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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, 2014

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
(Issuer's Telephone Number, Including Area Code)

(Former Name, Former Address and Former Fiscal Year, if Changed Since Last Report)

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	☐

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 $327,143,169 as of June 30, 2014 (the last business day of the registrant's most recently completed second fiscal quarter), based on a total of 81,176,965 shares of common stock held by non-affiliates and on a closing price of $4.03 as reported on the NASDAQ Capital Market on June 30, 2014.

As of February 10, 2015, there were 114,694,324 shares of the registrant's common stock, $.001 par value per share, outstanding.

DOCUMENTS INCORPORATED BY REFERENCE:

Portions of the definitive proxy statement for our 2015 annual meeting of stockholders, which is to be filed within 120 days after the end of the fiscal year ended December 31, 2014, are incorporated by reference into Part III of this Form 10-K, to the extent described in Part III.

ZIOPHARM Oncology, Inc. ***(a development stage enterprise)***
FORM 10-K
FOR THE FISCAL YEAR ENDED DECEMBER 31, 2014

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All trademarks, trade names and service marks appearing in this annual report on Form 10-K are the property of their respective owners

Special note regarding forward-looking statements

This Annual Report on Form 10-K contains, forward-looking statements within the meaning of Section 27A of the Securities Act of 1933, as amended, or the Securities Act, and Section 21E of the Exchange Act. These statements relate to future events or to our future operating or financial performance and involve known and unknown risks, uncertainties and other factors which may cause our actual results, performance or achievements to be materially different from any future results, performances or achievements expressed or implied by the forward-looking statements. Forward-looking statements may include, but are not limited to statements about:

- The progress, timing and results of preclinical and clinical trials involving our drug candidates;
- The progress of our research and development programs;
- Our plans or others' plans to conduct future clinical trials or research and development efforts;
- The risk that final trial data may not support interim analysis of the viability of our drug candidates;
- Our plans and expectations regarding partnering our drug candidates;
- The benefits to be derived from relationships with our collaborators;
- The receipt or anticipated receipt of regulatory clearances and approvals;
- Estimates of the potential markets for our drug candidates;
- Our ability to adequately protect our intellectual property rights;
- The use of proceeds from this offering;
- Our estimates of future revenues and profitability;
- Our estimates regarding our capital requirements and our ability to control costs; and
- Our need for additional funding and the period through which we anticipate our resources will sufficient to fund operations.

In some cases, you can identify forward-looking statements by terms such as "may," "will," "should," "could," "would," "expects," "plans," "anticipates," "believes," "estimates," "projects," "predicts," "potential" and similar expressions intended to identify forward-looking statements. These statements reflect our current views with respect to future events and are based on assumptions and subject to risks and uncertainties. Given these uncertainties, you should not place undue reliance on these forward-looking statements. We discuss many of these risks in greater detail under the heading "Risk factors" in Part I, Item 1A of this Annual Report on Form 10-K.

You should read Annual Report on Form 10-K with the understanding that our actual future results may be materially different from what we expect. We qualify all of the forward-looking statements in the foregoing documents by these cautionary statements.

Unless required by law, we undertake no obligation to update or revise any forward-looking statements to reflect new information or future events or developments. Thus, you should not assume that our silence over time means that actual events are bearing out as expressed or implied in such forward-looking statements.

PART I

Item 1. Business

General

ZIOPHARM Oncology, Inc. is a biopharmaceutical company that seeks to acquire, develop and commercialize, on its own or with commercial partners, a diverse portfolio of cancer therapies that can address unmet medical needs through synthetic biology. Pursuant to an exclusive channel collaboration agreement (or "ECC") with Intrexon Corporation, or Intrexon, we obtained rights to Intrexon's synthetic biology platform for use in the field of oncology, which included a clinical stage product candidate, Ad-RTS-IL-12 used with the oral activator veledimex. The synthetic biology platform is an industrialized engineering approach for molecular and cell biology and gene control. It employs an inducible gene-delivery system that enables controlled in vivo expression of genes that produce therapeutic proteins to treat cancer. Ad-RTS-IL-12 + veledimex uses this gene delivery system to produce Interleukin-12, or IL-12, a potent, naturally occurring anti-cancer protein. We have completed two Phase 2 studies evaluating Ad-RTS-IL-12 + veledimex, the first for the treatment of metastatic melanoma, and the second for the treatment of metastatic breast cancer; data from these Phase 2 studies was presented in December 2014. We are continuing to pursue intratumoral injection of Ad-RTS-IL-12 + veledimex in breast cancer and brain cancer.

In addition to our synthetic biology programs, Intrexon (and we, through our ECC agreement with Intrexon) recently obtained an exclusive, worldwide license to certain immuno-oncology technologies owned and licensed by The University of Texas M.D. Anderson Cancer Center, or MD Anderson, including technologies relating to novel chimeric antigen receptors, or CARs, natural killer, or NK cells and T cell receptors, or TCRs. Combining these technologies with Intrexon's technology suite and clinically tested RheoSwitch Therapeutic System®, or RTS®, IL-12 modules, we plan to develop CAR-T and other immune cells that will target and kill cancer cells. We plan to leverage the synergy between the platforms to accelerate a promising synthetic immuno-oncology pipeline, with up to five CAR-T therapies expected to enter the clinic in 2015 and programs for the development of allogeneic CAR-T therapies that can be used off-the-shelf expected to be initiated in 2016.

We plan to continue to combine Intrexon's technology suite with our capabilities to translate science to the patient, and to identify and develop additional products to stimulate or inhibit key pathways, including those used by the body's immune system, to treat cancer.

Enabling Technology

Synthetic biology entails the application of engineering principles to biological systems for the purpose of designing and constructing new biological systems or redesigning/modifying existing biological systems. Biological systems are governed by DNA, the building block of gene programs, which control cellular processes by coding for the production of 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. Synthetic biology 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. Synthetic biology 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.

On January 6, 2011, we entered into an Exclusive Channel Partner Agreement with Intrexon, which we refer to as the Channel Agreement, to develop and commercialize novel DNA-based therapeutics in the field of cancer

treatment by combining Intrexon's synthetic biology platform with our capabilities to translate science to the patient. As a result, our DNA synthetic biology platform employs an inducible gene-delivery system that enables regulated and controlled delivery of genes that produce therapeutic proteins to treat cancer. The first example of this regulated controlled delivery is achieved by producing IL-12, a potent, naturally occurring anti-cancer protein, under the control of Intrexon's proprietary biological "switch" to turn on and off (and on and off repeatedly) the therapeutic protein expression at the tumor site. We and Intrexon refer to this "switch" as the RheoSwitch Therapeutic System® or RTS® platform. Our initial drug candidate being developed using the synthetic biology platform is Ad-RTS-IL-12 + veledimex.

More detailed descriptions of our clinical development for each are set forth in this report under the caption "Prospectus supplement summary – Product candidates."

Immuno-oncology

Immuno-oncology, which 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 a highly efficient process known as immune surveillance. A central player in immune surveillance is a type of white blood cell known as the T cell. In healthy individuals, T cells 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 last five years, there has been substantial scientific progress in countering these evasion mechanisms using immunotherapies, or therapies that activate the immune system.

On January 13, 2015, we, together with Intrexon, entered into a license agreement with MD Anderson, which we refer to as the MD Anderson License. Pursuant to the MD Anderson License, we and Intrexon 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., professor of pediatrics at MD Anderson, as well as either co-exclusive or non-exclusive licenses under certain related technologies.

Combining the non-viral genetic engineering technologies we licensed from MD Anderson together with Intrexon's industrialized approach to gene engineering and cell control, we believe we can rapidly and efficiently reprogram T cells to express a particular CAR or TCR construct that will enable the T cell to recognize and target cancer cells. CAR-T cells target cell surface tumor antigens, such as CD-19, that exist on cancer cells and that are independent of human leukocyte antigens, or HLAs, and which we refer to as "public" antigens. TCR+ cells target tumor antigens that are dependent on HLAs and which we refer to as "private" antigens. Natural killer cells target tumors with loss of HLAs, or tumors with no antigens. Most CAR-T cell and TCR products currently being developed by competitors are autologous, or derived from the patient's own blood, and gene engineered with viral technology. As a result, the patient's blood must be harvested, shipped to a manufacturing facility where it is modified using a retrovirus to express the CAR or TCR, and then shipped back to be infused into the patient. The process can take several weeks to a month and is very labor intensive and costly. Currently, this complex technique can only be done in very sophisticated laboratories. We believe we will be able to manufacture our CAR-T cells and TCRs using non-viral methods, which we expect will enable a simpler process requiring only days or hours and result in a lower cost of manufacturing. Our non-viral methods could also potentially enable autologous point of care treatment, where a patient's own T cells would be modified at or near the point of care, for example, utilizing a local blood bank, to express the CAR-T or TCR construct and then infused back into the patient, potentially during the same visit. In addition, we intend to use our non-viral methods to develop allogeneic treatments that can be used off-the-shelf. An allogeneic off-the-shelf treatment would enable a patient to be treated with a CAR-T or TCR construct that is created from a separate healthy donor, personalized for that patient, and then distributed to the point of care. Our non-viral methods, which we believe are nimble, fast and less costly than other approaches, together with our industrialized, scalable

engineering approach are expected to enable highly efficient and less costly manufacturing approaches to gene engineered cell-based therapy. In addition, our proprietary RheoSwitch Therapeutic System® may give us the ability to control in vivo gene expression (on-off-on-off etc.) in CAR-T or TCR cells, which we believe could result in significantly lower toxicity compared to other products currently in development.

Cancer Overview

Cancer is a group of diseases characterized by either the runaway growth of cells or the failure of cells to die normally. Often, cancer cells spread to distant parts of the body, where they can form new tumors. Cancer can arise in any organ of the body and, according to the American Cancer Society, strikes slightly less than one of every two American men and a little more than one of every three American women at some point in their lives.

It is reported that there are more than 100 different varieties of cancer. Carcinomas, the most common type of cancer, originate in tissues that cover a surface or line a cavity of the body. Lymphomas are cancers of the lymph system, which is a circulatory system that bathes and cleanses the body's cells. Leukemias involve blood-forming tissues and blood cells. As their name indicates, brain tumors are cancers that begin in the brain, skin cancers, including melanomas, originate in the skin, while soft tissue sarcoma, or STS, arises in soft tissue. Cancers are considered metastatic if they spread through the blood or lymphatic system to other parts of the body to form secondary tumors.

Cancer is caused by a series of mutations (alterations) in genes that control cells' ability to grow and divide. Some mutations are inherited; others arise from environmental factors such as smoking or exposure to chemicals, radiation, or viruses that damage cells' DNA. The mutations cause cells to divide relentlessly or lose their normal ability to die.

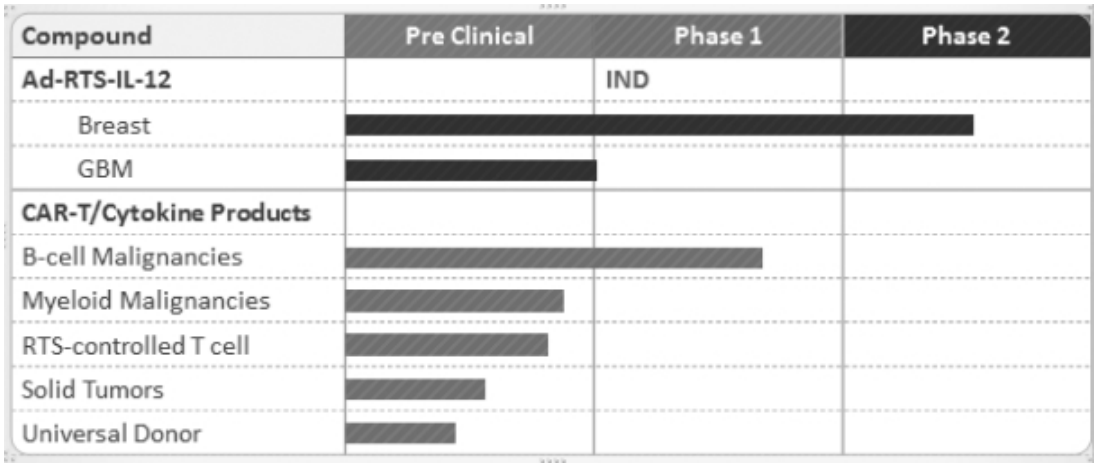
According to the American Cancer Society, it was estimated that about 1,658,370 new cases of cancer are expected to be diagnosed in 2015 and about 589,430 Americans are expected to die from cancer in 2015. The cost of treating cancer is significant. The Agency for Healthcare Research and Quality estimates that the direct medical cost of cancer in 2011 was $88.7 billion.

Cancer Treatments

Major treatments for cancer include surgery, radiotherapy, chemotherapy and immunotherapy. Newer approaches such as anti-angiogenic and targeted therapies are rapidly evolving. Other treatment for cancer may involve supportive care. While there are many experimental treatments under investigation, including DNA and other immunological based therapies, we believe cancer treatment will remain a significant unmet medical need.

Product Candidates

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



Synthetic Biology Programs:

Ad-RTS-IL-12 + veledimex

Ad-RTS-IL-12 + veledimex has been evaluated in two Phase 2 studies, the first for the treatment of metastatic melanoma, and the second for the treatment of unresectable recurrent or metastatic breast cancer. Ad-RTS-IL-12 + veledimex is our lead product candidate, which uses our gene delivery system to produce IL-12, a potent, naturally occurring anti-cancer protein.

More specifically, IL-12 is a potent immunostimulatory cytokine which activates and recruits dendritic cells that facilitate the cross-priming of tumor antigen-specific T cells. Intratumoral administration of Ad-RTS-IL-12 + veledimex, which allows for adjustment of IL-12 gene expression upon varying the dose of veledimex, is designed to reduce the toxicity elicited by systemic delivery of IL-12, and increase efficacy through high intratumoral expression.

