus Net)*, which clarifies the implementation guidance on principal versus agent considerations. In April 2016, the FASB issued ASU No. 2016-10, *Revenue from Contracts with Customers (Topic 606): Identifying Performance Obligations and Licensing*, which clarifies certain aspects of identifying performance obligations and licensing implementation guidance. In May 2016, the FASB issued ASU No. 2016-12, *Revenue from Contracts with Customers (Topic 606): Narrow-Scope Improvements and Practical Expedients*, which relates to disclosures of remaining performance obligations, as well as other amendments to guidance on collectability, non-cash consideration, and the presentation of sales and other similar taxes collected from customers. Collectively these amendments are referred to as "ASC 606".

ASC 606 clarifies the principles for recognizing revenue and develops a common revenue standard for U.S. GAAP and International Financial Reporting Standards, or IFRS. This standard removes inconsistencies and weaknesses between U.S. GAAP and IFRS in revenue requirements, provides a more robust framework for addressing revenue issues, improves comparability of revenue recognition practices across entities, industries, jurisdictions, and capital markets, provides more useful information to users of financial statements through improved disclosure requirements, and simplifies the preparation of financial statements by reducing the number of requirements to which an entity must refer. This update is effective for annual periods beginning after December 15, 2017, including interim periods within that reporting period. The Company adopted this standard using the modified retrospective approach on January 1, 2018. The Company has substantially completed our assessment and the implementation resulted in a cumulative effect adjustment to accumulated deficit as of

ZIOPHARM Oncology, Inc.

NOTES TO FINANCIAL STATEMENTS

3. Summary of Significant Accounting Policies (Continued)

January 1, 2018 of approximately $8.1 million and a corresponding increase to the contract liability (formerly deferred revenue). The adjustment is related to the Company's Ares Trading License and Collaboration Agreement (Note 7), which is the Company's sole contract outstanding at January 1, 2018 (Note 3). The Company has a full valuation allowance so there will be no effect on incomes taxes as a result of this adoption.

The Company will recognize collaboration revenue under certain of the Company's license or collaboration agreements that are within the scope of ASC 606. The terms of these agreements may contain multiple performance obligations, which may include licenses and research and development activities. The Company evaluates these agreements under ASC 606 to determine the distinct performance obligations.

Prior to recognizing revenue, the Company makes estimates of the transaction price, including variable consideration that are subject to a constraint. Amounts of variable consideration are included in the transaction price to the extent that it is probable that a significant reversal in the amount of cumulative revenue recognized will not occur and when the uncertainty associated with the variable consideration is subsequently resolved. Variable consideration may include nonrefundable upfront license fees, payments for research and development activities, reimbursement of certain third-party costs, payments based upon the achievement of specified milestones, and royalty payments based on product sales derived from the collaboration.

If there are multiple distinct performance obligations, including material rights, the Company allocates the transaction price to each distinct performance obligation based on its relative standalone selling price. The standalone selling price is generally determined based on the prices charged to customers or using expected cost plus margin. Revenue is recognized by measuring the progress toward complete satisfaction of the performance obligations using an input measure, in accordance with ASC-340-40, *Other Assets and Deferred Costs: Contracts with Customers*.

As it relates to the Ares Trading License and Collaboration Agreement (Note 7), the Company determined that there were three performance obligations; the first performance obligation consists of the license and research development services and the other two performance obligations are material rights as it relates to potential future targets that have not yet been identified. The transaction price of $57.5 million was allocated to the performance obligations based on their relative standalone selling prices.

In February 2016, the FASB issued ASU No. 2016-02, *Leases* (Topic 842), or ASU 2016-02. The guidance in this ASU supersedes the leasing guidance in *Leases* (Topic 840). Under the new guidance, lessees are required to recognize lease assets and lease liabilities on the balance sheet for all leases with terms longer than 12 months. Leases will be classified as either finance leases or operating leases, with classification affecting the pattern of expense recognition in the statement of operations. The new standard is effective for annual reporting periods beginning after December 15, 2018, including interim reporting periods within each annual reporting period. The Company is currently evaluating the impact of the adoption of this ASU on the financial statements.

In March 2016, the FASB issued ASU No. 2016-09, Compensation—Stock Compensation (Topic 718): *Improvements to Employee Share-Based Accounting*, or ASU 2016-09, to require changes to several areas of employee share-based payment accounting in an effort to simplify share-based reporting. ASU 2016-09 is effective for annual reporting periods beginning after December 15, 2016, including interim reporting periods within each annual reporting period. The Company adopted this standard on January 1, 2017. The update revises requirements in the following areas: minimum statutory withholding, accounting for income taxes, and forfeitures. Prior to adoption, the Company recognized share-based compensation, net of estimated forfeitures, over the vesting period of the grant. Upon adoption of ASU 2016-09, the Company elected to change its

ZIOPHARM Oncology, Inc.

NOTES TO FINANCIAL STATEMENTS

3. Summary of Significant Accounting Policies (Continued)

accounting policy to recognize forfeitures as they occur. The new forfeiture policy election was adopted using a modified retrospective approach with a cumulative effect adjustment recorded to retained earnings as of January 1, 2017. The update requires the Company to recognize the income tax effect of awards in the income statement when the awards vest or are settled. It also allows the Company to repurchase more of an employee's shares than it can today for tax withholding purposes without triggering a liability. The income tax related items had no effect on the current period presentation and the Company maintains a full valuation allowance against its deferred tax assets.

In August 2016, the FASB issued ASU No. 2016-15, *Classification of Certain Cash Receipts and Cash Payments*, or ASU 2016-15, to address how certain cash receipts and cash payments are presented and classified in the statement of cash flows in an effort to reduce existing diversity in practice. The update includes eight specific cash flow issues and provides guidance on the appropriate cash flow presentation for each. ASU 2016-15 is effective for annual reporting periods beginning after December 15, 2017, including interim reporting periods within each annual reporting period. The Company is currently evaluating the impact of the adoption of this ASU on the financial statements.

In November 2016, the FASB issued ASU No. 2016-18, *Statement of Cash Flows* (Topic 230): *Restricted Cash*, or ASU 2016-18, to clarify how entities should present restricted cash and restricted cash equivalents in the statement of cash flows. Under this new update, entities are required to show the changes in the total of cash, cash equivalents, restricted cash, and restricted cash equivalents in the statement of cash flows. This guidance will be applied retrospectively and is effective for annual reporting periods beginning after December 15, 2017, including interim reporting periods within each annual reporting period. The Company is currently evaluating the impact of the adoption of this ASU on the financial statements and does not expect there to be a material impact on the financial statements.

In May 2017, the FASB issued ASU No. 2017-09, *Compensation—Stock Compensation* (Topic 718): *Scope of Modification Accounting*, or ASU 2017-09, to clarify when to account for a change to the terms or conditions of a share-based payment award as a modification. Under this new guidance, modification accounting is required if the fair value, vesting conditions, or classification of the award changes as a result of the change in terms or conditions. ASU 2017-09 is effective for annual reporting periods beginning after December 15, 2017, including interim reporting periods within each annual reporting period. The Company does not expect the adoption of this guidance to have a material impact on the financial statements.

4. Property and Equipment, net

Property and equipment, net, consists of the following:

(in thousands)	December 31, 2017	December 31, 2016
Office and computer equipment	$ 1,215	$ 1,162
Software	913	907
Leasehold improvements	1,553	1,158
Research and development equipment	1,161	878
	4,842	4,105
Less: accumulated depreciation	(3,631)	(3,262)
Property and equipment, net	$ 1,211	$ 843

ZIOPHARM Oncology, Inc.

NOTES TO FINANCIAL STATEMENTS

4. Property and Equipment, net (Continued)

Depreciation charged to the statement of operations for the years ended December 31, 2017, 2016, and 2015 was $369 thousand, $290 thousand and $357 thousand, respectively.

5. Accrued Expenses

Accrued expenses consist of the following:

(in thousands)	December 31, 2017	2016
Clinical consulting services	$3,022	$2,342
Preclinical services	2,210	2,693
Employee compensation	1,919	1,446
Payroll taxes and benefits	1,017	646
Manufacturing services	902	1,116
Accrued vacation	361	294
Professional services	256	488
Other consulting services	222	28
Accrued rent	—	56
Total	$9,909	$9,109

6. Related Party Transactions

Collaborations with Intrexon/ Precigen

On January 6, 2011, the Company entered into the Channel Agreement with Intrexon (now Precigen) (Note 7). A director of the Company, Randal J. Kirk, is the chief executive officer, a director, and the largest stockholder of Intrexon.

On February 3, 2015, Intrexon purchased 1,440,000 shares of common stock in the Company's public offering upon the same terms as others that participated in the offering.