We reported the controlled local expression of IL-12 as an immunotherapeutic treatment of glioma (brain cancer) in animal models through the use of the RTS® at the October 2013 AACR-NCI-EORTC conference. Veledimex brain penetration was demonstrated in normal mice and monkeys with intact blood brain barriers. Treatment with Ad-RTS-IL-12 + veledimex and DC-RTS-IL-12 + veledimex both demonstrated dose-related increase in survival in the mouse GL-261 glioma model with no adverse clinical signs observed. In December 2013, we announced the unanimous approval of the Recombinant DNA Advisory Committee of the National Institutes of Health, or the RAC/NIH, for the initiation of a Phase 1 study of Ad-RTS-IL-12 + veledimex, in subjects with recurrent or progressive high grade gliomas. The U.S Food and Drug Administration, or FDA, has requested additional nonclinical information to support the Phase 1 study and this data has been generated. Subject to reaching agreement with the FDA, we anticipate initiation of the Phase 1 study during the first half of 2015. Glioblastoma is by far the most frequent malignant brain tumor and is associated with a particularly aggressive course and dismal prognosis. The current standard of care is based on surgical resection to the maximum feasible extent, followed by radiotherapy and concomitant adjuvant temozolomide. Such aggressive treatment, however, is associated with only modest improvements in survival resulting in a very high unmet medical need.

At the American Association for Cancer Research, or AACR, 2014 Annual Meeting, in April 2014, we presented data from a preclinical study conducted jointly by us and Intrexon demonstrating the anti-tumor effects and

tolerability of Ad-RTS-mIL-12 in a glioblastoma murine model. Veledimex was found to effectively cross the blood brain barrier, with dose-related increases in plasma and brain tissue exposure, and no accumulation in brain tissue following repeat dosing. The study data demonstrated that administration of Ad-RTS-mIL-12 + veledimex resulted in dose-related increases in survival of four- to five-fold, without exhibiting an adverse safety profile, when compared to median survival in vehicle control groups.

At the 17th Annual Meeting of the American Society of Gene and Cell Therapy, or ASGCT, in May 2014, we presented results demonstrating the potent anti-tumor and anti-cancer stem cell effects of Ad-RTS-IL-12 in a preclinical glioma model. Results from human and laboratory studies of Ad-RTS-IL-12 demonstrated that precise control of IL-12 gene expression levels can be achieved using Intrexon's RTS®. Rapid, tight modulation of in vivo expression of IL-12 using the activator ligand, veledimex, was demonstrated across these studies. When IL-12 expression was "switched on" it rapidly led to expression and an immune response. This immune response was characterized by an increase in tumor infiltrating lymphocytes with system wide immune activation. The data presented in May 2014 further demonstrated that Ad-RTS-IL-12 has potent anti-cancer effects in a glioma model, showing both a reduction in tumor mass and prolonged survival when compared to existing treatment standards. The data also showed a significant reduction in cancer stem cells, as measured by dramatically reduced nestin levels. Cancer stem cells are thought to play a critical role in recurrence and metastasis.

At the AACR 2014 Immunology and Immunotherapy Meeting in December 2014, together with Intrexon, we presented clinical results from the Ad-RTS-hIL-12 + veledimex studies in patients with advanced breast cancer and melanoma demonstrating local and systemic IL-12-mediated anti-cancer activity, as well as safety and control of both immune- and IL-12-mediated toxicity with use of the RTS® gene switch. In two open-label Phase 2 clinical studies, twelve patients with metastatic advanced stage breast cancer and twenty-six patients with metastatic melanoma were administered Ad-RTS-hIL-12. Following intra-tumoral injection of Ad-RTS-hIL-12, expression of IL-12 within patients was controlled by the RTS® gene switch using the oral activator ligand, veledimex, at doses ranging from 5mg to 160mg. All subjects had heavy tumor burden and disease progression at the time of enrollment, with mean number of prior therapies at 14 and 10 for breast cancer and melanoma patients, respectively. Treatment with Ad-RTS-hIL-12 + veledimex resulted in an increase in the immune cytokine IL-12 and downstream cytokines, IFN- g, IP-10 and IL-10, resulting in a significant increase in the number of CD8+ T-cells. Among seven evaluable subjects in the Phase 2 clinical study of Ad-RTS-IL-12 + veledimex in patients with recurrent or metastatic breast cancer, three had stable disease, including one triple negative breast cancer subject who crossed the primary endpoint of 16 week progression free survival, for a disease control rate (stable disease or better) of 43%. Target lesions and tumor burden were significantly reduced in approximately 40% of patients. In the Phase 1/2 study of Ad-RTS-hIL-12 + veledimex in subjects with unresectable stage III/IV melanoma, of eighteen evaluable subjects, one had a partial response and six had stable disease, for a disease control rate of 39%. In melanoma patients for whom a response was observed, there was evidence of local and systemic anti-cancer activity. The adverse event profile of Ad-RTS-hIL-12 + veledimex in both melanoma and breast cancer was predictable, reversible and characteristic of immune activation. The most common ³ Grade 3 treatment emergent adverse events, or TEAEs, in breast cancer and melanoma included neutropenia and electrolyte abnormalities (21%) each, LFTs increased (16%), leukopenia (13%) and pyrexia, hypotension, lymphopenia, anemia, and cytokine release syndrome (11%) each. Importantly, all TEAEs and SAEs ³ Grade 3 reversed rapidly upon discontinuation of veledimex oral dosing.

Also at the AACR 2014 Immunology and Immunotherapy Meeting in December 2014, together with Intrexon, we presented preclinical data supporting the potential for cytolytic activity against solid tumor targets with allogeneic, genetically-modified stem cells enabled for controlled release of cell-linking moieties, or CLMs, within the tumor micro-environment and preclinical data describing the development of a novel, high-throughput screening technology for rapidly identifying bi-specific antibodies capable of inducing targeted immunologic activity through the activation of T-cells or other immune cells against tumors. CLMs are small bi-specific antibody fragments capable of directing potent T-cell mediated tumor lysis by bridging the immunologic synapses of T-cells and surface targets on tumor cells. Previous studies have shown that the systemic distribution and pharmacokinetic profile of bi-specific antibodies limit their utility for many target/effector combinations. In

two preclinical studies, Intrexon and Ziopharm researchers interrogated a large number of CLM-based effectors for their ability to activate white blood cells from peripheral blood and lyse receptor target-positive tumor cells. Allogeneic, tumor targeting stem cells were then genetically modified to express CLMs within the tumor microenvironment using the RTS® platform as a mechanism for providing spatial and temporal control. The first study demonstrated the ability of Intrexon's proprietary image-based screening systems and rapid DNA assembly to screen a large number of EGFR and HER2 receptor-targeted CLM variants for their ability to recruit CD3+ T-cells and mediate selective cell killing against target positive cells in peripheral blood co-cultures. The image-based screening platform allowed for real time target cell killing information to be obtained, as well as kinetic cell morphologic analyses to understand the dynamics of killing activity, thereby shortening the developmental timeline to lead candidate selection. The second study validated these CLM candidates in scalable, allogeneic endometrial regenerative cells, or ERCs, genetically modified to express an anti-CD3-anti-EGFR CLM under RTS® ligand inducible control. Expression of CLMs under the RTS® inducible promoter provided effective control of CLM secretion and modulation of killing activity, with veledimex-dependent cytotoxicity of greater than 80% against an EGFR+ KRAS mutant lung cancer cell model. CLM-expressing ERCs were found to be effective in co-culture killing assays at cellular doses as low as 1% of target cells. These data supported the feasibility of localized cytolytic activity of CLM-secreting allogeneic cell therapy products against EGFR+ KRAS mutant solid tumor malignancies.

We have completed the Phase 2 monotherapy studies in melanoma and breast cancer using Ad-RTS-IL-12 + veledimex. Additionally, we expect a future trial with IL-12 in combination therapies with standard of care for breast cancer. As the treatment of advanced melanoma has undergone and continues to undergo a rapid evolution with the introduction and approval of highly promising new single and combination agents, the standard of care in this indication has become uncertain, resulting in a much more competitive and commercially unpredictable environment. As a result, we are pursuing intratumoral injection of Ad-RTS-IL-12 + veledimex in brain cancer and breast cancer, and will pause further development of Ad-RTS-IL-12 + veledimex in melanoma with intratumoral injection. However, through current strategic initiatives, we expect to utilize RTS-IL-12 + veledimex in cell based immunotherapy of melanoma and other cancers. We plan to initiate a Phase 1 trial to evaluate Ad-RTS-IL-12 + veledimex as a single agent in the treatment of patients with brain cancer in the first half of 2015.

CAR-T Cells

We are actively pursuing non-viral, genetic engineering technologies to develop novel CAR-T, NK and TCR cells. Combining this technology with Intrexon's industrialized synthetic biologic engineering and clinically tested and validated RTS IL-12 modules, represents a differentiated approach to genetically modified CAR-T cell and other immune cells. Employing novel cell engineering techniques and multigenic gene programs, we expect to implement next-generation non-viral adoptive cellular therapies based on designer cytokines and CARs under control of RTS® technology targeting both hematologic malignancies and solid tumors. We plan to leverage the synergy between the platforms to accelerate a promising synthetic immuno-oncology pipeline, with up to five CAR-T therapies expected to enter the clinic in 2015 and programs for the development of allogeneic CAR-T therapies that can be used off-the-shelf expected to be initiated in 2016.

Research suggests that T cells can be re-programmed to have a very strong anti-cancer therapeutic effect through the expression of CARs to redirect specificity to tumors without HLA restrictions. The signature event within this field has resulted from the infusion of T cells expressing CARs into patients with B cells leukemias and lymphomas. Many of these patients have responded to these new therapies with a durable and dramatic anti-tumor effect after infusing CD19-specific T cells. Despite the highly promising results that have been demonstrated by early researchers in the field, current technologies and approaches have shown a number of serious drawbacks, including toxicity, manufacturing complexity and expense. A particular problem is that infusions of T cells into patients with large amounts of disease have invariably led to significant issues of toxicity for recipient patients. These toxicities primarily involve three major, potentially catastrophic side-effects:

- The rapid killing of tumor cells releases a large number intracellular constituents that are very toxic to various organs and is called "tumor lysis syndrome" that can be fatal,

- the supra-physiologic release of cytokines ("cytokine storm") that causes fever, instability of blood pressure, mental status changes and on occasion, death, and
- on-target, and off-tissue toxicity represented by the concomitant damage of normal B cells and loss of humoral (antibody) immunity.

We expect to be able to tightly control expansion and activation of CAR-T cells in the body, which has the potential to alleviate or abrogate these toxicities.

MD Anderson's platform, which uses the exclusive Sleeping Beauty system, or SB system, generates and characterizes new CAR-T designs, which enables a high throughput approach to evaluate the CAR-T. This "EZ-CAR-T" non-viral system is used to fashion immuno-receptors that differ in specificity and ability to activate T cells. These CAR-T molecules are evaluated in a "go/no go" system based on serial killing and protection of T cells from activation-induced cell death. Non-viral gene transfer using the SB system is unique in the field of oncology. Examples of cell engineering techniques that we expect to employ with the SB system are induced pluripotent stem cell (iPSC) processing technologies combined with Laser-enabled Analysis and Processing, or LEAP®, which consists of computerized image-based selection and laser processing for very rapid cell identification and purification as well as AttSite® Recombinases, which involves stable, targeted gene integration and expression with proprietary serine recombinases. We believe the advanced DNA vectors derived from SB can be used to avoid the expense and manufacturing difficulty associated with creating CAR-T cells using viral vectors. After electroporation, the transposon/transposase improves the efficiency of integration of plasmids used to express CAR and other transgenes in T cells. Propagation of genetically modified T cells on activating and propagating cells, or AaPC, provide a competitive advantage over other non-viral methods of modification. The SB system combined with artificial antigen-presenting cells can selectively propagate and thus retrieve CAR+ T cells suitable for human application. T cells can also be genetically modified using these technologies to target a panel (several) cancer antigen targets. We are on the verge of implementing technology to manufacture "minimally-manipulated" T cells within days of gene transfer by electroporation.

We expect this platform will rapidly integrate with Intrexon's RTS® and multigenic control gene programs. The programs are also designed and built for rapid transition to universal donor products or minimally manipulated point of care products. Dr. Laurence Cooper and colleagues at MD Anderson recently published research which demonstrated that transformed, primary, and pluripotent stem cells can be permanently modified to eliminate HLA-A expression, demonstrating how to generate a priori cells from one allogeneic donor for infusion into multiple recipients representing a significant step towards our goal of on-demand therapy that can be pre-deployed at multiple sites and infused when needed. The primary factor limiting the development of a universal donor product is the existence of graft-vs-host response, or GVHD. GVHD occurs because the newly transplanted cells regard the recipient's body as foreign. When this happens, the newly transplanted cells attack the recipient's body. Additional research from Dr. Cooper and colleagues at MD Anderson suggests that "universal" allogeneic T cells generated from one donor could be administered to multiple recipients. This is achieved by genetically editing CD19-specific CAR+ T cells to eliminate expression of the endogenous aß TCR, the gene responsible for triggering GVHD, without compromising CAR-dependent effector functions. Genetically modified T cells are generated using the SB system to stably introduce the CD19-specific CAR with subsequent permanent deletion of a or ß TCR chains with nucleases. The translation of the SB system and AaPC for use in clinical trials highlights how a nimble and cost-effective approach to developing genetically modified T cells can be used to implement clinical trials infusing next-generation T cells with improved therapeutic potential. We are expanding our initial trials targeting CD19 and planning to conduct additional trials with re-designed CAR-Ts expanding beyond CD19+ tumor cells.