On March 27, 2015, the Company and Intrexon (now Precigen) entered into a Second Amendment to the Exclusive Channel Partner Agreement amending the Channel Agreement, which is referred to as the ECP Amendment. The ECP Amendment modified the scope of the parties' collaboration under the Channel Agreement in connection with the Ares Trading Agreement, which the Company and Intrexon (now Precigen) entered into with Ares Trading, on March 27, 2015. The ECP Amendment provided that Intrexon (now Precigen) will pay to the Company 50% of all payments that Precigen receives for upfronts, milestones and royalties under the Ares Trading Agreement (Note 7). The Amendment also reduces Intrexon's aggregate commitment under a Stock Purchase Agreement that the parties executed in connection with the initial Channel Agreement to purchase the Company's common stock from $50.0 million to $43.5 million, which has been satisfied.

On June 29, 2015, the Company re-purchased 3,711 shares of common stock from Intrexon, at a discount of 5% to the closing price of the Company's common stock on the date of purchase, which represented fractional shares that resulted from Intrexon's special stock dividend of the Company's shares to Intrexon's shareholders, for $34 thousand. On January 8, 2016, the Company re-purchased an additional 168 shares of common stock from Intrexon for $2 thousand at the same terms as the previous share purchase.

ZIOPHARM Oncology, Inc.

NOTES TO FINANCIAL STATEMENTS

6. Related Party Transactions (Continued)

On September 28, 2015, the Company entered into the GvHD Agreement with Precigen, whereby the Company was granted the right to use Precigen's technology directed towards *in vivo* expression of biologics to research, develop and commercialize products for use in the treatment or prevention of graft-versus-host disease, or GvHD (Note 7). The Company paid Precigen a technology access fee of $10.0 million in cash in October 2015 and agreed to reimburse Precigen for all research and development costs under the GvHD Agreement.

On June 29, 2016, the Company entered into the 2016 ECP Amendment, with Intrexon (now Precigen), amending the Channel Agreement, and the 2016 GvHD Amendment, amending their existing Exclusive Channel Collaboration Agreement, effective September 28, 2015, which the Company refers to as the GvHD Agreement. The 2016 ECP Amendment reduced the royalty percentage that the Company will pay to Intrexon (now Precigen) under the Channel Agreement on a quarterly basis from 50% to 20% of net profits derived in that quarter from the sale of ZIOPHARM Products (as defined in the Channel Agreement), calculated on a ZIOPHARM Product-by-ZIOPHARM Product basis, subject to certain expense allocations and other offsets provided in the Channel Agreement. The 2016 GvHD Amendment reduced the royalty percentage that the Company would pay to Intrexon (now Precigen) under the GvHD Agreement on a quarterly basis from 50% to 20% of net profits derived in that quarter from the sale of Products (as defined in the GvHD Agreement), subject to certain expense allocations and other offsets provided in the GvHD Agreement. The reductions in the royalty percentages provided by the 2016 ECP Amendment and the 2016 GvHD Amendment do not apply to sublicensing revenue or royalties under the Channel Agreement and GvHD Agreement, nor do they apply to any royalties or other payments made with respect to sublicensing revenue from the Company's existing collaboration with Merck Serono, the biopharmaceutical business of Merck KGaA.

In consideration for the execution and delivery of the 2016 ECP Amendment and the 2016 GvHD Amendment, the Company issued Intrexon 100,000 shares of its Series 1 preferred stock. Each share of the Company's Series 1 preferred stock has a stated value of $1,200, subject to appropriate adjustment in the event of any stock dividend, stock split, combination or other recapitalization, and certain other rights, preferences, privileges and obligations (Note 8). The holders of the shares of Series 1 preferred stock are entitled to receive a monthly dividend, payable in additional shares of Series 1 preferred stock, equal to $12.00 per preferred share held by such holder per month divided by the stated value of the preferred shares, rounded down to the nearest whole share.

During the year ended December 31, 2017, the Company issued an aggregate of 13,460 shares of Series 1 preferred stock to Intrexon, the holder of all of the outstanding shares of the Company's Series 1 preferred stock, as monthly dividend payments. The Company recorded such shares of Series 1 preferred stock at a fair value of $18.9 million, which is a component of temporary equity and recorded a loss on the change of the derivative liabilities in the amount of $1.3 million. See Notes 4 and 8 for additional discussion regarding the accounting for and valuation of these derivative financial instruments.

During the years ended December 31, 2017, 2016, and 2015, the Company expensed $21.4 million, $22.2 million, and $16.3 million, respectively, for services performed by Intrexon. As of December 31, 2017 and 2016, the Company recorded $6.8 million and $3.4 million, respectively, in current liabilities on its balance sheet for amounts due to Intrexon.

Collaboration with Precigen and MD Anderson

On January 13, 2015, the Company, together with Intrexon (now Precigen), entered into a license agreement with MD Anderson, which is referred to as the MD Anderson License. Pursuant to the MD Anderson License, the

ZIOPHARM Oncology, Inc.

NOTES TO FINANCIAL STATEMENTS

6. Related Party Transactions (Continued)

Company and Precigen hold an exclusive, worldwide license to certain technologies owned and licensed by MD Anderson, including technologies relating to novel CAR+ T-cell therapies arising from the laboratory of Laurence Cooper, M.D., Ph.D., who is now the Company's Chief Executive Officer and was formerly a professor of pediatrics at MD Anderson and now currently a visiting scientist under that institution's policies, as well as either co-exclusive or non-exclusive licenses under certain related technologies. In partial consideration for entering into the MD Anderson License, the Company issued MD Anderson an aggregate of 11,722,163 shares of common stock for which the Company incurred a $67.3 million charge recorded in 2015. The Company has determined that the rights acquired in the MD Anderson License represent in-process research and development with no alternative future use. During the year ending December 31, 2017, the Company made four quarterly payments totaling $13.0 million, bringing the total aggregate payments to $39.2 million under this arrangement. Subsequent to the balance sheet date, the Company made the final payment of $2.7 million bringing our total prepayment to $34.6 million for programs to be conducted at MD Anderson.

7. Commitments and Contingencies

Operating Leases

Prior to December 31, 2012, the Company entered into an operating lease in New York, NY for office space. In accordance with this agreement, the Company entered into a letter of credit in the amount of $388 thousand, naming the Company's landlord as beneficiary. In January 2012, the Company amended the lease agreement, adding additional office space. The collateral for the letter of credit is restricted cash and recorded in other current assets on the balance sheet as of December 31, 2017. The collateral for the letter of credit was recorded in other current assets on the balance sheet as of December 31, 2016. The lease for office space in New York, NY expires in October 2018.

On October 17, 2013, the Company entered into a sublease agreement to lease all of its New York office space to a subtenant. The Company remains primarily liable to pay rent on the original lease. The Company recorded a loss on the sublease in the amount of $729 thousand for the year ended December 31, 2013, representing the remaining contractual obligation of $2.3 million, less $1.6 million in payments from its subtenant. The Company continues to maintain the $388 thousand letter of credit in respect of the New York office space and recorded in other current assets on the balance sheets.

Prior to December 31, 2012, the Company entered into separate operating lease agreements for various spaces in a building in Boston, MA. In June 2012, the Company re-negotiated a master lease for the Company's Boston office space to incorporate all three lease agreements under the same master agreement, which was originally set to expire in August 2016. On December 21, 2015 and April 15, 2016, the Company renewed the sublease for the Company's corporate headquarters in Boston, MA through August 31, 2021. As of December 31, 2017, and 2016, a total security deposit of $128 thousand is included in deposits on the balance sheet.

On January 30, 2018, the Company entered into a lease agreement for office space in Houston, TX at MD Anderson. Under the terms of the Houston lease agreement, we lease approximately two hundred and ten square feet and are required to make rental payments at an average monthly rate of approximately $1 thousand through April 2021. Upon signing the lease agreement, the company expensed approximately $40 thousand for rent expense for the period beginning in May 2015 through December 2017. The $40 thousand for rent expense incurred from May 2015 through December 2017, and all future rent expense incurred in Houston, will be deducted from our prepayment at MD Anderson described in the license agreement section below.

ZIOPHARM Oncology, Inc.

NOTES TO FINANCIAL STATEMENTS

7. Commitments and Contingencies (Continued)

Future net minimum lease payments under operating leases as of December 31, 2017 are as follows (in thousands):

2018	1,129
2019	723
2020	736
2021	489
2022 and beyond	—
	3,077
Less: contractual sublease income	(278)
Future minimum lease payments, net	$2,799

Total rent expense was approximately $0.7 million, $0.3 million, and $1.0 million for the years ended December 31, 2017, 2016, and 2015, respectively.

The Company records rent expense on a straight-line basis over the term of the lease. Accordingly, the Company has recorded a liability for deferred rent at December 31, 2017 and 2016 of $145 thousand ($141 thousand current and $1 thousand long-term) and $281 thousand ($155 thousand current and $126 thousand long-term) respectively, which is recorded in deferred rent on the balance sheet.

License Agreements

Exclusive Channel Partner Agreement with Precigen for the Cancer Programs

On January 6, 2011, the Company entered into the Channel Agreement with Intrexon (now Precigen), that governs a “channel partnering” arrangement in which the Company uses Precigen’s technology to research, develop and commercialize products in which DNA is administered to humans for expression of anti-cancer effectors for treatment or prophylaxis of cancer, which the Company collectively refers to as the Cancer Program. This Channel Agreement establishes committees comprising representatives of us and Precigen that govern activities related to the Cancer Program in the areas of project establishment, chemistry, manufacturing and controls, clinical and regulatory matters, commercialization efforts and intellectual property.

The Channel Agreement grants us a worldwide license to use patents and other intellectual property of Precigen in connection with the research, development, use, importing, manufacture, sale, and offer for sale of products involving DNA administered to humans for expression of anti-cancer effectors for the purpose of treatment or prophylaxis of cancer, which are collectively referred to as the Ziopharm Products. Such license is exclusive with respect to any clinical development, selling, offering for sale or other commercialization of Ziopharm Products, and otherwise is non-exclusive. Subject to limited exceptions, the Company may not sublicense these rights without Precigen’s written consent.

Under the Channel Agreement, and subject to certain exceptions, the Company is responsible for, among other things, the performance of the Cancer Program, including the development, commercialization and certain aspects of manufacturing of Ziopharm Products. Precigen is responsible for establishing manufacturing capabilities and facilities for the bulk manufacture of products developed under the Cancer Program, certain other aspects of manufacturing and costs of discovery-stage research with respect to platform improvements and costs of filing, prosecution and maintenance of Precigen’s patents.

ZIOPHARM Oncology, Inc.

NOTES TO FINANCIAL STATEMENTS

7. Commitments and Contingencies (Continued)

After the 2016 Exclusive Channel Partner (ECP) Amendment, discussed below, and subject to certain expense allocations and other offsets provided in the Channel Agreement, the Company is obligated to pay Precigen on a quarterly basis 20% of net profits derived in that quarter from the sale of Ziopharm Products, calculated on a Ziopharm Product-by- Ziopharm Product basis. The Company likewise agreed to pay Precigen on a quarterly basis 50% of revenue obtained in that quarter from a sublicensor in the event of a sublicensing arrangement. In addition, in partial consideration for each party's execution and delivery of the Channel Agreement, the Company entered into a stock purchase agreement with Precigen.

Upon termination of the Channel Agreement, the Company may continue to develop and commercialize any Ziopharm Product that, at the time of termination:

- Is being commercialized by us;
- Has received regulatory approval;
- Is a subject of an application for regulatory approval that is pending before the applicable regulatory authority; or
- Is the subject of at least an ongoing Phase 2 clinical trial (in the case of a termination by Precigen due to an uncured breach or a voluntary termination by us), or an ongoing Phase 1 clinical trial in the field (in the case of a termination by us due to an uncured breach or a termination by Precigen following an unconsented assignment by us or its election not to pursue development of a Superior Therapy (as defined in the Channel Agreement)).

With respect to these "retained" Ziopharm Products, the Company's obligation to pay 20% of net profits derived from the sale of Ziopharm Products and 50% of revenue derived from a sublicensor will survive termination of the Channel Agreement.

Amendment of Collaborations with Precigen

On March 27, 2015, the Company, together with Intrexon, now Precigen, entered into an ECP Amendment, amending the Channel Agreement. The ECP Amendment modifies the scope of the parties' collaboration under the Channel Agreement in connection with the Ares Trading Agreement discussed below. Pursuant to the ECP Amendment, the chimeric antigen receptor T-cell products to be developed and commercialized pursuant to the Ares Trading Agreement shall be included within the Precigen/ Ziopharm collaboration under the Channel Agreement. The ECP Amendment provides that Precigen will pay us fifty percent of all payments Precigen receives for upfronts, milestones and royalties under the Ares Trading Agreement.

On June 29, 2016, the Company entered into (1) the 2016 ECP Amendment with Intrexon (now Precigen), amending the Channel Agreement, and (2) the 2016 GvHD Amendment, amending the Exclusive Channel Collaboration Agreement the Company entered into with Intrexon (now Precigen) in September 2015, or the GvHD Agreement. The 2016 ECP Amendment reduced the royalty percentage that the Company will pay to Precigen under the Channel Agreement on a quarterly basis from 50% to 20% of net profits derived in that quarter from the sale of Ziopharm Products, calculated on a Ziopharm Product-by- Ziopharm Product basis, subject to certain expense allocations and other offsets provided in the Channel Agreement. The 2016 GvHD Amendment reduced the royalty percentage that the Company would pay to Precigen under the GvHD Agreement on a quarterly basis from 50% to 20% of net profits derived in that quarter from the sale of Products (as defined in the GvHD Agreement), subject to certain expense allocations and other offsets provided in the GvHD Agreement. The reductions in the royalty percentages provided by the 2016 ECP Amendment and the

ZIOPHARM Oncology, Inc.

NOTES TO FINANCIAL STATEMENTS

7. Commitments and Contingencies (Continued)

2016 GvHD Amendment do not apply to sublicensing revenue or royalties under the Channel Agreement and GvHD Agreement, nor do they apply to any royalties or other payments made with respect to sublicensing revenue from the existing collaboration with Ares Trading S.A., or Ares Trading, a subsidiary of the biopharmaceutical business of Merck KGaA. The Company has recently announced the decision to stop pursuing the development of engineered cell therapy strategies for targeted treatment of GvHD. The Company has reverted the rights under the GvHD Agreement back to Precigen [and are in the process of winding down the related activities].

In consideration for the execution and delivery of the 2016 ECP Amendment and the 2016 GvHD Amendment, the Company agreed to issue to Intrexon 100,000 shares of its Series 1 preferred stock. Each share of Series 1 preferred stock has a stated value of $1,200, subject to appropriate adjustment in the event of any stock dividend, stock split, combination or other recapitalization, and certain other rights, preferences, privileges and obligations (see Note 9 to the accompanying financial statements).

Exclusive Channel Collaboration Agreement with Precigen for GvHD

On September 28, 2015, the Company entered into the GvHD Agreement with Intrexon (now Precigen), whereby the Company would use Precigen's technology directed towards *in vivo* expression of effectors to research, develop and commercialize products for use in the treatment or prevention of GvHD. The GvHD Agreement granted us a worldwide license to use specified patents and other intellectual property of Precigen in connection with the research, development, use, importing, manufacture, sale, and offer for sale of products developed under the GvHD Agreement.

The Company paid Intrexon a technology access fee of $10.0 million in cash in October 2015 and agreed to reimburse Intrexon for all related research and development costs pursuant to the GvHD Agreement. The Company has determined that the rights acquired in the GvHD Agreement represent in-process research and development with no alternative future use. Accordingly, the Company recorded a charge of $10.0 million to research and development expense in September 2015.

As a result of an in-depth review of the Company's research and development portfolio, the determination was made that the pursuit of GvHD as an indication was not a material part of its corporate strategy and therefore have decided to stop pursuing the development of engineered cell therapy strategies, used either separately or in combination, for targeted treatment of GvHD. The Company has reverted the rights under the GvHD program back to Precigen [and are in the process of winding down the related activities]. The Company made this decision to focus its efforts and resources on the development of the Controlled IL-12 and Sleeping Beauty platforms for the treatment of oncology indications.

License Agreement—The University of Texas MD Anderson Cancer Center

On January 13, 2015, the Company, together with Intrexon (now Precigen), entered into a License Agreement, or the MD Anderson License, with The University of Texas MD Anderson Cancer Center, or MD Anderson. Pursuant to the MD Anderson License, the Company, together with Precigen, hold an exclusive, worldwide license to certain technologies owned and licensed by MD Anderson including technologies relating to novel chimeric antigen receptor, or CAR, T-cell therapies, non-viral gene transfer systems, genetic modification and/or propagation of immune cells and other cellular therapy approaches, Natural Killer, or NK Cells, and T-cell receptors, or TCRs, arising from the laboratory of Laurence Cooper, M.D., Ph.D., who became the Company's Chief Executive Officer in May 2015 and was formerly a tenured professor of pediatrics at MD Anderson and is

ZIOPHARM Oncology, Inc.

NOTES TO FINANCIAL STATEMENTS

7. Commitments and Contingencies (Continued)

now currently a visiting scientist under that institution's policies, as well as either co-exclusive or non-exclusive licenses under certain related technologies.

Pursuant to the terms of the MD Anderson License, MD Anderson received consideration consisting of $50.0 million in shares of common stock (or 10,124,561 shares), and $50.0 million in shares of Intrexon's common stock, in each case based on a trailing 20 day volume weighted average of the closing price the Company's and Intrexon's common stock ending on the date prior to the announcement of the entry into the MD Anderson License, collectively referred to as the License Shares, pursuant to the terms of the License Shares Securities Issuance Agreement described below. The License Shares were issued to MD Anderson on March 11, 2015, pursuant to the terms of the MD Anderson License.