Anticipated Milestones

We expect the following milestones to occur in 2015 and 2016:

- Intra-tumoral IL-12 RheoSwitch® programs:
  - Early data is expected in the fourth quarter of 2015 for our Phase 1/2 study in Breast Cancer with standard of care.
  - Early data is expected in the fourth quarter of 2015 for our Phase 1 study of Glioblastoma multiforme (GBM).
- CAR-T programs:
  - We expect to initiate two Phase 1 studies of next-generation CD19 CARs in the second quarter of 2015.
  - We expect to initiate a Phase 1 study of next-generation CAR with an inducible cytokine in the fourth quarter of 2015.
  - We expect to initiate a novel CAR for myeloid malignancies in the fourth quarter of 2015.
  - We expect to receive interim data on two Phase 1 CARs studies in advanced leukemia and lymphomas in the fourth quarter of 2015.
- We expect to initiate other leukemia and solid tumor CAR-T cell studies in 2016.
- We expect to initiate allogeneic, off-the-shelf T-cell studies in 2016.

Data from all programs is expected in 2015 and 2016. We are also evaluating additional potential preclinical candidates and continuing discovery efforts aimed at identifying other potential product candidates under our Channel Agreement with Intrexon. In addition, we may seek to enhance our pipeline in synthetic biology through focused strategic transactions, which may include acquisitions, partnerships and in-licensing activities. We are actively seeking to out-license some or all of our small molecule programs to further support our synthetic biology efforts.

Small Molecule Programs

In addition to our synthetic biology programs discussed above, we have certain rights to three small molecule programs, palifosfamide (or isophosphoramide mustard), darinaparsin and indibulin, all of which we are no longer actively pursuing. With respect to palifosfamide, in March 2013, we announced that the pivotal Phase 3 study, PICASSO 3, did not meet its primary endpoint of progression-free survival, and that we would terminate our development program in metastatic soft tissue sarcoma. In addition, we recently received the overall survival endpoint data from our study of palifosfamide in combination with carboplatin and etoposide chemotherapy versus carboplatin and etoposide alone in chemotherapy naïve patients with metastatic small cell lung cancer, which we refer to as MATISSE. This data will be submitted for presentation at a scientific forum during the first half of 2015.

We are seeking transactions with third parties for the possible out-license of palifosfamide. With respect to darinaparsin, we have entered into an amended and restated global licensing agreement with Solasia Pharma K.K., or Solasia, on July 31, 2014 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. During 2014, we determined to no longer pursue clinical development of indibulin.

Development plans

As of December 31, 2014, we have approximately $42.8 million of cash and cash equivalents. Taking into account our receipt of approximately $94.6 million in net proceeds from our February 2015 public offering of

common stock, and given our development plans, we anticipate cash resources will be sufficient to fund our operations into the first quarter of 2017. This 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, including the factors discussed in the "Risk Factors" section of this form 10-K and the uncertainties applicable to our forecast for the overall sufficiency of our capital resources. 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. In particular, 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 Intrexon, agreed to enter into a research and development agreement pursuant to which we will 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 and $20 million per year. In addition, we also expect to enter into additional collaboration and technology transfer agreements with MD Anderson and Intrexon 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. Further, in light of our entry into the MD Anderson License, we expect to establish operations in Houston, Texas that will enable us to join and collaborate with the MD Anderson academic and medical community, which may require that we add headcount in the future, and which could add to our general and administrative expenses going forward. 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 was entered into on January 13, 2015 and is only beginning to be implemented, therefore the actual costs associated therewith may be significantly in excess of forecasted amounts.

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.

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 in order 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 Intrexon Corporation

On January 6, 2011, we entered into an Exclusive Channel Partner Agreement, or the Channel Agreement, with Intrexon that governs a "channel partnering" arrangement in which we use Intrexon's technology directed towards *in vivo* expression of effectors in connection with the development of Ad-RTS-IL-12 + veledimex and DC-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 establishes committees comprised of representatives of us and Intrexon 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 Intrexon 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 collectively refer 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 the rights described without Intrexon'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. Intrexon is responsible for the costs of 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 Intrexon's patents.

Subject to certain expense allocations and other offsets provided in the Channel Agreement, we will pay Intrexon on a quarterly basis 50% of net profits derived in that quarter from the sale of ZIOPHARM Products, calculated on a ZIOPHARM Product-by- ZIOPHARM Product basis. We have likewise agreed to pay Intrexon 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 Intrexon (see Note 2 to the financial statements, Financings).

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 Intrexon 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 Intrexon following an unconsented assignment by us or our election not to pursue development of a Superior Therapy).

Our obligation to pay 50% of net profits or revenue described above with respect to these "retained" products will survive termination of the Channel Agreement.

License Agreement—The University of Texas M. D. Anderson Cancer Center

On January 13, 2015, we, together with Intrexon, entered into a license agreement, or the License, with MD Anderson. Pursuant to the License, we and Intrexon hold an exclusive, worldwide license to certain technologies owned and licensed by MD Anderson including technologies relating to novel chimeric antigen receptor (CAR) T-cell therapies arising from the laboratory of Laurence Cooper, M.D., Ph.D., professor of pediatrics at MD Anderson, as well as either co-exclusive or non-exclusive licenses under certain related technologies.

Pursuant to the terms of the License, MD Anderson will receive, within sixty days of the date of the License, consideration of $50 million in shares of our common stock (or 10,124,561 shares), and $50 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 announcement of the entry into the License, collectively referred to as the License Shares, pursuant to the terms of the License Shares Securities Issuance Agreement described below. We and Intrexon also agreed to reimburse MD Anderson for out of pocket expenses for maintaining patents covering the licensed technologies.

In addition, pursuant to the License, MD Anderson has agreed to transfer to us certain existing research programs described in the License and to grant to Intrexon and us certain additional technology rights related thereto. In connection with such transfer, the terms of the License also require us and Intrexon to enter into a research and development agreement with MD Anderson pursuant to which we will provide funding for certain research and development activities of MD Anderson for a period of three years, in an amount between $15 and $20 million per year. The first quarterly payment of $3.75 million due under this arrangement is required to be made by us within 60 days of the date of the License.

The term of the 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 License; provided, however, that following the expiration of the term, we and Intrexon 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 License and subject to a 90 day cure period, MD Anderson will have the right to convert the License into a non-exclusive license if we and Intrexon 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 License and subject to a 180 day cure period, MD Anderson will have the right to terminate the License with respect to specific technology(ies) funded by the government or subject to a third party contract if we and Intrexon 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 License if we and Intrexon fail to timely deliver the shares due in consideration for the License. MD Anderson may also terminate the agreement with written notice upon material breach by us and Intrexon, if such breach has not been cured within 60 days of receiving such notice. In addition, the License will terminate upon the occurrence of certain insolvency events for both us and Intrexon and may be terminated by the mutual written agreement of us, Intrexon and MD Anderson.

On January 9, 2015, in order to induce MD Anderson to enter into the License on an accelerated schedule, we and Intrexon entered into a letter agreement, or the Letter Agreement, pursuant to which MD Anderson will receive consideration of $7.5 million in shares of the 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 the our and Intrexon's common stock ending on the date prior to the Letter Agreement, collectively referred to as the Incentive Shares, in the event that the License was entered into on or prior to 8:00 am pacific time on January 14, 2015, referred to as the Accelerated Closing Deadline. The Incentive Shares will be issued to MD Anderson within sixty days of the date of the License pursuant to the terms of the Incentive Shares Securities Issuance Agreement described below.

In connection with the entry into the License, on January 13, 2015, we entered into a Securities Issuance Agreement with MD Anderson, or the License Shares Securities Issuance Agreement, pursuant to which we agreed to issue and sell the License Shares to MD Anderson in consideration for the License. The closing of the issuance and sale of the License Shares under the License Shares Securities Issuance Agreement will occur within sixty days of the date of the License, subject to customary closing conditions.

In connection with the entry into the Letter Agreement, on January 13, 2015, we entered into a Securities Issuance Agreement with MD Anderson, or the Incentive Shares Securities Issuance Agreement, pursuant to which we agreed to issue and sell the Incentive Shares to MD Anderson in consideration for the execution and delivery of the License on or prior to the Accelerated Closing Deadline in connection with the Letter Agreement.

The closing of the issuance and sale of the Incentive Shares under the Incentive Shares Securities Issuance Agreement will occur within sixty days of the date of the License, subject to customary closing conditions.

Also in connection with the License and the issuance of the License Shares and the Incentive Shares, on January 13, 2015, we and MD Anderson entered into a Registration Rights Agreement, or the Registration Rights Agreement, pursuant to which 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 our common stock held by MD Anderson on the date that the Registration Statement is filed, within 15 days of the closing under the License Shares Securities Issuance Agreement. Under the Registration Rights Agreement, we are obligated to use our reasonable best efforts to cause the Registration Statement to be declared effective as promptly as practicable after filing and in no event later than 120 days of the closing under the License Shares Securities Issuance Agreement and 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.

License Agreement with DEKK-Tec, Inc.

On October 15, 2004, the Company entered into a license agreement with DEKK-Tec, Inc., pursuant to which it was granted an exclusive, worldwide license for palifosfamide.

In consideration for the license rights, DEKK-Tec is entitled to receive payments upon achieving certain milestones in varying amounts which on a cumulative basis may total $4.0 million. Of the aggregate milestone payments, most will be creditable against future royalty payments as referenced below. Additionally, the Company issued DEKK-Tec an option to purchase 27,616 shares of the Company's common stock for $0.02 per share, of which 13,808 options are still outstanding. DEKK-Tec is entitled to receive single digit percentage royalty payments on the sales of palifosfamide should it be approved for commercial sale. The Company's obligation to pay royalties will terminate on a country-by-country basis upon the expiration of all valid claims of patents in such country covering licensed product, subject to earlier termination in the event of defaults by the parties under the license agreement. No milestones under the license agreement have been reached or expensed since 2010.

License Agreement with Southern Research Institute

On December 22, 2004, the Company entered into an Option Agreement with the Southern Research Institute, or SRI, pursuant to which the Company was granted an exclusive option to obtain an exclusive license to SRI's interest in certain intellectual property, including exclusive rights related to certain isophosphoramide mustard analogs. On February 5, 2007, the Company exercised its option and entered into the exclusive license agreement. Under the license agreement, the Company is required to remit minimum annual royalty payments of $25 thousand until the first commercial sale of a licensed product. These payments were made for the years ended December 31, 2014, 2013, and 2012. The Company may be required to make payments upon achievement of certain milestones in varying amounts which on a cumulative basis could total up to $775 thousand. In addition, SRI will be entitled to receive single digit percentage royalty payments on the sales of a licensed product in any country until all licensed patents rights in that country which are utilized in the product have expired. No milestones under the license agreement were reached or expensed since the agreement's inception.

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

On August 24, 2004, we entered into a patent and technology license agreement with The Board of Regents of the University of Texas System, acting on behalf of The University of Texas M. D. Anderson Cancer Center 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.

The Company issued options to purchase 50,222 shares outside the 2003 Stock Option Plan for $0.002 per share following the successful completion of certain clinical milestones, of which 37,666 have vested. The remaining 12,556 shares will vest 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. In addition, the Licensors are entitled to receive certain milestone payments. The Company may be required to make additional payments 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.

The license agreement also contains other provisions customary and common in similar agreements within the industry, such as the right to sublicense the Company rights under the agreement. However, if the Company sublicenses its rights prior to the commencement of a pivotal study i.e. a human clinical trial intended to provide the substantial evidence of efficacy necessary to support the filing of an approvable NDA, the Licensors will be entitled to receive a share of the payments received by the Company in exchange for the sublicense (subject to certain exceptions). The term of the license agreement extends until the expiration of all claims under patents and patent applications associated with the licensed technology, subject to earlier termination in the event of defaults by the Company or the Licensors under the license agreement, or if the Company becomes bankrupt or insolvent. No milestones under the license agreement were reached or expensed during the years ended December 31, 2014, 2013, or 2012.

Collaboration Agreement with Solasia Pharma K.K.

On March 7, 2011, the Company entered into a License and Collaboration Agreement with Solasia Pharma K.K., or Solasia.

Pursuant to the License and Collaboration Agreement, the Company granted Solasia an exclusive license to develop and commercialize darinaparsin in both IV and oral forms and related organic arsenic molecules, in all indications for human use in a pan- Asian/Pacific territory comprised of 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. Under the License and Collaboration Agreement, the Company provided Solasia with drug product to conduct clinical trials. These transfers were accounted for as a reduction of research and development costs and an increase in collaboration receivables. The agreement provides that Solasia will be responsible for the development and commercialization of darinaparsin in the pan-Asian/Pacific territory.

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

The $5.0 million upfront payment received in March 2011 is being amortized over the period of the Company's research and development effort. The Company originally estimated this period to be 75 months. In accordance with the amended and restated License and Collaboration Agreement with Solasia, the Company is no longer obligated to continue their research and development efforts in connection with the upfront payment. However, there are certain deliverables that are included in the amended and restated License and Collaboration Agreement including transfer of intellectual property and prior research and development results, which were originally estimated by management to be completed by March 31, 2015 when the amended and restated License and Collaboration Agreement was signed in July 2014. Management reassessed the period of performance related to the remaining transitional services to be completed under the agreement and determined that the services are now expected to be completed by December 31, 2015. As a result, the Company has determined that the estimated remaining period for delivering the transitional services at September 30, 2014 was 15 months through December 31, 2015. Accordingly, the Company has recorded $1.4 million in revenue during the twelve months ended December 31, 2014 while the remaining deferred revenue balance of $1.4 million at December 31, 2014 has been classified as current.

License Agreement with Baxter Healthcare Corporation

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 each of the years ended December 31, 2014, 2013, and 2012, the installment payments of $250 thousand were met and expensed.