On January 9, 2015, in order to induce MD Anderson to enter into the MD Anderson License on an accelerated schedule, the Company, together with Intrexon entered into a letter agreement, or the Letter Agreement, pursuant to which MD Anderson received consideration of $7.5 million in shares of common stock (or 1,597,602 shares), and $7.5 million in shares of Intrexon's common stock, in each case based on a trailing 20-day volume-weighted average of the closing price of the Company's and Intrexon's common stock ending on the date prior to the execution of the Letter Agreement, collectively referred to as the Incentive Shares, in the event that the MD Anderson License was entered into on January 14, 2015. The Incentive Shares were issued to MD Anderson on March 11, 2015, pursuant to the terms of the Incentive Shares Securities Issuance Agreement described below.

On August 17, 2015, the Company, Intrexon (now Precigen) and MD Anderson entered into a research and development agreement, or the Research and Development Agreement, to formalize the scope and process for the transfer by MD Anderson, pursuant to the terms of the MD Anderson License, of certain existing research programs and related technology rights, as well as the terms and conditions for future collaborative research and development of new and ongoing research programs.

Pursuant to the Research and Development Agreement, the Company, Intrexon (now Precigen) and MD Anderson have agreed to form a joint steering committee that will oversee and manage the new and ongoing research programs. As provided under the MD Anderson License, the Company provided funding for research and development activities in support of the research programs under the Research and Development Agreement for a period of three years and in an amount of no less than $15.0 million and no greater than $20.0 million per year. During the twelve months ended December 31, 2017, the Company made payments in the aggregate amount of $13.0 million to MD Anderson compared to $15.0 million during the twelve months ended December 31, 2016. The decrease in cash paid to MD Anderson during 2017 is a result of approved expenditures incurred by us being deducted from the April, July, and October quarterly payments. As of December 31, 2017, MD Anderson had used $7.3 million to offset costs incurred pursuant to the MD Anderson License and the Research and Development Agreement. The net balance of cash resources on hand at MD Anderson is $31.9 million, of which $18.5 million is included in other current assets and the remaining $13.4 million is included in non-current assets at December 31, 2017. Subsequent to the balance sheet date, the final payment to MD Anderson was made in January 2018 for $2.7 million.

The term of the MD Anderson License expires on the last to occur of (a) the expiration of all patents licensed thereunder, or (b) the twentieth anniversary of the date of the MD Anderson License; provided, however, that following the expiration of the term of the MD Anderson License, the Company, together with Precigen, shall then have a fully-paid up, royalty free, perpetual, irrevocable and sublicensable license to use the licensed intellectual property thereunder. After ten years from the date of the MD Anderson License and subject to a 90-day cure period, MD Anderson will have the right to convert the MD Anderson License into a non-exclusive

ZIOPHARM Oncology, Inc.

NOTES TO FINANCIAL STATEMENTS

7. Commitments and Contingencies (Continued)

license if the Company and Precigen are not using commercially reasonable efforts to commercialize the licensed intellectual property on a case-by-case basis. After five years from the date of the MD Anderson License and subject to a 180-day cure period, MD Anderson will have the right to terminate the MD Anderson License with respect to specific technology(ies) funded by the government or subject to a third-party contract if the Company and Precigen are not meeting the diligence requirements in such funding agreement or contract, as applicable. MD Anderson may also terminate the agreement with written notice upon material breach by us and Precigen, if such breach has not been cured within 60 days of receiving such notice. In addition, the MD Anderson License will terminate upon the occurrence of certain insolvency events for both us and Precigen and may be terminated by the mutual written agreement of us, Precigen and MD Anderson.

In connection with the MD Anderson License and the issuance of the License Shares and the Incentive Shares, on January 13, 2015, the Company, together with MD Anderson, entered into a Registration Rights Agreement, or the Registration Rights Agreement, pursuant to which the Company agreed to file a “resale” registration statement, or the Registration Statement, registering the resale of the License Shares, the Incentive Shares and any other shares of the common stock held by MD Anderson on the date that the Registration Statement is filed. Under the terms of the Registration Rights Agreement, the Company is obligated to maintain the effectiveness of the Registration Statement until all securities therein are sold or are otherwise can be sold pursuant to Rule 144, without any restrictions. A prospectus supplement under the Company’s already effective registration statement on Form S-3 (File No. 333-201826) was filed on April 1, 2015 in satisfaction of its obligations under the Registration Rights Agreement.

The Company determined that the rights acquired in the MD Anderson License represented in process research and development with no alternative future use. Accordingly, the Company recorded a charge of $67.3 million to research and development expense in 2015, representing the fair value of the 11,722,163 shares of its common stock on the date the MD Anderson License was executed.

Ares Trading License and Collaboration Agreement

On March 27, 2015, the Company, together with Intrexon (now Precigen), signed a worldwide License and Collaboration Agreement, or the Ares Trading Agreement, with Ares Trading S.A., or Ares Trading, a subsidiary of the biopharmaceutical business of Merck KGaA, Darmstadt, Germany, through which the parties established a collaboration for the research and development and commercialization of certain products for the prophylactic, therapeutic, palliative or diagnostic use for cancer in humans.

Under the collaboration, Ares Trading has elected two CAR^+ T targets for which the Company will perform certain research activities that will, in part, be funded by Ares Trading. Once these candidates reach investigational new drug, or IND, stage, the programs will be transferred to Ares Trading for clinical development and commercialization. The Company is expected to perform multiple preclinical development programs, each consisting of the development of one product candidate, pursuant to the agreement. The Company, together with Precigen, will also independently conduct research and development on other CAR^+ T candidates, with Ares Trading having the opportunity during clinical development to opt-in to these candidates for additional payments to us and Precigen.

Precigen is entitled to receive $5.0 million, from Ares Trading, payable in equal quarterly installments over two years for each identified product candidate, which will be used to fund discovery work. The Company is responsible for costs exceeding the quarterly installments and all other costs of the preclinical research and development. For the twelve months ended December 31, 2017, the Company has expensed $1.6 million under the Ares Trading Agreement, respectively.

ZIOPHARM Oncology, Inc.

NOTES TO FINANCIAL STATEMENTS

7. Commitments and Contingencies (Continued)

Ares Trading paid a non-refundable upfront fee of $115.0 million to Intrexon as consideration for entry into the Ares Trading Agreement. Pursuant to the ECP Amendment, the Company was entitled to receive 50% of the upfront fee, or $57.5 million, which was received from Intrexon in July 2015.

The Ares Trading Agreement provides for up to $60.0 million in development milestone payments, up to $148.0 million in regulatory milestone payments and up to $205.0 million in commercial milestone payments for each product candidate. Development milestone payments are triggered upon initiation of a defined phase of clinical research for a product candidate. Regulatory milestone payments are triggered upon approval to market a product candidate by the FDA, or other global regulatory authorities. Commercial milestone payments are triggered when an approved pharmaceutical product reaches certain defined levels of net sales by the licensee. The Ares Trading Agreement also provides for up to $50.0 million of one-time payments upon the achievement of certain technical milestones evidenced by the initiation of a defined phase of clinical research. All development, regulatory and technical milestones are considered substantive based on the contingent nature of the milestone, specifically reviewing factors such as the scientific, clinical, regulatory, commercial and other risks that must be overcome to achieve the milestone as well as the level of effort and investment required. Accordingly, such amounts will be recognized as revenue in full in the period in which the associated milestone is achieved, assuming all other revenue recognition criteria are met. All commercial milestones will be accounted for in the same manner as royalties and recorded as revenue upon achievement of the milestone, assuming all other revenue recognition criteria are met. The next potential milestone payment that Precigen could be entitled to receive under the Ares Trading Agreement is a $15.0 million substantive milestone for the initiation of a Phase 1 clinical trial. In addition, to the extent any of the product candidates licensed by Ares Trading are commercialized, Precigen would be entitled to receive royalties ranging from the lower-single digits to the low-teens of net sales derived from the sale of products developed under agreement. Precigen will pay 50% of all milestone and royalty payments that it receives under the Ares Trading Agreement to us pursuant to the ECP Amendment.

The term of the Ares Trading Agreement commenced in May 2015 and may be terminated by either party in the event of a material breach as defined in the agreement and may be terminated voluntarily by Ares Trading upon 90 days written notice to us.

The Company considered FASB Accounting Standards Codification 605-25, *Multiple-Element Arrangements*, in evaluating the appropriate accounting for the Ares Trading Agreement. In accordance with this guidance, the Company identified the license and research and development services as the deliverables in the arrangement. The Company concluded that the license does not have standalone value independent from the research and development services. Accordingly, the Ares Trading Agreement is accounted for by us as a single unit of accounting. The $57.5 million upfront payment received by us was recorded as deferred revenue and is being recognized over the estimated period of performance of the research and development services which are currently estimated to be nine years, beginning with the commencement of the research and development services. During the three and twelve months ended December 31, 2017 and 2016, the Company recognized $1.6 million, each quarter, of revenue related to the Ares Trading Agreement. As of December 31, 2017, the remaining balance of deferred revenue associated with the upfront payment is $41.5 million, of which $6.4 million is current and $35.1 million is classified as long-term. As of December 31, 2016, the remaining balance of deferred revenue associated with the upfront payment was $47.9 million, of which $6.4 million was current and $41.5 million was classified as long term.

ZIOPHARM Oncology, Inc.

NOTES TO FINANCIAL STATEMENTS

7. Commitments and Contingencies (Continued)

Patent and Technology License Agreement—The University of Texas MD Anderson Cancer Center and the Texas A&M University System

On August 24, 2004, the Company entered into a patent and technology license agreement with MD Anderson and the Texas A&M University System, which the Company refers to, collectively, as the Licensors. Under this agreement, were granted an exclusive, worldwide license to rights (including rights to U.S. and foreign patent and patent applications and related improvements and know-how) for the manufacture and commercialization of two classes of organic arsenicals (water- and lipid-based) for human and animal use. The class of water-based organic arsenicals includes darinaparsin.

The Company issued options to purchase 50,222 shares outside of its stock option plans following the successful completion of certain clinical milestones, of which 37,666 shares have vested. The remaining 12,556 shares vested upon enrollment of the first patient in a multi-center pivotal clinical trial *i.e.* a human clinical trial intended to provide the substantial evidence of efficacy necessary to support the filing of an approvable New Drug Application, or NDA. An expense of $87 thousand was charged to research and development expense for the vesting event which occurred in March 2016. This trial was initiated by Solasia Pharma K.K., or Solasia, on March 28, 2016 and triggered a $1.0 million milestone payment to us from Solasia which was received in May 2016. An equivalent of $1.0 million milestone payment was subsequently made to MD Anderson and reported net. In addition, the Licensors are entitled to receive certain milestone payments. In addition, the Company may be required to make additional payments to the Licensors (as defined in the MD Anderson License) upon achievement of certain other milestones in varying amounts which, on a cumulative basis could total up to an additional $4.5 million. In addition, the Licensors are entitled to receive single digit percentage royalty payments on sales from a licensed product and will also be entitled to receive a portion of any fees that the Company may receive from a possible sublicense under certain circumstances.

Collaboration Agreement with Solasia Pharma K.K.

On March 7, 2011, the Company entered into a License and Collaboration Agreement with Solasia. Pursuant to the License and Collaboration Agreement, the Company granted Solasia an exclusive license to develop and commercialize darinaparsin in both intravenous and oral forms and related organic arsenic molecules, in all indications for human use in a pan-Asian/Pacific territory comprising Japan, China, Hong Kong, Macau, Republic of Korea, Taiwan, Singapore, Australia, New Zealand, Malaysia, Indonesia, Philippines and Thailand.

As consideration for the license, the Company received an upfront payment of $5.0 million to be used exclusively for further clinical development of darinaparsin outside of the pan-Asian/Pacific territory and will be entitled to receive additional payments of up to $32.5 million in development-based milestones and up to $53.5 million in sales-based milestones. The Company will also be entitled to receive double digit royalty payments from Solasia based upon net sales of licensed products in the applicable territories, once commercialized, and a percentage of sublicense revenues generated by Solasia. The $5.0 million upfront payment received in March 2011 was amortized over the period of the research and development effort, which was completed in March 2016.

On July 31, 2014, the Company entered into an amendment and restatement of the License and Collaboration Agreement granting Solasia an exclusive worldwide license to develop and commercialize darinaparsin, and related organoarsenic molecules, in both intravenous and oral forms in all indications for human use. In exchange, the Company will be eligible to receive from Solasia development- and sales-based milestones, a royalty on net sales of darinaparsin, once commercialized, and a percentage of any sublicense revenues generated by Solasia.

ZIOPHARM Oncology, Inc.

NOTES TO FINANCIAL STATEMENTS

7. Commitments and Contingencies (Continued)

Solasia will be responsible for all costs related to the development, manufacturing and commercialization of darinaparsin. The Company's Licensors, as defined in the agreement, will receive a portion of all milestone and royalty payments made by Solasia to us in accordance with the terms of the license agreement with the Licensors.

On March 28, 2016, Solasia initiated a multi-center pivotal clinical trial intended to provide substantial evidence of efficacy necessary to support the filing of an application for an NDA for darinaparsin in certain of the territories assigned to Solasia. The initiation of the trial on March 28, 2016 triggered a $1.0 million milestone payment from Solasia to us which was received in May 2016. The Company subsequently made an equivalent payment to MD Anderson as the ultimate licensor of darinaparsin (see above).

License Agreement with Baxter Healthcare S.A.

On November 3, 2006, the Company entered into a definitive Asset Purchase Agreement for indibulin and a License Agreement to proprietary nanosuspension technology with affiliates of Baxter Healthcare S.A. The purchase included the entire indibulin intellectual property portfolio as well as existing drug substance and capsule inventories. The terms of the Asset Purchase Agreement included an upfront cash payment and an additional payment for existing inventory. During the year ending December 31, 2017, the Company made the final payment of $250 thousand under the asset agreement. The Company are not actively pursuing the development of indibulin.

8. Income Taxes

There is no provision for income taxes because the Company has incurred operating losses since inception. The reported amount of income tax expense for the years differs from the amount that would result from applying domestic federal statutory tax rates to pretax losses primarily because of the changes in the valuation allowance. Significant components of the Company's deferred tax assets at December 31, 2017 and 2016 are as follows:

(in thousands)	December 31, 2017	2016
Net operating loss carryforwards	$ 89,098	$ 100,790
Start-up and organizational costs	37,488	59,360
Research and development credit carryforwards	32,395	34,845
Stock compensation	1,330	2,014
Capitalized acquisition costs	5,822	9,389
Deferred revenue	11,126	18,636
Depreciation	136	227
Other	993	1,537
	178,388	226,798
Less valuation allowance	(178,388)	(226,798)
Effective tax rate	$ —	$ —

Deferred income taxes reflect the net tax effects of temporary differences between the carrying amount of assets and liabilities for financial reporting purposes and the amounts used for income tax purposes. At December 31, 2017, the Company has aggregate net operating loss carryforwards for federal tax purposes of approximately $342 million and $299 million for Federal and state purposes, respectively, available to offset future federal and

ZIOPHARM Oncology, Inc.

NOTES TO FINANCIAL STATEMENTS

8. Income Taxes (Continued)

state taxable income to the extent permitted under the Internal Revenue Code, or IRC, expiring in varying amounts through 2037. Additionally, the Company has approximately $35 million of research and development credits at December 31, 2017, expiring in varying amounts through 2037, which may be available to reduce future taxes.

In March 2016, the FASB issued ASU No. 2016-09, “Improvements to Employee Share-Based Payment Accounting” (ASU 2016-09), which is intended to simplify several aspects of accounting for share-based payment transactions, including the income tax effects, statutory withholding requirements, forfeitures, and classification on the statement of cash flows. ASU 2016-09 is effective for annual reporting periods after December 15, 2016, including interim reporting periods within each annual reporting period. The Company adopted this standard on January 1, 2017. The update revises requirements in the following areas: minimum statutory withholding, accounting for income taxes, and forfeitures. Prior to adoption, the Company recognized share-based compensation, net of estimated forfeitures, over the vesting period of the grant. Upon adoption of ASU 2016-09, the Company elected to change its accounting policy to recognize forfeitures as they occur. The net forfeiture policy election was adopted using a modified retrospective approach with a cumulative effect adjustment of $122 thousand recorded to retained earnings as of January 1, 2017. The update requires the Company to recognize the income tax effect of awards in the income statement when the awards vest or are settled without triggering a liability. The income tax related items had no effect on the current period presentation and the Company maintains a full valuation allowance against its deferred tax assets. As a result, an accumulated excess tax benefit of 10.2 million was recognized as a deferred tax asset with a full valuation allowance against it. Additionally, we continued to estimate the number of awards expected to be vested. The adoption had no material impact on our financial statements for the 2017 tax year or the interim periods within.
Under the IRC Section 382, certain substantial changes in the Company’s ownership may limit the amount of net operating loss carryforwards that can be utilized in any one year to offset future taxable income.

Section 382 of the IRC provides limits to which a corporation that has undergone a change in ownership (as defined) can utilize any net operating loss, or NOL, and general business tax credit carryforwards it may have. The Company commissioned an analysis to determine whether Section 382 could limit the use of its carryforwards in this manner. After completing the analysis, it was determined an ownership change had occurred in February 2007. As a result of this change, the Company’s NOL’s and general business tax credits from February 23, 2007 and prior would be completely limited under IRC Section 382. The deferred tax assets related to NOL’s and general business credits have been reduced by $11.2 million and $636 thousand, respectively, as a result of the change. The Company updated the IRC Section 382 analysis through December 31, 2014. It was determined a change of ownership occurred on February 28, 2011. The Company’s NOL’s were not further limited as a result of the change. The Company updated the IRC Section 382 analysis through December 31, 2016 and it was determined that there was no further change in ownership.

The Company has provided a valuation allowance for the full amount of these net deferred tax assets, since it is more likely than not that these future benefits will not be realized. However, these deferred tax assets may be available to offset future income tax liabilities and expenses. The valuation allowance decreased by $48.4 million in 2017 primarily due to the change in the federal tax rate, net operating loss carryforwards, and the increase in research and development credits.