Collaboration Agreement with Harmon Hill, LLC

On April 8, 2008, the Company signed a collaboration agreement for Harmon Hill, LLC, or Harmon Hill, to provide consulting and other services for the development and commercialization of oncology therapeutics by ZIOPHARM. The Company expensed $200 thousand during the year ended December 31, 2012 under this agreement. This agreement expired on November 8, 2012.

On June 27, 2013, the Company signed a new collaboration agreement with Harmon Hill to provide consulting and other services for the development and commercialization of oncology therapeutics by ZIOPHARM, effective April 1, 2013. Under the agreement the Company has agreed to pay Harmon Hill $15 thousand per month for the consulting services. Subject to renewal or extension by the parties, the term of the agreement is for a one year period. The Company expensed $135 thousand and $180 thousand for the years ended December 31, 2013 and 2014, respectively.

CRO Services Agreement with Novella Clinical, Inc.

On December 4, 2008, the Company entered into a Master Clinical Research Organization Services Agreement with Novella Clinical, Inc., or Novella, under which Novella provides CRO services in support of our clinical trials. The work order for the newest trial being conducted by Novella was signed on November 2, 2012. Novella was entitled to cumulative payments of up to $790 thousand under these arrangements, which is payable in varying amounts upon Novella achieving specified milestones. During the year ended December 31, 2012, the Company expensed $256 thousand upon the achievement of various milestones. During the year ended December 31, 2013, two database related milestones and one site activation related milestone were met and expensed totaling $136 thousand.

On August 18, 2014 and November 6, 2014, the Company entered into two amendments of the Master Clinical Research Organization Services Agreement with Novella. The amendment reflects the removal of data management, statistical and clinical study report services, as well as a change in the timeline and scope of clinical trial support. During the year ended December 31, 2014, three clinical milestones were met and expensed totaling $236 thousand.

CRO Services Agreement with MS Clinical Services, LLC.

On July 24, 2014, the Company entered into a Master Clinical Research Organization Services Agreement with MS Clinical Services, LLC., or Medsource, under which Medsource provides CRO services in support of our clinical trials. There are no milestones associated with this agreement.

CRO Services Agreement with PPD Development, L. P.

The Company was party to a Master Clinical Research Organization Services Agreement with PPD Development, L. P., or PPD, dated January 29, 2010, a related work order dated June 25, 2010 and a related work order dated April 8, 2011 under which PPD provides clinical research organization, or CRO, services in support of the Company's clinical trials. During the years ended December 31, 2012 and 2013, the Company expensed $3.8 million and $9.2 million respectively. There are no remaining milestones related to this agreement.

CRO Services Agreement with Pharmaceutical Research Associates, Inc.

On December 13, 2011, the Company entered into a Master Clinical Research Organization Services Agreement with Pharmaceutical Research Associates, Inc., or PRA, under which PRA provides CRO services in support of our clinical trials. During the years ended December 31, 2012 and 2013, the Company expensed $7.3 million and $2.2 million, respectively. There are no remaining milestones related to this agreement.

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 Factors*"* section of this report for information about certain risks and uncertainties that may affect our patent position and proprietary rights.

Additional information as of December 31, 2014 about material patents and other proprietary rights covering our product candidates is set forth below.

Palifosfamide

The patent estate covering palifosfamide compositions, methods of use, methods of manufacture, formulations, combination therapies and analogs includes seven issued U.S. patents (one of which is scheduled to expire in 2031, one of which is scheduled to expire in 2030, two of which are scheduled to expire in 2029, one of which is scheduled to expire in 2027, one of which is scheduled to expire in 2025, and one of which is scheduled to expire in 2020), four pending U.S. patent applications, sixty-five issued foreign patents in Europe, Canada, Japan and Australia and other countries and thirty-five pending foreign patent applications in Europe, Canada, Japan, Australia and other countries. Some of these patent assets are in-licensed from DEKK-Tec, Inc., some are in-licensed from Southern Research Institute, and some are owned by us.

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

The patent estate licensed to us by Intrexon covering Ad-RTS-IL-12 + veledimex and DC-RTS-IL-12 + veledimex compositions, methods of use, methods of manufacture, and formulations includes over one hundred issued U.S. patents and applications which are scheduled to expire starting in 2018 and include coverage through at least 2031. 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.

Darinaparsin

The patent estate covering darinaparsin compositions, methods of use, methods of manufacture, formulations, polymorphic forms, analogs and combination therapies includes ten issued U.S. patents (two of which are scheduled to expire in 2029, one of which is scheduled to expire in 2027, three of which are scheduled to expire in 2026, one of which is scheduled to expire in 2025 and three of which are scheduled to expire in 2023), three pending U.S. patent applications, forty issued foreign patents in Europe, Japan, Australia and other countries and fifty-one pending foreign patent applications in Europe, Canada, Japan, Australia and other countries. Some of these patent assets are in-licensed from The University of Texas M. D. Anderson Cancer Center and the Texas A&M University System and some have been assigned to Solasia.

CAR-T Cells

We have recently in-licensed from The University of Texas M.D. Anderson Cancer Center a technology portfolio that includes intellectual property directed to certain CAR-T cell 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 The University of Texas M.D. Anderson Cancer Center intellectual property flow to the Company via our agreement with Intrexon.

Governmental Regulation

The research, development, testing, manufacture, labeling, promotion, advertising, distribution, and marketing, among other things, of our products are extensively regulated by governmental authorities in the United States and other countries. In the United States, the FDA regulates drugs under the Federal Food, Drug, and Cosmetic Act, or the FDCA, and biologics under the Public Health Service Act, or PSHA, as well as their respective implementing regulations. Failure to comply with the applicable U.S. requirements may subject us to administrative or judicial sanctions, such as FDA refusal to approve pending NDAs or Biologics License Applications, or BLAs, warning letters, product recalls, product seizures, total or partial suspension of production or distribution, injunctions, and/or criminal prosecution. Moreover, if our product candidates are approved by the FDA, government coverage and reimbursement policies will both directly and indirectly affect our ability to successfully commercialize our product candidates, and such coverage and reimbursement policies will be affected by future healthcare reform measures. In addition, we may be subject to state and federal laws, including anti-kickback statutes and false claims statutes as well as data privacy laws that restrict certain business practices in the biopharmaceutical industry.

Product Approval Process. None of our product candidates may be marketed in the United States until it has received FDA approval. The steps required before a drug or biologic product may be marketed in the United States include:

- Preclinical laboratory tests, animal studies, and formulation studies;
- Submission to the FDA of an IND for human clinical testing, which must become effective before human clinical trials may begin;
- Adequate and well-controlled human clinical trials to establish the safety and efficacy of the product for each indication;
- Submission to the FDA of NDA or BLA;
- Satisfactory completion of an FDA inspection of the manufacturing facility or facilities at which the product is produced to assess compliance with current good manufacturing practices, or cGMPs; and
- FDA review and approval of the NDA or BLA.

Preclinical tests include laboratory evaluation of product chemistry, pharmacokinetics, toxicity, immunogenicity and formulation, as well as animal studies. The conduct of the preclinical tests and formulation of the products for testing must comply with federal regulations and requirements. The results of the preclinical tests, together with manufacturing information and analytical data, are submitted to the FDA as part of an IND application, which must become effective before human clinical trials may begin. An IND automatically takes effect 30 calendar days after receipt by the FDA, unless before that time the FDA applies a clinical hold and raises safety concerns or questions about issues such as the design of the trials as outlined in the IND. In such a case, the IND sponsor and the FDA must resolve any outstanding FDA concerns or questions before clinical trials may proceed. We cannot be certain that submission of an IND will result in the FDA allowing a clinical trial to be initiated.

Clinical trials involve the administration of an investigational drug or biologic to human subjects under the supervision of qualified investigators. Clinical trials are conducted according to protocols that detail the study objectives, the parameters to be used in monitoring participants' safety, and the effectiveness criteria by which the investigational product will be evaluated. Each protocol must be submitted to the FDA as part of the IND.

Clinical trials are typically conducted in three sequential phases, but the phases may overlap. The study protocol and informed consent information for study subjects in a clinical trial must also be approved by an Institutional Review Board for each institution where the trial will be conducted. Study subjects must sign an informed consent form before participating in a clinical trial. Phase 1 usually involves the initial introduction of the investigational product into people to evaluate its short-term safety, dosage tolerance, metabolism,

pharmacokinetics, and pharmacologic actions and, if possible, to gain an early indication of its effectiveness. Phase 2 usually involves trials in a limited patient population in order to (1) evaluate dosage tolerance and appropriate dosage; (2) identify possible adverse effects and safety risks; and (3) evaluate preliminarily the efficacy of the drug for specific indications. Phase 3 trials usually continue to evaluate clinical efficacy and further test for safety by using the product in its final form in an expanded patient population. There can be no assurance that Phase 1, Phase 2, or Phase 3 testing will be completed successfully within any specified period of time, if at all. Furthermore, the sponsoring company or the FDA may suspend clinical trials at any time on various grounds, including a finding that the subjects or patients are being exposed to an unacceptable health risk.

The FDCA permits the FDA and the IND sponsor to agree in writing on the design and size of clinical studies intended to form the primary basis of a claim of effectiveness in an NDA or BLA. This process is known as Special Protocol Assessment, or SPA, and can be a somewhat lengthy process. An agreement may not be changed by the sponsor or the FDA after the trial begins, except (1) with the written agreement of the sponsor and the FDA, or (2) if the director of the FDA reviewing division determines that "a substantial scientific issue essential to determining the safety or effectiveness of the drug" was identified after the testing began.

Assuming successful completion of the required clinical testing, the results of the preclinical studies and of the clinical studies, together with other detailed information, including information on the manufacture and composition of the product candidate, are submitted to the FDA in the form of an NDA or BLA requesting approval to market the product for one or more indications. The testing and approval process requires substantial time, effort, and financial resources. The FDA reviews the application and may deem it to be inadequate to support the registration, and companies cannot be sure that any approval will be granted on a timely basis, if at all. The FDA may also refer the application to the appropriate external advisory committee, typically a panel of clinicians, for review, evaluation and a recommendation as to whether the application should be approved. The FDA is not bound by the recommendations of the advisory committee.

The goals of the NDA/BLA are to provide enough information to permit FDA to reach the following key decisions:

- Is the product safe and effective in its proposed use(s), and do its benefits outweigh its risks?
- Is the product's proposed labeling (package insert) appropriate, and what should it contain? Are measures necessary to mitigate risks of use of the product (referred to as Risk Evaluation and Mitigation Strategies, or REMS)?
- Are the methods used in manufacturing the product and the controls used to maintain its quality adequate to preserve identity, strength, quality, and purity?

The FDA has various programs, including orphan drug, fast track, priority review, and accelerated approval, which are intended to expedite or simplify the process for developing and reviewing drugs, and/or provide for approval on the basis surrogate endpoints, or provide financial incentives and market exclusivity. Generally, drugs that may be eligible for one or more of these programs are those for serious or life-threatening conditions, those with the potential to address unmet medical needs, and those that provide meaningful benefit over existing treatments. A company cannot be certain that any of its investigational drugs will qualify for any of these programs, or that, if a drug does qualify, the review time will be reduced.

Before approving an NDA or BLA, the FDA usually will inspect the facility or the facilities at which the drug is manufactured and will not approve the product unless cGMP compliance is satisfactory. If the FDA evaluates the NDA or BLA and the manufacturing facilities and deems them to be acceptable, the FDA may issue an approval letter, or in many cases, a complete response letter. The complete response letter contains the conditions that must be met in order to secure final approval of the NDA or BLA. When and if those conditions have met with the FDA's satisfaction, the FDA will issue an approval letter. The approval letter authorizes commercial

marketing of the drug or biologic for specific indications. As a condition of NDA/BLA approval, the FDA may require post-marketing testing and surveillance to monitor the drug's safety or efficacy, or impose other conditions.

After approval, certain changes to the approved drug product, such as adding new indications, initiating certain manufacturing changes, or making certain additional labeling claims, are subject to further FDA review and approval. Before a company can market a drug product for any additional indication(s), it must obtain additional approval from the FDA. Obtaining approval for a new indication generally requires that additional clinical studies be conducted. A company cannot be sure that any additional approval for new indications for any product candidate will be approved on a timely basis, or at all.

Post-approval Requirements. Often times, even after a drug has been approved by the FDA for sale, the FDA may require that certain post-approval requirements be satisfied, including the conduct of additional clinical studies. If such post-approval conditions are not satisfied, the FDA may withdraw its approval of the drug. In addition, holders of an approved NDA are required to: (1) report certain adverse reactions to the FDA; (2) comply with certain requirements concerning advertising and promotional labeling for their products; and (3) continue to have quality control and manufacturing procedures conform to cGMP. The FDA periodically inspects the sponsor's records relating to safety reporting and/or manufacturing facilities; this latter effort includes assessment of cGMP compliance. Accordingly, manufacturers must continue to expend time, money, and effort in the area of production and quality control to maintain cGMP compliance. We intend to use third-party manufacturers to produce our products in clinical and commercial quantities, and future FDA inspections may identify compliance issues at the facilities of our contract manufacturers that may disrupt production or distribution, or require substantial resources to correct. In addition, discovery of problems with a product after approval may result in restrictions on a product, manufacturer, or holder of an approved NDA or BLA, including withdrawal of the product from the market.

Patent Challenge Process Regarding ANDAs. The Hatch-Waxman Act provides incentives for generic pharmaceutical manufacturers to challenge patents on branded pharmaceutical products and/or their methods of use, as well as to develop products comprising non-infringing forms of the patented drugs. The Hatch-Waxman legislation places significant burdens on the Abbreviated New Drug Application, or ANDA, filer to ensure that such challenges are not frivolous, but also offers the opportunity for significant financial reward if the challenge is successful.