Income taxes using the federal statutory income tax rate differ from the Company’s effective tax rate primarily due to non-deductible expenses related to the Company’s issuance of preferred stock along with the change in the valuation allowance on deferred tax assets.

ZIOPHARM Oncology, Inc.

NOTES TO FINANCIAL STATEMENTS

8. Income Taxes (Continued)

A reconciliation of income tax expense (benefit) at the statutory federal income tax rate and income taxes as reflected in the financial statements is as follows:

	Year Ended December 31,		
(in thousands)	**2017**	**2016**	**2015**
Federal income tax at statutory rates	34%	34%	34%
State income tax, net of federal tax benefit	4%	1%	5%
Research and development credits	3%	3%	3%
Stock compensation	-1%	-1%	-1%
Channel rights	0%	-25%	0%
Research and development true-up	-7%	0%	0%
Officers compensation	-2%	0%	0%
Other	-3%	0%	0%
Federal rate change	-124%	0%	0%
Increase in valuation allowance	96%	-12%	-41%
Effective tax rate	0%	0%	0%

The Company adopted ASC740, “Accounting for Uncertain Tax Positions” on January 1, 2007. ASC740 clarifies the accounting for uncertainty in income taxes recognized in an enterprise’s financial statements in accordance with FASB Statement No. 109, “Accounting for Income Taxes.” ASC 740 prescribes a recognition threshold and measurement of a tax position taken or expected to be taken in a tax return. The Company did not establish any additional reserves for uncertain tax liabilities upon adoption of ASC 740. A summary of the company’s adjustments to its uncertain tax positions in the years ended December 31, 2017, 2016, and 2015 are as follows:

(in thousands)	
Balance at December 31, 2014	$ 238
Increase/Decrease for tax positions related to the current year	—
Increase/Decrease for tax positions related to prior years	—
Decrease for settlements with applicable taxing authorities	—
Decrease for previous year’s lapses of statute of limitations	(20)
Decrease for impact of §382 limitations	(218)
Decrease for lapses of statute of limitations	—
Balance at December 31, 2015	$ —
Increase/Decrease for tax positions related to the current year	—
Increase/Decrease for tax positions related to prior years	—
Decreases for settlements with applicable taxing authorities	—
Decrease for lapses of statute of limitations	—
Balance at December 31, 2016	$ —
Increase/Decrease for tax positions related to the current year	—
Increase/Decrease for tax positions related to prior years	—
Decrease for settlements with applicable taxing authorities	—
Decrease for lapses of statute of limitations	—
Balance at December 31, 2017	$ —

The Company has not recognized any interest and penalties in the statement of operations because of the Company’s net operating losses and tax credits that are available to be carried forward. When necessary, the

ZIOPHARM Oncology, Inc.

NOTES TO FINANCIAL STATEMENTS

8. Income Taxes (Continued)

Company will account for interest and penalties related to uncertain tax positions as part of its provision for federal and state income taxes. The Company does not expect the amounts of unrecognized benefits will change significantly within the next twelve months.

The Company is currently open to audit under the statute of limitations by the Internal Revenue Service and state jurisdictions for the years ended December 31, 1999 through 2017.

The Tax Cuts and Jobs Act, or the "Tax Act," was enacted in December 2017. The act significantly changes US tax law by, among other things, lowering US corporate income tax rates, implementing a territorial tax system, and imposing a one-time transition tax on deemed repatriated earnings of foreign subsidiaries. The Tax Act reduces the US corporate income tax rate from 35% to 21%, effective January 1, 2018. Deferred tax assets and liabilities are measured using enacted tax rates expected to apply to taxable income in the years in which those temporary differences are expected to reverse. As a result of the reduction in the US corporate tax rate from 35% to 21% under the Tax Act, the Company revalued its ending net deferred tax assets at December 31, 2017. There was no impact as a result of the revaluation of the deferred tax assets as the calculated provisional tax benefit of approximately $67.0 million was offset by the Company's subsequent change in valuation allowance.

The SEC staff issued Staff Accounting Bulletin (SAB 118) to address the application of US GAAP in situations when a registrant does not have the necessary information available, prepared or analyzed in reasonable detail to complete the accounting for certain income tax effects of the Tax Act and allows the registrant to record provisional amounts during the measurement period. We are in the process of analyzing the impact of the various provisions of the Tax Act. We expect to complete our analysis within the measurement period in accordance with SAB 118.

9. Preferred Stock and Stockholders' Equity (Deficit)

On April 26, 2006, the date of the Company's annual stockholders meeting that year, the shareholders approved the adoption of an Amended and Restated Certificate of Incorporation pursuant to which the Company has 280,000,000 shares of authorized capital stock, of which 250,000,000 shares are designated as common stock (par value $.001 per share), and 30,000,000 shares are designated as preferred stock (par value $.001 per share).

Common Stock

On February 3, 2015, the Company entered into an underwriting agreement with J.P. Morgan Securities LLC, as representative of the several underwriters named therein, relating to the issuance and sale of 10,000,000 shares of our common stock. The price to the public in the offering was $8.75 per share, and the underwriters agreed to purchase the shares from the Company pursuant to the underwriting agreement at a purchase price of $8.225 per share. Under the terms of the underwriting agreement, the Company also granted the underwriters an option, exercisable for 30 days, to purchase up to an additional 1,500,000 shares of common stock at a purchase price of $8.225 per share. The offering was made pursuant to the Company's registration statement on Form S-3 (SEC File No. 333-201826) previously filed with the SEC, and a prospectus supplement thereunder. The underwriters purchased the 10,000,000 shares and the additional 1,500,000 shares on February 9 and 17, 2015, respectively. The net proceeds from the offering were approximately $94.3 million after deducting underwriting discounts and estimated offering expenses paid by the Company.

ZIOPHARM Oncology, Inc.

NOTES TO FINANCIAL STATEMENTS

9. Preferred Stock and Stockholders' Equity (Deficit) (Continued)

On January 13, 2015, the Company, together with Intrexon (now Precigen), entered into the MD Anderson License. Pursuant to the terms of the MD Anderson License, MD Anderson received consideration of 11,722,163 shares of the Company's common stock (see Note 7).

On May 11, 2017, the Company sold in an underwritten offering an aggregate of 9,708,738 shares of its common stock. The price to the investor in the offering was $5.15 per share, and the underwriters agreed to purchase the shares from the Company pursuant to the Company's registration statement on Form S-3ASR (File No. 333-201826) previously filed with the SEC, and a prospectus supplement thereunder. The net proceeds from the offering were approximately $47.3 million after deducting underwriting commissions and estimated offering expenses payable by the Company.

Preferred Stock

The Company's Board of Directors are authorized to designate any series of Preferred Stock, to fix and determine the variations in relative rights, preferences, privileges and restrictions as between and among such series.

On June 29, 2016, the Company entered into the 2016 ECP Amendment and 2016 GvHD Amendment with Intrexon (now Precigen) (see Note 7). In consideration for the execution and delivery of the 2016 ECP Amendment and the 2016 GvHD Amendment, the Company issued to Intrexon 100,000 shares of its newly designated Series 1 preferred stock. Each share of the Company's Series 1 preferred stock has a stated value of $1,200, subject to appropriate adjustment in the event of any stock dividend, stock split, combination or other recapitalization. The Series 1 preferred stock has the following rights and preferences and certain other rights, preferences, privileges and obligations.

Conversion

All shares of Series 1 preferred stock shall automatically convert into shares of common stock upon the public announcement of the first approval in the United States of (i) a ZIOPHARM Product under the Channel Agreement, (ii) a Product under the GvHD Agreement or (iii) a Product under the Ares Trading Agreement, which the Company refers to as the Conversion Event Date. On the second business day following the Conversion Event Date, each of Series 1 preferred stock shall convert into a number of shares of common stock equal to the stated value of such Series 1 preferred stock, divided by the greater of (i) the volume weighted average closing price of common stock as reported by The Nasdaq Stock Market, LLC over the 20 trading days ending on the Conversion Event Date or (ii) $1.00 per share; however, without shareholder approval in accordance with the Nasdaq listing rules, the Company will not affect any conversion of the Series 1 preferred stock into shares of common stock in excess of 19.9% of the lesser of (i) the pre-transaction outstanding shares of common stock or (ii) the outstanding shares of common stock at the time of conversion. In addition, without shareholder approval in accordance with the Nasdaq listing rules, the Company will not affect any conversion of the Series 1 preferred stock into common stock to the extent that the number of shares of common stock issued in such conversion would constitute a change of control under the Nasdaq listing rules.

Dividends

The Series 1 preferred stock provides for a monthly dividend, payable in additional shares of Series 1 preferred stock, equal to $12.00 per share, per month divided by the stated value per share, or the PIK Dividend; provided, that if any shares of Series 1 preferred stock are not converted on the Conversion Event Date (discussed below),

ZIOPHARM Oncology, Inc.