If there is a patent listed for the branded drug in the FDA's Orange Book at the time of submission of the ANDA or at any time before the ANDA is approved and the generic company intends to market the generic equivalent prior to the expiration of that patent, the generic company includes a certification asserting that the patent is invalid, unenforceable and/or not infringed, a so-called "paragraph IV certification."

After receiving notice from the FDA that its application is acceptable for review or immediately if the ANDA has been amended to include a paragraph IV certification after the application was submitted to the FDA, the company filing a generic application is required to send the patent holder and the holder of the NDA for the brand-name drug a notice explaining why it believes that the patents in question are invalid, unenforceable or not infringed. Upon receipt of the notice from the generic applicant, the patent holder has 45 days during which to bring a patent infringement suit in federal district court against the generic applicant in order to obtain the 30 month automatic stay.

If a suit is commenced by the patent holder during the 45-day period, the Hatch-Waxman Act provides for an automatic stay on the FDA's ability to grant final approval of the ANDA for the generic product. Patent holders may only obtain one 30-month stay with respect to patents that were listed at the time an ANDA was filed. The period during which the FDA may not approve the ANDA and the patent challenger therefore may not market the generic product is 30 months, or such other period as may be ordered by the court. The 30-month period may or may not, and often does not, coincide with the timing of the resolution of the lawsuit or the expiration of a

patent, but if the patent challenge is successful or the challenged patent expires during the 30-month period, the FDA may approve the generic drug for marketing, assuming there are no other obstacles to approval such as periods of non-patent exclusivity given to the NDA holder.

Under the Hatch-Waxman Act, any developer of a generic drug that is considered first to have filed its ANDA for review by the FDA, and whose filing includes a paragraph IV certification, may be eligible to receive a 180-day period of generic market exclusivity. This period of market exclusivity may provide the patent challenger with the opportunity to earn a return on the risks taken and its legal and development costs and to build its market share before other generic competitors can enter the market. If the ANDA of the first applicant accepted for filing is withdrawn, the 180-day exclusivity period is forfeited and unavailable to any other applicant.

Coverage and Reimbursement. Market acceptance and sales of any product candidates that we develop will depend on coverage and reimbursement policies of third-party payors and may be affected by future healthcare reform measures. Government health administration authorities, private health insurers and other organizations generally decide which drugs they will pay for and establish reimbursement levels for health care. In particular, in the U.S., private health insurers and other third-party payers often provide reimbursement for products and services based on the level at which the government (through the Medicare or Medicaid programs) provides reimbursement for such treatments. In the U.S., the European Union and other potentially significant markets for our product candidates, government authorities and third-party payers are increasingly attempting to limit or regulate the price of medical products and services, particularly for new and innovative products and therapies, which has resulted in lower average selling prices. Further, the increased emphasis on managed healthcare in the U.S. and on country and regional pricing and reimbursement controls in the European Union will put additional pressure on product pricing, reimbursement and usage, which may adversely affect our future product sales and results of operations. These pressures can arise from rules and practices of managed care groups, judicial decisions and governmental laws and regulations related to Medicare, Medicaid and healthcare reform, pharmaceutical reimbursement policies and pricing in general.

In the United States and foreign jurisdictions, there have been a number of legislative and regulatory changes to the healthcare system that could affect our future results of operations. In particular, there have been and continue to be a number of initiatives at the United States federal and state level that seek to reduce healthcare costs. The Medicare Prescription Drug, Improvement, and Modernization Act of 2003, or the MMA, imposed new requirements for the distribution and pricing of prescription drugs for Medicare beneficiaries. Under Part D, Medicare beneficiaries may enroll in prescription drug plans offered by private entities which provide coverage of outpatient prescription drugs. Part D plans include both stand-alone prescription drug benefit plans and prescription drug coverage as a supplement to Medicare Advantage plans. Unlike Medicare Part A and B, Part D coverage is not standardized. Part D prescription drug plan sponsors are not required to pay for all covered Part D drugs, and each drug plan can develop its own drug formulary that identifies which drugs it will cover and at what tier or level. However, Part D prescription drug formularies must include drugs within each therapeutic category and class of covered Part D drugs, though not necessarily all the drugs in each category or class. Any formulary used by a Part D prescription drug plan must be developed and reviewed by a pharmacy and therapeutic committee. Government payment for some of the costs of prescription drugs may increase demand for our products for which we receive marketing approval. However, any negotiated prices for our future products covered by a Part D prescription drug plan will likely be lower than the prices we might otherwise obtain. Moreover, while the MMA applies only to drug benefits for Medicare beneficiaries, private payors often follow Medicare coverage policy and payment limitations in setting their own payment rates. Any reduction in payment that results from Medicare Part D may result in a similar reduction in payments from non-governmental payors.

The American Recovery and Reinvestment Act of 2009 provides funding for the federal government to compare the effectiveness of different treatments for the same illness. A plan for the research will be developed by the Department of Health and Human Services, the Agency for Healthcare Research and Quality and the National Institutes for Health, and periodic reports on the status of the research and related expenditures will be made to

Congress. Although the results of the comparative effectiveness studies are not intended to mandate coverage policies for public or private payors, it is not clear what effect, if any, the research will have on the sales of any product, if any such product or the condition that it is intended to treat is the subject of a study. It is also possible that comparative effectiveness research demonstrating benefits in a competitor's product could adversely affect the sales of our product candidates. If third-party payors do not consider our products to be cost-effective compared to other available therapies, they may not cover our products as a benefit under their plans or, if they do, the level of payment may not be sufficient to allow us to sell our products on a profitable basis.

The U.S. and some foreign jurisdictions are considering or have enacted a number of additional legislative and regulatory proposals to change the healthcare system in ways that could affect our ability to sell our products profitably. Among policy makers and payers in the U.S. and elsewhere, there is significant interest in promoting changes in healthcare systems with the stated goals of containing healthcare costs, improving quality and/or expanding access. In the U.S., the pharmaceutical industry has been a particular focus of these efforts and has been significantly affected by major legislative initiatives, including, most recently, the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Affordability Reconciliation Act, or collectively, the PPACA, which became law in the U.S. in March 2010 and substantially changes the way healthcare is financed by both governmental and private insurers.

Federal and State Fraud and Abuse Laws. In addition to FDA restrictions on marketing of pharmaceutical products, several other types of state and federal laws have been applied to restrict certain business practices in the biopharmaceutical industry in recent years. These laws include anti-kickback and false claims statutes.

The federal Anti-Kickback Statute prohibits, among other things, knowingly and willfully offering, paying, soliciting, or receiving remuneration to induce or in return for purchasing, leasing, ordering, or arranging for the purchase, lease, or order of any healthcare item or service reimbursable under Medicare, Medicaid, or other federally financed healthcare programs. The term "remuneration" has been broadly interpreted to include anything of value, including for example, gifts, discounts, the furnishing of supplies or equipment, credit arrangements, payments of cash, waivers of payment, ownership interests and providing anything at less than its fair market value. The Anti-Kickback Statute has been interpreted to apply to arrangements between pharmaceutical manufacturers on one hand and prescribers, purchasers, and formulary managers on the other. Although there are a number of statutory exemptions and regulatory safe harbors protecting certain common activities from prosecution, the exemptions and safe harbors are drawn narrowly, and our practices may not in all cases meet all of the criteria for statutory exemptions or safe harbor protection. Practices that involve remuneration that may be alleged to be intended to induce prescribing, purchases, or recommendations may be subject to scrutiny if they do not qualify for an exemption or safe harbor. 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 statute has been violated. The reach of the Anti-Kickback Statute was also broadened by the PPACA, which, among other things, amends the intent requirement of the federal Anti-Kickback Statute. Pursuant to the statutory amendment, a person or entity no longer needs to have actual knowledge of this statute or specific intent to violate it in order to have committed a violation. In addition, the PPACA 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 civil False Claims Act (discussed below) or the civil monetary penalties statute, which imposes penalties against any person who is determined to have presented or caused to be presented a claim to a federal health program that the person knows or should know is for an item or service that was not provided as claimed or is false or fraudulent.

The federal False Claims Act prohibits any person from knowingly presenting, or causing to be presented, a false claim for payment to the federal government or knowingly making, using, or causing to be made or used a false record or statement material to a false or fraudulent claim to the federal government. As a result of a modification made by the Fraud Enforcement and Recovery Act of 2009, a claim includes "any request or demand" for money or property presented to the U.S. government. Recently, several pharmaceutical and other healthcare companies

have been prosecuted under these laws for allegedly providing free product to customers with the expectation that the customers would bill federal programs for the product. Other companies have been prosecuted for causing false claims to be submitted because of the companies' marketing of the product for unapproved, and thus non-reimbursable, uses. Many states also have statutes or regulations similar to the federal Anti-Kickback Statute and False Claims Act, which state laws apply to items and services reimbursed under Medicaid and other state programs, or, in several states, apply regardless of the payer. Also, the federal Health Insurance Portability and Accountability Act of 1996, or HIPAA, created new federal criminal statutes that prohibit knowingly and willfully executing a scheme to defraud any healthcare benefit program, including private third-party payers 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.

Because of the breadth of these laws and the narrowness of the federal Anti-Kickback Statute's safe harbors, it is possible that some of our business activities could be subject to challenge under one or more of such laws. Such a challenge could have a material adverse effect on our business, financial condition and results of operations. If we obtain FDA approval for any of our product candidates and begin commercializing those products in the United States, our operations may be directly, or indirectly, through our customers, distributors, or other business partners, subject to various federal and state fraud and abuse laws, including, without limitation, anti-kickback statutes and false claims statutes. These laws may impact, among other things, our proposed sales, marketing and education programs.

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 and Clinical Health Act, or HITECH, and its implementing regulations, imposes certain requirements relating to the privacy, security and transmission of individually identifiable health information. Among other things, HITECH makes HIPAA's privacy and security standards directly applicable to "business associates"—independent contractors or agents of covered entities that receive or obtain protected health information in connection with providing a service on behalf of a covered entity. HITECH also increased the civil and criminal penalties that may be imposed against covered entities, business associates and possibly other persons, and gave state attorneys general new authority to file civil actions for damages or injunctions in federal courts to enforce the federal HIPAA laws and seek attorney's fees and costs associated with pursuing federal civil actions. In addition, state laws govern the privacy and security of health information in certain circumstances, many of which differ from each other in significant ways and may not have the same effect, thus complicating compliance efforts.

If our operations are found to be in violation of any of the federal and state laws described above or any other governmental regulations that apply to us, we may be subject to penalties, including criminal and significant civil monetary penalties, damages, fines, imprisonment, exclusion of products from reimbursement under government programs, and the curtailment or restructuring of our operations, any of which could adversely affect our ability to operate our business and our results of operations. To the extent that any of our product candidates are ultimately sold in a foreign country, we may be subject to similar foreign laws and regulations, which may include, for instance, applicable post-marketing requirements, including safety surveillance, anti-fraud and abuse laws, and implementation of corporate compliance programs and reporting of payments or transfers of value to healthcare professionals.

Employees

As of February 10, 2015 we had 27 employees.

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 effect 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 Commission 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. Our internet site is www.ziopharm.com. None of the information on our internet site is part of this report, unless expressly noted.

Available Information

Our website address is www.ziopharm.com. Information contained on our website is not incorporated by reference into this report unless expressly noted. 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 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 consider carefully 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, through our License with MD Anderson and Intrexon and our Channel Agreement with Intrexon, nonviral adoptive cellular therapies based on designer cytokines and novel chimeric antigen receptor (CAR) T-cell therapies are new approaches to cancer treatment that present significant challenges in a competitive landscape and the success of our efforts depends in large part on our owned and licensed intellectual property, and our efforts may be affected by litigation and developments in intellectual property law outside of our control.

We intend to employ technologies licensed from MD Anderson pursuant to the MD Anderson License described above in "Summary—Recent developments", and from Intrexon, pursuant to our existing Channel Agreement with Intrexon, to pursue the development and commercialization of nonviral adoptive cellular therapies based on cytokines and CARs under control of the RTS® technology 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 T-cell therapies for cancer;
- developing and deploying consistent and reliable processes for engineering a patient's T-cells ex vivo and infusing the engineered T-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;
- 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; and
- not infringing the intellectual property rights, in particular, the patent rights, of third parties, including competitors developing alternative CAR T-cell therapies

We cannot be sure that T-cell immunotherapy technologies that we intend to develop in partnership with MD Anderson and Intrexon 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.

Our CAR-T 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 CAR-T product candidates, and any failure to obtain, or delays in obtaining, sponsorship of investigational new drug applications, or INDs, or in filing new 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, 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 conduct by MD Anderson to date may not be replicated in future clinical trials. Our CAR-T 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 CAR-T and other early-stage product candidate development programs may adversely affect our ability to continue development and commercialization of our synthetic biology product candidates.

The biopharmaceutical industry, and the rapidly evolving market for developing genetically engineered T-cells in particular, is characterized by intense competition and rapid innovation. Genetically engineering T-cells faces significant competition in the CAR technology space from multiple companies and their collaborators, such as Novartis/University of Pennsylvania, Bluebird bio/Celgene/Baylor College of Medicine, Kite Pharma/National Cancer Institute, Juno Therapeutics/Fred Hutchinson Cancer Research Center/Memorial Sloan-Kettering Cancer Center/Seattle Children's Research Institute, Cellectis/Pfizer and Adaptimmune/GSK. We face competition from non-cell based treatments offered by other companies such as Amgen, AstraZeneca, Bristol-Myers, Incyte, Merck, and Roche. 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. 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.