NOTES TO FINANCIAL STATEMENTS

9. Preferred Stock and Stockholders' Equity (Deficit) (Continued)

then the rate of the PIK Dividend on all remaining unconverted shares of Series 1 preferred stock shall automatically increase from $12.00 to $24.00 per share, per month.

Liquidation Preference

In the event of any voluntary or involuntary liquidation, dissolution or winding up of the Company or a change of control or sale, lease transfer or exclusive license of all or substantially all of the Company's assets prior to the conversion of the Series 1 preferred stock into shares of common stock, then the Series 1 preferred stock will participate in the proceeds of the transaction on a pro rata basis along with common stock, treating the Series 1 preferred stock as if it had been converted into a number of shares of common stock equal to the aggregate stated value of the Series 1 preferred stock, divided by the volume weighted average closing price of common stock over the 20 trading days ending on the public announcement of such voluntary or involuntary liquidation, dissolution or winding up of the Company or change of control or sale, lease transfer or exclusive license of all or substantially all of the Company's assets. Alternatively, the Company may redeem the Series 1 preferred stock at a redemption price equal to the pro rata amount that the Series 1 preferred stock would have received if it had been converted using the same formula.

Voting Rights

The Series 1 preferred stock does not have any voting rights except that the Company may not, without the consent of the holders of a majority of the outstanding shares of the Series 1 preferred stock, voting as a separate class, (i) amend, alter or repeal any provision of its Certificate of Incorporation in a manner that adversely affects the powers, preferences or rights of the Series 1 preferred stock in a manner that is more adverse than the effect on any other class or series of the Company's capital stock; (ii) (A) create, or authorize the creation of, or issue or obligate itself to issue shares of, any additional class or series of the Company's capital stock unless the same ranks junior or pari passu to the Series 1 preferred stock with respect to the distribution of assets on the liquidation, dissolution or winding up of the Company, the payment of dividends and rights of redemption, or (B) reclassify, alter or amend any existing security that is junior or pari passu to the Series 1 preferred stock with respect to the distribution of assets on the liquidation, dissolution or winding up of the Company, the payment of dividends or rights of redemption, if such reclassification, alteration or amendment would render such other security senior to the Series 1 preferred in respect of any such right, preference or privilege; or (iii) enter into any transaction (or series of related transactions) the effect of which would adversely affect the holders of the Series 1 preferred stock in a manner that is more adverse than the effect on any other class or series of capital stock.

Analysis

The Company analyzed the features of the Series 1 preferred stock and determined that the conversion option and the Company's right to redeem the shares at liquidation are embedded derivatives that required bifurcation from the Series 1 preferred stock in accordance with FASB ASC 815, *Derivatives and Hedging*. The embedded derivatives were valued as described below at $0.9 million. Upon issuance of the shares on July 1, 2016 the Company recorded the fair value of the derivatives as a liability and the fair value of the Series 1 preferred stock of $118.2 million as a component of temporary equity. Furthermore, because of the temporary equity classification, the carrying value of the Series 1 preferred stock will not be accreted to redemption value unless or until its redemption becomes probable.

The fair value of the Series 1 preferred stock was estimated using a probability-weighted approach and a Monte Carlo simulation model. The fair value of the embedded derivatives was estimated using the "with" and

ZIOPHARM Oncology, Inc.

NOTES TO FINANCIAL STATEMENTS

9. Preferred Stock and Stockholders' Equity (Deficit) (Continued)

"without" method where the preferred stock was first valued with all of its features ("with" scenario) and then without derivatives subject to the valuation analysis ("without" scenario). The fair value of the derivatives was then estimated as the difference between the fair value of the preferred stock in the "with" scenario and the preferred stock in the "without" scenario. The model also takes into account, management estimates of clinical success/failure based upon market studies and probability of potential conversion and liquidation events. If these estimates were different, the valuations would change, and that change could be material. Inputs to the models included the following:

Risk-free interest rate	1.04%
Expected dividend rate	0
Expected volatility	70.50%
Preferred stock conversion limit—percentage of outstanding common stock	19.90%
Preferred conversion floor price	$ 1.00

During the year ended December 31, 2017, the Company issued an aggregate of 13,460 shares of Series 1 preferred stock to Intrexon, the holder of all of the outstanding shares of its Series 1 preferred stock, as monthly dividend payments. The Company recorded such shares of Series 1 preferred stock at a fair value of $18.9 million, which is a component of temporary equity and recorded a loss on the change in fair value of the derivative liabilities in the amount of $1.3 million (Note 10).

10. Derivative Financial Instruments

The Company determined that certain embedded features related to the Series 1 preferred stock are derivative financial instruments. The company values the embedded derivative financial instruments related to the Series 1 preferred stock as Level 3 financial liabilities (Note 3).

Fair values of derivative instruments to be classified as derivative liabilities on the balance sheet consist of the following:

($ in thousands) Liability derivatives:	Balance Sheet Location	Fair Value
December 31, 2017:		
Derivative liabilities	Liabilities	$ 2,424

The change in the derivative liability for the year ended December 31, 2017 and 2016 consists of the following:

($ in thousands)	Fair Value
Balance, June 30, 2016	$ 694
Dividends	44
Change in fair value	124
Balance, December 31, 2016	$ 862
Dividends	267
Change in fair value	1,295
Balance, December 31, 2017	$ 2,424

ZIOPHARM Oncology, Inc.

NOTES TO FINANCIAL STATEMENTS

10. Derivative Financial Instruments (Continued)

The fair value of the Series 1 preferred stock dividends was estimated using a probability-weighted approach and a Monte Carlo simulation model. The fair value of the embedded derivatives was estimated using the "with" and "without" method where the preferred stock was first valued with all of its features ("with" scenario) and then without derivatives subject to the valuation analysis ("without" scenario). The fair value of the derivatives was then estimated as the difference between the fair value of the preferred stock in the "with" scenario and the preferred stock in the "without" scenario. The model also takes into account, management estimates of clinical success/failure based upon market studies and probability of potential conversion and liquidation events. If these estimates were different, the valuations would change, and that change could be material. Inputs to the models included the following:

	December 31,	
	2017	2016
Risk-free interest rate	1.92 - 2.12%	1.04% - 1.69%
Expected dividend rate	0	0
Expected volatility	68.7 - 80.4%	70.5% - 72.70%
Preferred stock conversion limit—percentage of outstanding common stock	19.90%	19.90%
Preferred conversion floor price	$1.00	$1.00

See Notes 3 and 7 for additional discussion regarding the accounting for and valuation of these derivative financial instruments.

11. Stock Option Plan

The Company adopted the 2012 Equity Incentive Plan, or the 2012 Plan, in May 2012, under which the Company initially reserved for the issuance of 4,000,000 shares of its common stock. The 2012 Plan was approved by the Company's stockholders on June 20, 2012. On June 18, 2014, the date of the Company's annual stockholders meeting, the Company's stockholders approved an amendment to the 2012 Plan increasing the total shares reserved by 5,000,000 shares, for a total of 9,000,000 shares.

As of December 31, 2017, the Company had outstanding options issued to its employees to purchase up to 3,214,635 shares of the Company's common stock, to its directors to purchase up to 627,500 shares of the Company's common stock, as well as options to consultants in connection with services rendered to purchase up to 10,000 shares of the Company's common stock.

Stock options to employees generally vest ratably in annual installments over three years, commencing on the first anniversary of the grant date and have contractual terms of ten years. Stock options to directors generally vest ratably over one or three years and have contractual terms of ten years. Stock options are valued using the Black-Scholes option pricing model and compensation is recognized based on such fair value over the period of vesting on a straight-line basis. The Company has also reserved an aggregate of 526,364 additional shares for issuance under options granted outside of the 2003 and 2012 Plans.

Proceeds from the option exercises during the years ended December 31, 2017, 2016, and 2015 amounted to $0.1 million, $0.7 million and $4.6 million respectively. The intrinsic value of these options amounted to $0.3 million, $1.5 million and $23.8 million for years ended December 31, 2017, 2016 and 2015, respectively.

ZIOPHARM Oncology, Inc.

NOTES TO FINANCIAL STATEMENTS

11. Stock Option Plan (Continued)

Transactions under the 2012 Plan for the years ending December 31, 2017, 2016, and 2015 were as follows:

(in thousands, except share and per share data)	Number of Shares	Weighted-Average Exercise Price	Weighted-Average Contractual Term (Years)	Aggregate Intrinsic Value
Outstanding, December 31, 2014	6,505,663	$ 4.07		
Granted	427,800	10.47		
Exercised	(3,249,160)	3.95		
Cancelled	(202,835)	4.36		
Outstanding, December 31, 2015	3,481,468	4.96		
Granted	362,800	6.40		
Exercised	(234,833)	4.57		
Cancelled	(144,100)	6.43		
Outstanding, December 31, 2016	3,465,335	5.07		
Granted	688,800	5.27		
Exercised	(180,000)	3.67		
Cancelled	(122,000)	6.64		
Outstanding, December 31, 2017	3,852,135	$ 5.12	6.47	$ 1,152
Options exercisable, December 31, 2017	2,925,502	$ 5.12	5.58	$ 1,152
Options exercisable, December 31, 2016	2,671,835	$ 4.40	5.88	$ 3,383
Options available for future grant at December 31, 2017	303,928			

In September 2017, the Company granted an option for 500,000 shares of its common stock, with an exercise price of $6.16 per share, which vests ratably in annual installments over three years, commencing on the first anniversary of the grant date and have contractual terms of ten years. This option was granted outside of the 2012 plan and therefore, is not included in the table above. The grant date fair value was $2.2 million. As of December 31, 2017, all 500,000 options are outstanding.

At December 31, 2017, total unrecognized compensation costs related to non-vested stock options outstanding amounted to $5.1 million. The cost is expected to be recognized over a weighted-average period of 1.73 years.

Restricted Stock

In December 2017, the Company issued 838,000 shares of restricted stock to its employees, which vest ratably in annual installments over three years, commencing on the first anniversary of the grant date. In December 2017, the Company issued 69,032 shares of restricted stock to its non-employee directors, which vest in their entirety on the one-year anniversary of the grant date. In December 2016, the Company issued 625,750 shares of restricted stock to its employees, which vest ratably in annual installments over three years, commencing on the first anniversary of the grant date. In December 2016, the Company issued 86,020 shares of restricted stock to its non-employee directors, which vest in their entirety on the one-year anniversary of the grant date. In May, June and December 2015, the Company issued 1,000,000, 50,000 and 403,083 shares of restricted stock to its employees, respectively, which vest ratably in annual installments over three years, commencing on the first anniversary of the grant date. In September and December 2015, the Company issued 4,186 and 133,305 shares of restricted stock to its non-employee directors, which vested in their entirety at December 31, 2015 and on the one-year anniversary of the grant date respectively.

ZIOPHARM Oncology, Inc.

NOTES TO FINANCIAL STATEMENTS

11. Stock Option Plan (Continued)

In May, June and December 2017, the Company repurchased 132,000, 16,666 and 245,602 shares at average prices of $7.12, $6.11 and $4.14, respectively to cover payroll taxes. In May, June and December 2016, the Company repurchased 116,667, 6,667 and 119,873 shares at average prices of $6.86, $7.74 and $5.35, respectively to cover payroll taxes. In September and December 2015, the Company repurchased 7,669 and 16,709 shares at average prices of $11.57 and $8.31, respectively to cover payroll taxes. A summary of the status of non-vested restricted stock as of December 31, 2017, 2016 and 2015 is as follows:

	Number of Shares	Weighted-Average Grant Date Fair Value
Non-vested, December 31, 2014	144,508	$ 4.70
Granted	1,590,574	9.01
Vested	(148,694)	4.88
Cancelled	—	—
Non-vested, December 31, 2015	1,586,388	9.00
Granted	711,770	5.35
Vested	(617,666)	8.90
Cancelled	—	—
Non-vested, December 31, 2016	1,680,492	7.49
Granted	907,032	4.14
Vested	(778,965)	7.66
Cancelled	—	—
Non-vested, December 31, 2017	1,808,559	$ 5.74

As of December 31, 2017, there was $8.2 million of total unrecognized stock-based compensation expense related to non-vested restricted stock arrangements. The expense is expected to be recognized over a weighted-average period of 1.59 years.

12. Employee Benefit Plan

The Company sponsors a qualified 401(k) retirement plan under which employees are allowed to contribute certain percentages of their pay, up to the maximum allowed under Section 401(k) of the IIRC. The Company may make contributions to this plan at its discretion. The Company contributed approximately $90 thousand, $75 thousand, and $47 thousand to this plan during the years ended December 31, 2017, 2016, and 2015, respectively.

ZIOPHARM Oncology, Inc.

NOTES TO FINANCIAL STATEMENTS

13. Selected Quarterly Information (Unaudited)
(in thousands, except per share amount)

Year Ended December 31, 2017	First Quarter	Second Quarter	Third Quarter	Fourth Quarter
Revenue	$ 1,597	$ 1,597	$ 1,598	$ 1,597
Total operating expenses	15,562	14,611	14,676	15,033
Loss from operations	(13,965)	(13,014)	(13,078)	(13,436)
Preferred stock dividends	(4,171)	(4,865)	(4,903)	(4,999)
Net (loss) applicable to common shareholders	(19,658)	(17,727)	(17,604)	(18,272)
Loss per share, basic and diluted	$ (0.15)	$ (0.13)	$ (0.13)	$ (0.12)

Year Ended December 31, 2016	First Quarter	Second Quarter	Third Quarter	Fourth Quarter
Revenue	$ 1,969	$ 1,697	$ 1,598	$ 1,597
Total operating expenses	14,009	132,939	12,512	12,708
Loss from operations	(12,040)	(131,242)	(10,914)	(11,111)
Preferred stock dividends	—	—	(3,591)	(3,532)
Net (loss) applicable to common shareholders	(12,019)	(131,200)	(14,445)	(14,756)
Loss per share, basic and diluted	$ (0.09)	$ (1.01)	$ (0.11)	$ (0.11)

CONSENT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

We consent to the incorporation by reference in the Registration Statements (Nos. 333-129884, 333-134280, 333-142701, 333-160496, 333-167925, 333-185433, 333-199304 and 333-220804) on Forms S-8 and Registration Statements (Nos. 333-134279, 333-141014, 333-161453, 333-162160, 333-163517, 333-166444, 333-174292, 333-177793, and 333-201826) on Forms S-3 of our report dated March 1, 2018 relating to the financial statements and the effectiveness of internal control over financial reporting of ZIOPHARM Oncology, Inc., appearing in this Annual Report on Form 10-K of ZIOPHARM Oncology, Inc. for the year ended December 31, 2017.

/s/ RSM US LLP

Boston, Massachusetts
March 1, 2018

CERTIFICATION OF PRINCIPAL EXECUTIVE OFFICER

I, Laurence J.N. Cooper, certify that:

1. I have reviewed this annual report on Form 10-K of ZIOPHARM Oncology, Inc.;

2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;

3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;

4. The registrant's other certifying officer(s) and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) for the registrant and have:

   a) Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;

   b) Designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;

   c) Evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and

   d) Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and

5. The registrant's other certifying officer(s) and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):

   a) All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and

   b) Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Date: March 1, 2018

/s/ Laurence J.N. Cooper

Laurence J.N. Cooper, M.D., Ph.D.
Chief Executive Officer
(Principal Executive Officer)

CERTIFICATION OF PRINCIPAL FINANCIAL OFFICER

I, Kevin G. Lafond, certify that:

1. I have reviewed this annual report on Form 10-K of ZIOPHARM Oncology, Inc.;

2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;

3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;

4. The registrant's other certifying officer(s) and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) for the registrant and have:

   a) Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;

   b) Designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;

   c) Evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and

   d) Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and

5. The registrant's other certifying officer(s) and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):

   a) All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and

   b) Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Date: March 1, 2018

/s/ Kevin G. Lafond
Kevin G. Lafond
Senior Vice President, Chief Accounting Officer and Treasurer
(Principal Financial and Accounting Officer)

CERTIFICATION PURSUANT TO
18 U.S.C. SECTION 1350,
AS ADOPTED PURSUANT TO
SECTION 906 OF THE SARBANES-OXLEY ACT OF 2002

In connection with the Annual Report of ZIOPHARM Oncology, Inc. (the "Company") on Form 10-K for the year ended December 31, 2017, as filed with the Securities and Exchange Commission on the date hereof (the "Report"), I, Laurence J.N. Cooper, Principal Executive Officer of the Company, certify, pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002, that:

(1) The Report fully complies with the requirements of Section 13(a) or 15(d) of the Securities Exchange Act of 1934; and

(2) The information contained in the Report fairly presents, in all material respects, the financial condition and result of operations of the Company.

/s/ Laurence J.N. Cooper
Laurence J.N. Cooper, M.D., Ph.D.
Chief Executive Officer
(Principal Executive Officer)
March 1, 2018

CERTIFICATION PURSUANT TO
18 U.S.C. SECTION 1350,
AS ADOPTED PURSUANT TO
SECTION 906 OF THE SARBANES-OXLEY ACT OF 2002

In connection with the Annual Report of ZIOPHARM Oncology, Inc. (the "Company") on Form 10-K for the year ended December 31, 2017, as filed with the Securities and Exchange Commission on the date hereof (the "Report"), I, Kevin G. Lafond, Principal Financial and Accounting Officer of the Company, certify, pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002, that:

(1) The Report fully complies with the requirements of Section 13(a) or 15(d) of the Securities Exchange Act of 1934; and

(2) The information contained in the Report fairly presents, in all material respects, the financial condition and result of operations of the Company.

/s/ Kevin G. Lafond
Kevin G. Lafond
Senior Vice President, Chief Accounting Officer and Treasurer
(Principal Financial and Accounting Officer)
March 1, 2018