We are dependent on patents, know-how, and proprietary technology that are licensed from others, particularly MD Anderson and Intrexon. 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 Intrexon, 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 Intrexon 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 with MD Anderson; 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, 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 U.S. PTO, 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, 2014, we had a net loss of $31.8 million, and, as of December 31, 2014, we have incurred approximately $372.6 million of cumulative net losses 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 Intrexon, 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 License with MD Anderson; and
- Commence providing funding for certain research and development activities of MD Anderson pursuant to the terms of the 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 synthetic biology, 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, 2014, we have approximately $42.8 million of cash and cash equivalents. Taking into account our receipt of approximately $94.6 million in net proceeds from our February 2015 public offering of common stock, and given our development plans, we anticipate cash resources will be sufficient to fund our operations into the first quarter of 2017. We do not know whether additional financing will be available on terms favorable or acceptable to us when needed, if at all. Our business is highly cash-intensive and our ability to continue operations after our current cash resources are exhausted depends on our ability to obtain additional financing and/or achieve profitable operations, as to which no assurances can be given. If adequate additional funds are not available when required, or if we are unsuccessful in entering into partnership agreements for the further development of our products, we will be required to delay, reduce or eliminate planned preclinical and clinical trials and may be forced to terminate the approval process for our product candidates from the FDA or other regulatory authorities. In addition, we could be forced to discontinue product development, forego attractive business opportunities or pursue merger or divestiture strategies. In the event we are unable to obtain additional financing, we may be forced to cease operations altogether.

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, 2014, we had incurred approximately $372.6 million of cumulative net losses and had approximately $42.8 million of cash and cash equivalents. Taking into account our receipt of approximately $94.6 million in net proceeds from our February 2015 public offering of common stock, and given our development plans, we anticipate cash resources will be sufficient to fund our operations into the first quarter of 2017. 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. We have estimated the sufficiency of our cash resources based in part on the discontinuation of the PICASSO 3 pivotal trial for first-line metastatic STS and our adaptive Phase 3 trial for first-line SCLC for IV palifosfamide. Also our estimates include the advancement of our synthetic biology product candidates in the clinic under our Channel Agreement with Intrexon 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 additional product candidates 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 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. For example, despite positive findings in earlier clinical trials, our product candidate palifosfamide failed to meet the primary endpoint of the Phase 3 PICASSO 3 trial. 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 Investigational New Drug, or IND, submission or in the conduct of these trials.

‘See also “Risk Factors— *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 file an NDA or BLA, with 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 designations for darinaparsin for the treatment of peripheral T-cell lymphoma in both the United States and Europe, and we may be able to receive additional Orphan Drug designation from the FDA and the European Medicines Agency, or EMA, for 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 drug candidates is long, complex, and costly. Unless and until we receive approval from the FDA and/or other 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 products candidates use a synthetic biology 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 synthetic 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 adverse events, which could also lead to negative publicity.

The synthetic 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 synthetic biological technologies only for use in a controlled laboratory and industrial environment, the release of such synthetic 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.

Our use of synthetic biology to develop product candidates may become subject to increasing regulation in the future.

Most of the laws and regulations concerning synthetic biology relate to the end products produced using synthetic biology, but that may change. For example, the Presidential Commission for the Study of Bioethical Issues in December 2010 recommended that the federal government oversee, but not regulate, synthetic biology research. The Presidential Commission also recommended that the government lead an ongoing review of developments in the synthetic biology field and that the government conduct a reasonable risk assessment before the field release of synthetic organisms. Synthetic biology may become subject to additional government regulations as a result of the recommendations, which could require us to incur significant additional capital and operating expenditures and other costs in complying with these laws and regulations.

The technology on which our Channel Agreement with Intrexon Corporation is based in part on early stage technology in the field of human oncologic therapeutics.

Our Channel Agreement with Intrexon contemplates our using Intrexon's advanced transgene engineering platform for the controlled and precise cellular production of anti-cancer effectors. The synthetic biology effector platform in which we have acquired rights represents early-stage technology in the field of human oncology biotherapeutic, with DC-RTS-IL-12 + veledimex having completed a Phase 1 study in melanoma and Ad-RTS-IL-12 + veledimex having completed two Phase 2 studies, in melanoma and breast cancer. The Company is continuing to pursue intratumoral injection of Ad-RTS-IL-12 + veledimex in brain cancer and breast cancer. Although we plan to leverage Intrexon's synthetic biology 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 Intrexon.

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

The synthetic biology platform, in which we have acquired rights for cancer indications from Intrexon, includes two existing product candidates, Ad-RTS-IL-12+ veledimex and DC-RTS-IL-12 + veledimex. Upon entry into the Channel Agreement with Intrexon, we assumed responsibility for the clinical development of these product candidates, which we expect will increase the level of our overall research and development expenses significantly going forward. 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 synthetic biology products are greater than the corresponding costs associated with clinical trials for small molecule candidates. In addition to increased research and development costs, prior to the adoption of our April 2013 workforce reduction plan, we added headcount in part to support our Channel Agreement endeavors, and we may need to do so again in the future which would add to our general and administrative expenses going forward.

Although our forecasts for expenses and the sufficiency of our capital resources takes into account our plans to develop the Intrexon products, 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.

We may not be able to retain the exclusive rights licensed to us by Intrexon Corporation 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 Intrexon's technology directed towards in vivo expression of effectors in connection with the development of Ad-RTS-IL-12+ veledimex and DC-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 Intrexon 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 Intrexon'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.

Intrexon 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 Intrexon that is a "Superior Therapy" as defined in the Channel Agreement. We may voluntarily terminate the Channel Agreement upon 90 days written notice to Intrexon. 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 Intrexon 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 Intrexon following an unconsented assignment by us or our election not to pursue development of a Superior Therapy).

Our obligation to pay 50% of net profits or revenue 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 Intrexon Corporation*" with respect to these "retained" products will survive termination of the Channel Agreement.

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 The University of Texas M.D. Anderson Cancer Center

Pursuant to the MD Anderson License with MD Anderson, we, together with Intrexon, obtained an exclusive, worldwide license to certain technologies owned and licensed by MD Anderson including technologies relating to novel CAR-T cell, T-NK and TCR cell therapies arising from the laboratory of Laurence Cooper, M.D., Ph.D., professor of pediatrics 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 Intrexon, agreed to

enter into a research and development agreement pursuant to which we will 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 and $20 million per year. In addition, we also expect to enter into additional collaboration and technology transfer agreements with MD Anderson and Intrexon 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.

In addition, in light of our entry into the MD Anderson License with MD Anderson, we expect to build a base of operations in Houston, Texas to join and collaborate with the MD Anderson academic and medical community, which may require that we add headcount in the future, and which could add to our general and administrative expenses going forward.

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 was entered into on January 13, 2015 and is 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, the final terms and conditions of the research and development agreement contemplated by the MD Anderson License, costs associated with opening a new operational facility in Houston, Texas, 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 Intrexon by The University of Texas M.D. Anderson Cancer Center to technologies relating to novel chimeric antigen receptor (CAR) T-cell therapies and other related technologies.

Under the MD Anderson License, we, together with Intrexon, received an exclusive, worldwide license to certain technologies owned and licensed by MD Anderson including technologies relating to novel CAR-T cell, T-NK and TCR cell therapies arising from the laboratory of Laurence Cooper, M.D., Ph.D., professor of pediatrics at MD Anderson, as well as either co-exclusive or non-exclusive licenses under certain related technologies. When combined with Intrexon's technology suite and ZIOPHARM's clinically tested RheoSwitch Therapeutic System® 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 tightly 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 Intrexon 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 Intrexon 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 Intrexon 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 Intrexon 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 Intrexon, 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 Intrexon and may be terminated by the mutual written agreement of us, Intrexon 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 process;
- 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. Jonathan Lewis, our Chief Executive Officer, Caesar J. Belbel, our Executive Vice President and Chief Legal Officer and our principal scientific, regulatory, and medical advisors. Mr. Belbel's employment is governed by a written employment agreement, while our previously effective written employment agreement with Dr. Lewis expired in accordance with its terms in January 2015. Dr. Lewis and Mr. Belbel 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 Dr. Lewis and Mr. Belbel, 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 drug 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 drug 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 New Drug Application, or NDA, or 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 NDAs or 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 an NDA or 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 an NDA or BLA for regulatory approval of our product candidates or whether such an NDA or BLA will be accepted. Because we do not anticipate generating revenues unless and until we submit one or more NDAs or BLAs and thereafter obtain requisite FDA approvals, the timing of our NDA or 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. If our product candidates or similar products or product candidates under development by third parties demonstrate unacceptable adverse events, we may be required to halt or delay further clinical development of our product candidates. The FDA, the EMA 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. Any of these occurrences may harm our business, financial condition and prospects significantly.

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 studies in support of approval of an NDA or 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. For example, despite positive findings in earlier clinical trials, our product candidate palifosfamide failed to meet the primary endpoints of the Phase 3 PICASSO 3 trial, causing us to suspend clinical development of palifosfamide in soft tissue sarcoma. 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 NDAs or 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 biology 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, no gene therapy products have been approved in the United States and only one product has been approved in Europe.

We have recently focused our product research and development efforts on our synthetic biology product candidates under our Channel Agreement with Intrexon. These products, including Ad-RTS-IL-12+ veledimex, are based on gene therapy technology. 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 synthetic biology 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 studies or commercializing our synthetic biology 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, only one gene therapy product, UniQure's Glybera, which received marketing authorization from the EMA in 2012, has been approved in Europe but has not yet been launched for commercial sale, which makes 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.

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 studies 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 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. For example, our planned Phase 1 clinical trial of Ad-RTS-IL-12 + veledimex, in subjects with recurrent or progressive high grade gliomas (brain cancer) received approval from the NIH RAC in December 2013, but the FDA requested additional nonclinical

information prior to permitting clinical study initiation, which we are currently generating. 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 synthetic biology 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 Intrexon on the manufacturing and scale-up of Intrexon 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 Intrexon 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 agencies to ensure strict compliance with 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 drug 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 drug 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 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 drug 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 drug candidates receives marketing approval, the accompanying label may limit the approved use of our drug, 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 drugs to ensure drugs 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 FDCA 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 adverse events 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 drug;

- 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 European Union 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 drug 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 drugs 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 approves 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 drugs do not obtain coverage adequate reimbursement from payors.

Our ability to commercialize our drugs, 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. 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 them 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 European Union, 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.

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 proposals in recent years that change the healthcare system in ways that could impact our future ability to sell our product candidates profitably. For example, the Medicare Prescription Drug, Improvement, and Modernization Act of 2003 established a new Part D prescription drug benefit, which became effective January 1, 2006. Under the prescription drug benefit, Medicare beneficiaries can obtain prescription drug coverage from private sector plans that are permitted to limit the number of prescription drugs that are covered in each therapeutic category and class on their formularies. If any of our product candidates that are approved by the FDA are not widely included on the formularies of these plans, our ability to market our products to the Medicare population could suffer.

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 recently, 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 PPACA, which includes measures that significantly change the way healthcare is financed by both governmental and private insurers. Among the provisions of the PPACA 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, beginning in 2011;
- An increase in the statutory minimum rebates a manufacturer must pay under the Medicaid Drug Rebate Program, retroactive to January 1, 2010, to 23% 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, beginning in 2011;
- Extension of manufacturers' Medicaid rebate liability to covered drugs dispensed to individuals who are enrolled in Medicaid managed care organizations, effective March 23, 2010;
- Expansion of eligibility criteria for Medicaid programs by, among other things, allowing states to offer Medicaid coverage to additional individuals beginning in April 2010 and by adding new mandatory eligibility categories for certain individuals with income at or below 133% of the Federal Poverty Level beginning in 2014, thereby potentially increasing both the volume of sales and manufacturers' Medicaid rebate liability; 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, beginning in 2011;
- Expansion of the entities eligible for discounts under the Public Health Service pharmaceutical pricing program, effective in January 2010;
- A new requirement to annually report drug samples that manufacturers and distributors provide to physicians, effective April 1, 2012;
- 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;
- Creation of the Independent Payment Advisory Board which, beginning in 2014, will have authority to recommend certain changes to the Medicare program that could result in reduced payments for prescription drugs and those recommendations could have the effect of law even if Congress does not act on the recommendations; and
- Establishment of a Center for Medicare Innovation at CMS to test innovative payment and service delivery models to lower Medicare and Medicaid spending, potentially including prescription drug spending beginning by January 1, 2011.

In addition, other legislative changes have been proposed and adopted since the PPACA was enacted. 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 up to 2% per fiscal year, which went into effect on April 1, 2013. 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. 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. 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:

- The federal Anti-Kickback Statute, which constrains 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 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; and

- New requirements to report certain financial arrangements with physicians and teaching hospitals, as defined in the PPACA 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, with data collection required as of August 1, 2013 and reporting to the Centers for Medicare & Medicaid Services, or CMS, to be required by March 31, 2014 and by the 90th day of each subsequent calendar year;
- 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, 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 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 PPACA, among other things, amends the intent requirement of the federal anti-kickback and 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 PPACA 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 civil and criminal penalties, damages, fines, exclusion from participation in United States federal or state health care programs, and the curtailment or restructuring of our operations. Any penalties, damages, fines, curtailment or restructuring of our operations 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 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, 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 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 have not experienced additional ownership changes, or that we will not experience an ownership change as a result of this offering. As a result, our NOLs and R&D credits 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 biology product candidates may face competition in the future from follow-on biologics.

With the enactment of the Biologics Price Competition and Innovation Act of 2009, or BPCIA, as part of the Patient Protection and Affordable Care Act, an abbreviated pathway for the approval of follow-on biological products was created. The new abbreviated regulatory pathway establishes legal authority for the FDA to review and approve biosimilar biologics, including the possible designation of a biosimilar as "interchangeable" with an existing brand product. 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. 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.

In his proposed budget for fiscal year 2014, President Obama proposed to cut this 12-year period of exclusivity down to seven years. He also proposed to prohibit additional periods of exclusivity due to minor changes in product formulations, a practice often referred to as "evergreening." It is possible that Congress may take these or other measures to reduce or eliminate periods of exclusivity.

The new law is complex and is only beginning to be interpreted and implemented by the FDA. As a result, its ultimate impact is subject to uncertainty, and could have a material adverse effect on the future commercial prospects for our biological products. Since enactment of the BCPIA, the FDA has issued several draft guidance documents discussing the biosimilar pathway, but to date, no biosimilar or interchangeable product has been approved. Although it is unclear what final implementation of the BCPIA will entail, such FDA implementation could have a material adverse effect on the future commercial prospects for our product candidates.

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 United States and foreign intellectual property with respect to our small molecule product candidates, with respect to the Intrexon technology, including the existing Intrexon product candidates, and with respect to CAR-T, NK and TCR cell therapies arising from the laboratory of Laurence Cooper, M.D., Ph.D., professor of pediatrics at MD Anderson. Under our Channel Agreement with Intrexon, Intrexon 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 Intrexon 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 License Agreement with MD Anderson, future filings and applications require the agreement of each of MD Anderson, Intrexon 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 Intrexon may prosecute the application directly. Although under the agreement MD has agreed to review and incorporate any reasonable comments that we or Intrexon 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 Intrexon 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, Intrexon 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 U.S. PTO 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 Intrexon 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 drug 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 Intrexon, 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 drug 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 biology, which we are pursuing under our Channel Agreement with Intrexon, 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 biology, 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 Intrexon is early-stage technology and we are just beginning 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 biology 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 U.S. PTO and foreign patent agencies in several stages over the lifetime of the patent. The U.S. PTO 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 with Intrexon and under our License with MD Anderson. 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 of our common stock has been highly volatile. The stock market from time to time experiences significant price and volume fluctuations unrelated to the operating performance of particular companies. In addition, factors such as fluctuations in our operating results, future sales of our common stock, announcements of the timing and amount of product sales, 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, laboratory or clinical trial results, government regulation, FDA determinations on the approval of a product candidate NDA submission, developments in patent or other proprietary rights, public concern as to the safety of drugs developed by us or others, changes in reimbursement policies, comments made by securities analysts and general market conditions may have a substantial effect on the market price of our common stock.

We are subject to Sarbanes-Oxley and the reporting requirements of federal securities laws, which can be expensive.

As a public reporting company, we are subject to the Sarbanes-Oxley Act of 2002, as well as to the information and reporting requirements of the Securities Exchange Act of 1934, as amended, or the Exchange Act, and other federal securities laws. As a result, we incur significant legal, accounting, and other expenses that we would not incur as a private company, including costs associated with our public company reporting requirements and corporate governance requirements. As an example of public reporting company requirements, we evaluate the effectiveness of disclosure controls and procedures and of our internal control over financing reporting in order to allow management to report on such controls. Sarbanes-Oxley generally requires that a public reporting company's independent registered public accounting firm attest to the effectiveness of the company's internal control over financial reporting as of the end of each fiscal year in the company's Annual Report on Form 10-K. In addition, any updates to our finance and accounting systems, procedures and controls, which may be required as a result of our ongoing analysis of internal controls, or results of testing by our independent auditor, may require significant time and expense. As a company with limited accounting resources, a significant amount of management's time and attention has been and will continue to be diverted from our business to ensure compliance with these regulatory requirements. This diversion of management's time and attention may have a material adverse effect on our business, financial condition and results of operations.

Management is working to continuously monitor and improve internal controls and has set in place controls to mitigate the potential segregation of duties risk. In the event significant deficiencies or material weaknesses are

identified in our internal control over financial reporting that we cannot remediate in a timely manner, or if we are unable to receive a positive attestation from our independent registered public accounting firm with respect to our internal controls over financial reporting, investors and others may lose confidence in the reliability of our financial statements and the trading price of our common stock and ability to obtain any necessary equity or debt financing could suffer. In addition, in the event that our independent registered public accounting firm is unable to rely on our internal controls over financial reporting in connection with its audit of our financial statements, and in the further event that it is unable to devise alternative procedures in order to satisfy itself as to the material accuracy of our financial statements and related disclosures, we may be unable to file our periodic reports with the United States Securities and Exchange Commission, or SEC. This would likely have an adverse effect on the trading price of our common stock and our ability to secure any necessary additional equity or debt financing, and could result in the delisting of our common stock from the NASDAQ Capital Market, which would severely limit the liquidity of our common stock.

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 capital 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 stock price is volatile and may decline regardless of our operating performance, and you may not be able to resell your shares at or above the price at which you purchased such shares.

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;
- Changes in operating performance and stock market valuations of other biopharmaceutical companies generally, or those that develop and commercialize cancer drugs in particular;
- The financial projections we may provide to the public, any changes in these projections or our failure to meet these projections;
- 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 SEC and announcements relating to product development, litigation and intellectual property impacting us or our business;
- 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;
- 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 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.

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, 2014, our executive officers, directors and holders of five percent or more of our outstanding common stock, beneficially owned, in the aggregate, 18.8% 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

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 consists of four floors, occupying approximately twenty-six thousand square feet, which are leased pursuant to a lease agreement that expires August 2016 under which we are required to make rental payments at an average monthly rate of approximately $63 thousand through the remainder of the lease term. The company is actively pursuing a subtenant to lease a portion of the space in the Boston Office that was vacated by a previous subtenant, in October 2014.

We also maintain office space in New York, which is subject to a lease agreement that expires in October 2018. Under the terms of the lease, we lease approximately seven thousand square feet and are required to make rental payments at an average monthly rate of approximately $41 thousand through the remainder of the term of the lease. On October 17, 2013, the Company entered into a sublease agreement to lease approximately seven thousand square feet to a subtenant. Under the sublease agreement, the Company will 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 the Company with a security deposit of an irrevocable standby letter of credit for approximately $167 thousand.

We also leased office space in Germantown, MD. The Maryland office space was subject to a lease agreement that would have expired in March 2014. On July 16, 2012, the Germantown, Maryland office was closed. Under the terms of the lease, we leased approximately two thousand square feet and were required to make rental payments at an average monthly rate of approximately $4 thousand through the remainder of the lease. In June 2013, we paid off the remainder of the Germantown, Maryland lease obligation.(see Note 8 to the financial statements, Commitments and Contingencies).

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.

While the outcome of these proceedings and claims cannot be predicted with certainty, there are no matters, as of December 31, 2014, 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.

	2014		2013	
Quarter Ended	High	Low	High	Low
March 31	$5.42	$3.81	$5.18	$3.09
June 30	$4.80	$2.96	$3.94	$2.11
September 30	$4.01	$2.64	$2.62	$1.52
December 31	$5.07	$2.43	$5.71	$1.72

Record Holders

As of February 10, 2015, we had approximately 170 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 10, 2015, we had approximately 16,121 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

None.

Issuer Purchases of Equity Securities

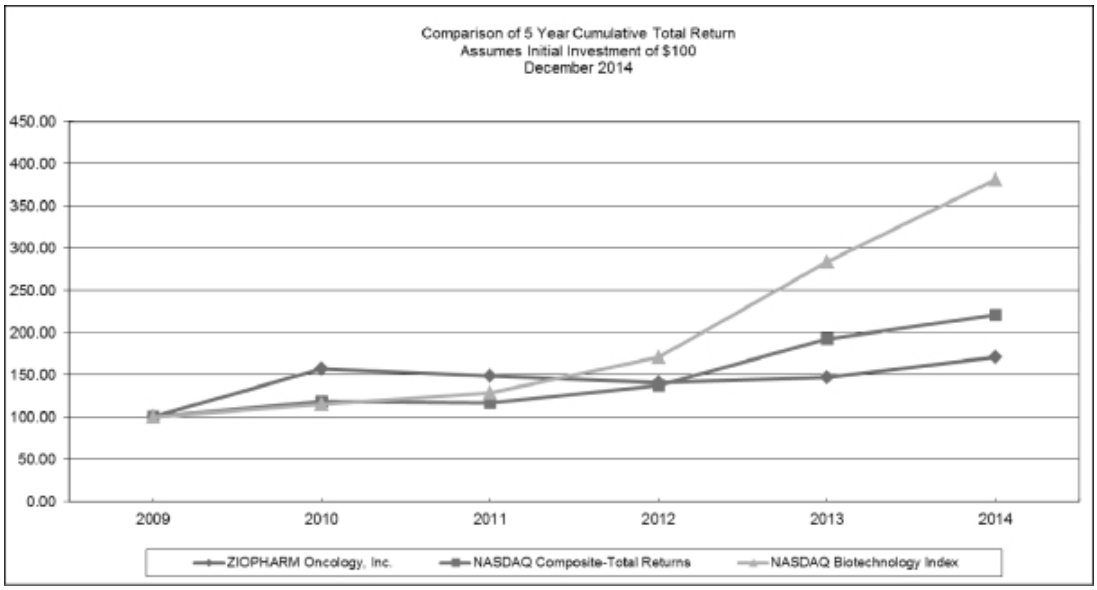
During the three months ended December 31, 2014, we purchased 81,702 shares of restricted stock from employees to cover withholding taxes due from the employees at the time that applicable forfeiture restrictions lapsed. The following table provides information about these purchases of restricted shares for the three months ended December 31, 2014:

Period	Total Number of Shares Purchased	Average Price Paid Per Share
October 1 to 31, 2014	—	$ —
November 1 to 30, 2014	—	—
December 1 to 31, 2014	81,702	5.04
Total	81,702	

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, 2009 and tracks it through December 31, 2014.



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,				
	2014	2013	2012	2011	2010
	(in thousands, except per share amounts)				
Statements of Operations Data:					
Research contract revenue	$ 1,373	$ 800	$ 800	$ 667	$ —
Total operating expenses	44,872	58,513	102,969	72,067	24,546
Loss from operations	43,499	(57,713)	(102,169)	(71,400)	(24,546)
Other income (expense), net	(5)	(579)	(13)	39	765
Change in fair value of warrants	11,723	1,185	6,050	7,583	(8,889)
Net loss	(31,781)	(57,107)	(96,132)	(63,778)	(32,670)
Basic and diluted net loss per share	$ (0.31)	$ (0.66)	$ (1.22)	$ (0.97)	$ (0.71)
Weighted average number of common shares outstanding: basic and diluted	101,130,710	85,943,175	78,546,112	66,003,789	46,003,996

	Year Ended December 31,				
	2014	2013	2012	2011	2010
			(in thousands)		
Balance Sheet Data:					
Cash and cash equivalents	$42,803	$68,204	$73,306	$104,713	$60,392
Total assets	45,237	71,754	83,404	108,108	61,520
Warrant liabilities	—	11,776	12,962	19,425	27,311
Total liabilities	11,396	22,371	34,959	36,501	30,967
Stockholders' equity	33,841	49,383	48,445	71,607	30,553

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

The following "Management's Discussion and Analysis of Financial Condition and Results of Operations," as well as disclosures included under the heading "Business" and elsewhere in this Form 10-K, include "forward-looking statements" within the meaning of the Private Securities Litigation Reform Act of 1995. This Act provides a safe harbor for forward-looking statements to encourage companies to provide prospective information about themselves so long as they identify these statements as forward-looking and provide meaningful cautionary statements identifying important factors that could cause actual results to differ from the projected results. All statements other than statements of historical fact we make in this Form 10-K are forward-looking. In particular, statements preceded by, followed by or that include the words "intends", "estimates", "plans", "believes", "expects", "anticipates", "should", "could" or similar expressions, are forward-looking statements. These statements include, but are not limited to, statements regarding future sales and operating results; growth and trends of our company and our industry, generally; growth of the markets in which we participate; international events; product performance; the acquisition of or investment in other entities; the construction of new or refurbishment of existing facilities by us; our ability to successfully develop and commercialize our therapeutic products; our ability to expand our long-term business opportunities; financial projections and estimates and their underlying assumptions; and future performance. All of such statements are subject to certain risks and uncertainties, many of which are difficult to predict and generally beyond our control, that could cause actual results to differ materially from those expressed in, or implied or projected by, the forward-looking information and statements. These risks and uncertainties include, but are not limited to: whether Ad-RTS-IL-12 + veledimex, the CAR-T programs , or any of our other therapeutic products will advance further in the clinical trials process and whether and when, if at all, they will receive final approval from the FDA or equivalent foreign regulatory agencies and for which indications; whether Ad-RTS-IL-12 + veledimex, the CAR-T programs and our other therapeutic products will be successfully marketed if approved; whether any of our synthetic biology platform discovery and development efforts will be successful; our ability to achieve the results contemplated by our collaboration agreements; the strength and enforceability of our intellectual property rights; competition from pharmaceutical and biotechnology companies; the development of and our ability to take advantage of the market for DNA-based biotherapeutics; our ability to raise additional capital to fund our operations on terms acceptable to us; general economic conditions; and the other risk factors contained in this Annual Report on Form 10-K. Forward-looking statements reflect our current expectations and are inherently uncertain. Our actual results may differ significantly from our expectations. We assume no obligation to update this forward-looking information. The section herein entitled "Risk Factors" describes some, but not all, of the factors that could cause these differences.

The following discussion and analysis should be read in conjunction with our historical financial statements and the notes to those financial statements which are included in Item 8 of Part II of this Form 10-K.

Business Overview

ZIOPHARM Oncology, Inc. is a biopharmaceutical company that seeks to acquire, develop and commercialize, on its own or with commercial partners, a diverse portfolio of cancer therapies that can address unmet medical

needs through synthetic biology. Pursuant to an exclusive channel collaboration agreement (or "ECC") with Intrexon Corporation, or Intrexon, we obtained rights to Intrexon's synthetic biology platform for use in the field of oncology, which included a clinical stage product candidate, Ad-RTS-IL-12 used with the oral activator veledimex. The synthetic biology platform is an industrialized engineering approach for molecular and cell biology and gene control. It employs an inducible gene-delivery system that enables controlled in vivo expression of genes that produce therapeutic proteins to treat cancer. Ad-RTS-IL-12 + veledimex uses this gene delivery system to produce Interleukin-12, or IL-12, a potent, naturally occurring anti-cancer protein. We have completed two Phase 2 studies evaluating Ad-RTS-IL-12 + veledimex, the first for the treatment of metastatic melanoma, and the second for the treatment of metastatic breast cancer; data from these Phase 2 studies was presented in December 2014. We are continuing to pursue intratumoral injection of Ad-RTS-IL-12 + veledimex in breast cancer and brain cancer.

In addition to our synthetic biology programs, Intrexon (and we, through our ECC agreement with Intrexon) recently obtained an exclusive, worldwide license to certain immuno-oncology technologies owned and licensed by The University of Texas M.D. Anderson Cancer Center, or MD Anderson, including technologies relating to novel chimeric antigen receptors, or CARs, natural killer, or NK cells and T cell receptors, or TCRs. Combining these technologies with Intrexon's technology suite and clinically tested RheoSwitch Therapeutic System®, or RTS®, IL-12 modules, we plan to develop CAR-T and other immune cells that will target and kill cancer cells. We plan to leverage the synergy between the platforms to accelerate a promising synthetic immuno-oncology pipeline, with up to five CAR-T therapies expected to enter the clinic in 2015 and programs for the development of allogeneic CAR-T therapies that can be used off-the-shelf expected to be initiated in 2016.

We plan to continue to combine Intrexon's technology suite with our capabilities to translate science to the patient, and to identify and develop additional products to stimulate or inhibit key pathways, including those used by the body's immune system, to treat cancer."

Enabling Technology

Synthetic biology entails the application of engineering principles to biological systems for the purpose of designing and constructing new biological systems or redesigning/modifying existing biological systems. Biological systems are governed by DNA, the building block of gene programs, which control cellular processes by coding for the production of 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. Synthetic biology 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. Synthetic biology 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.

On January 6, 2011, we entered into an Exclusive Channel Partner Agreement with Intrexon, which we refer to as the Channel Agreement, to develop and commercialize novel DNA-based therapeutics in the field of cancer treatment by combining Intrexon's synthetic biology platform with our capabilities to translate science to the patient. As a result, our DNA synthetic biology platform employs an inducible gene-delivery system that enables regulated and controlled delivery of genes that produce therapeutic proteins to treat cancer. The first example of this regulated controlled delivery is achieved by producing IL-12, a potent, naturally occurring anti-cancer protein, under the control of Intrexon's proprietary biological "switch" to turn on and off (and on and off repeatedly) the therapeutic protein expression at the tumor site. We and Intrexon refer to this "switch" as the RheoSwitch Therapeutic System® or RTS® platform. Our initial drug candidate being developed using the synthetic biology platform is Ad-RTS-IL-12 + veledimex.

More detailed descriptions of our clinical development for each are set forth in this report under the caption "Business summary – Product candidates."

Immuno-oncology

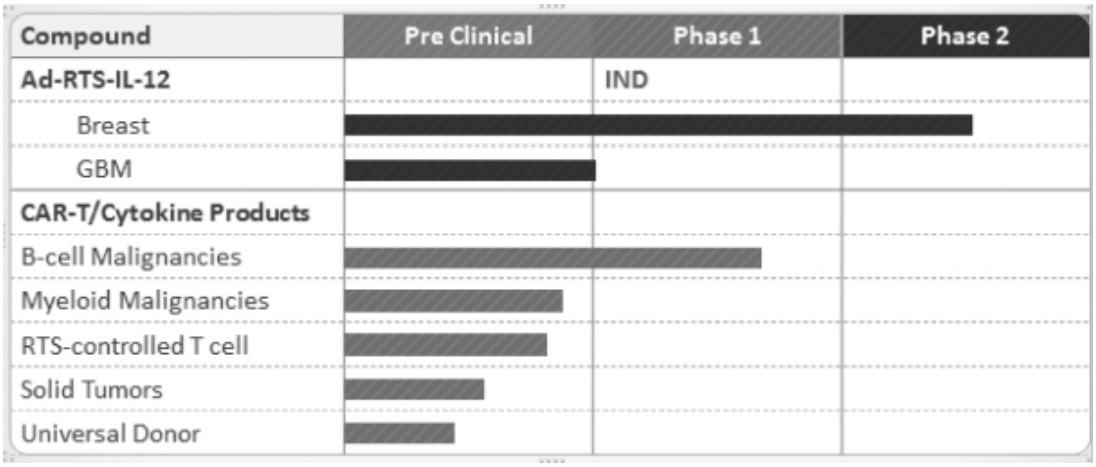
Immuno-oncology, which utilizes a patient's own immune system to treat cancer, is one of the most actively pursued areas of research by biotechnology and pharmaceutical companies today. Cancer cells contain mutated proteins and may overexpress other proteins usually found in the body at low levels. The immune system typically recognizes unusual or aberrant cell protein expression and eliminates these cells in a highly efficient process known as immune surveillance. A central player in immune surveillance is a type of white blood cell known as the T cell. In healthy individuals, T cells 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 last five years, there has been substantial scientific progress in countering these evasion mechanisms using immunotherapies, or therapies that activate the immune system.

On January 13, 2015, we, together with Intrexon, entered into a license agreement with MD Anderson, which we refer to as the MD Anderson License. Pursuant to the MD Anderson License, we and Intrexon 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., professor of pediatrics at MD Anderson, as well as either co-exclusive or non-exclusive licenses under certain related technologies.

Combining the non-viral genetic engineering technologies we licensed from MD Anderson together with Intrexon's industrialized approach to gene engineering and cell control, we believe we can rapidly and efficiently reprogram T cells to express a particular CAR or TCR construct that will enable the T cell to recognize and target cancer cells. CAR-T cells target cell surface tumor antigens, such as CD-19, that exist on cancer cells and that are independent of human leukocyte antigens, or HLAs, and which we refer to as "public" antigens. TCR+ cells target tumor antigens that are dependent on HLAs and which we refer to as "private" antigens. Natural killer cells target tumors with loss of HLAs, or tumors with no antigens. Most CAR-T cell and TCR products currently being developed by competitors are autologous, or derived from the patient's own blood, and gene engineered with viral technology. As a result, the patient's blood must be harvested, shipped to a manufacturing facility where it is modified using a retrovirus to express the CAR or TCR, and then shipped back to be infused into the patient. The process can take several weeks to a month and is very labor intensive and costly. Currently, this complex technique can only be done in very sophisticated laboratories. We believe we will be able to manufacture our CAR-T cells and TCRs using non-viral methods, which we expect will enable a simpler process requiring only days or hours and result in a lower cost of manufacturing. Our non-viral methods could also potentially enable autologous point of care treatment, where a patient's own T cells would be modified at or near the point of care, for example, utilizing a local blood bank, to express the CAR-T or TCR construct and then infused back into the patient, potentially during the same visit. In addition, we intend to use our non-viral methods to develop allogeneic treatments that can be used off-the-shelf. An allogeneic off-the-shelf treatment would enable a patient to be treated with a CAR-T or TCR construct that is created from a separate healthy donor, personalized for that patient, and then distributed to the point of care. Our non-viral methods, which we believe are nimble, fast and less costly than other approaches, together with our industrialized, scalable engineering approach are expected to enable highly efficient and less costly manufacturing approaches to gene engineered cell-based therapy. In addition, our proprietary RheoSwitch Therapeutic System® may give us the ability to control in vivo gene expression (on-off-on-off etc.) in CAR-T or TCR cells, which we believe could result in significantly lower toxicity compared to other products currently in development.

Product candidates

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



Synthetic Biology Programs:

Ad-RTS-IL-12 + veledimex

Ad-RTS-IL-12 + veledimex has been evaluated in two Phase 2 studies, the first for the treatment of metastatic melanoma, and the second for the treatment of unresectable recurrent or metastatic breast cancer. Ad-RTS-IL-12 + veledimex is our lead product candidate, which uses our gene delivery system to produce IL-12, a potent, naturally occurring anti-cancer protein.

More specifically, IL-12 is a potent immunostimulatory cytokine which activates and recruits dendritic cells that facilitate the cross-priming of tumor antigen-specific T cells. Intratumoral administration of Ad-RTS-IL-12 + veledimex, which allows for adjustment of IL-12 gene expression upon varying the dose of veledimex, is designed to reduce the toxicity elicited by systemic delivery of IL-12, and increase efficacy through high intratumoral expression.

We reported the controlled local expression of IL-12 as an immunotherapeutic treatment of glioma (brain cancer) in animal models through the use of the RTS® at the October 2013 AACR-NCI-EORTC conference. Veledimex brain penetration was demonstrated in normal mice and monkeys with intact blood brain barriers. Treatment with Ad-RTS-IL-12 + veledimex and DC-RTS-IL-12 + veledimex both demonstrated dose-related increase in survival in the mouse GL-261 glioma model with no adverse clinical signs observed. In December 2013, we announced the unanimous approval of the Recombinant DNA Advisory Committee of the National Institutes of Health, or the RAC/NIH, for the initiation of a Phase 1 study of Ad-RTS-IL-12 + veledimex, in subjects with recurrent or progressive high grade gliomas. The U.S Food and Drug Administration, or FDA, has requested additional nonclinical information to support the Phase 1 study and this data has been generated. Subject to reaching agreement with the FDA, we anticipate initiation of the Phase 1 study during the first half of 2015. Glioblastoma is by far the most frequent malignant brain tumor and is associated with a particularly aggressive course and dismal prognosis. The current standard of care is based on surgical resection to the maximum feasible extent, followed by radiotherapy and concomitant adjuvant temozolomide. Such aggressive treatment, however, is associated with only modest improvements in survival resulting in a very high unmet medical need.

At the American Association for Cancer Research, or AACR, 2014 Annual Meeting, in April 2014, we presented data from a preclinical study conducted jointly by us and Intrexon demonstrating the anti-tumor effects and

tolerability of Ad-RTS-mIL-12 in a glioblastoma murine model. Veledimex was found to effectively cross the blood brain barrier, with dose-related increases in plasma and brain tissue exposure, and no accumulation in brain tissue following repeat dosing. The study data demonstrated that administration of Ad-RTS-mIL-12 + veledimex resulted in dose-related increases in survival of four- to five-fold, without exhibiting an adverse safety profile, when compared to median survival in vehicle control groups.

At the 17th Annual Meeting of the American Society of Gene and Cell Therapy, or ASGCT, in May 2014, we presented results demonstrating the potent anti-tumor and anti-cancer stem cell effects of Ad-RTS-IL-12 in a preclinical glioma model. Results from human and laboratory studies of Ad-RTS-IL-12 demonstrated that precise control of IL-12 gene expression levels can be achieved using Intrexon's RTS®. Rapid, tight modulation of in vivo expression of IL-12 using the activator ligand, veledimex, was demonstrated across these studies. When IL-12 expression was "switched on" it rapidly led to expression and an immune response. This immune response was characterized by an increase in tumor infiltrating lymphocytes with system wide immune activation. The data presented in May 2014 further demonstrated that Ad-RTS-IL-12 has potent anti-cancer effects in a glioma model, showing both a reduction in tumor mass and prolonged survival when compared to existing treatment standards. The data also showed a significant reduction in cancer stem cells, as measured by dramatically reduced nestin levels. Cancer stem cells are thought to play a critical role in recurrence and metastasis.

At the AACR 2014 Immunology and Immunotherapy Meeting in December 2014, together with Intrexon, we presented clinical results from the Ad-RTS-hIL-12 + veledimex studies in patients with advanced breast cancer and melanoma demonstrating local and systemic IL-12-mediated anti-cancer activity, as well as safety and control of both immune- and IL-12-mediated toxicity with use of the RTS® gene switch. In two open-label Phase 2 clinical studies, twelve patients with metastatic advanced stage breast cancer and twenty-six patients with metastatic melanoma were administered Ad-RTS-hIL-12. Following intra-tumoral injection of Ad-RTS-hIL-12, expression of IL-12 within patients was controlled by the RTS® gene switch using the oral activator ligand, veledimex, at doses ranging from 5mg to 160mg. All subjects had heavy tumor burden and disease progression at the time of enrollment, with mean number of prior therapies at 14 and 10 for breast cancer and melanoma patients, respectively. Treatment with Ad-RTS-hIL-12 + veledimex resulted in an increase in the immune cytokine IL-12 and downstream cytokines, IFN- g, IP-10 and IL-10, resulting in a significant increase in the number of CD8+ T-cells. Among seven evaluable subjects in the Phase 2 clinical study of Ad-RTS-IL-12 + veledimex in patients with recurrent or metastatic breast cancer, three had stable disease, including one triple negative breast cancer subject who crossed the primary endpoint of 16 week progression free survival, for a disease control rate (stable disease or better) of 43%. Target lesions and tumor burden were significantly reduced in approximately 40% of patients. In the Phase 1/2 study of Ad-RTS-hIL-12 + veledimex in subjects with unresectable stage III/IV melanoma, of eighteen evaluable subjects, one had a partial response and six had stable disease, for a disease control rate of 39%. In melanoma patients for whom a response was observed, there was evidence of local and systemic anti-cancer activity. The adverse event profile of Ad-RTS-hIL-12 + veledimex in both melanoma and breast cancer was predictable, reversible and characteristic of immune activation. The most common ³ Grade 3 treatment emergent adverse events, or TEAEs, in breast cancer and melanoma included neutropenia and electrolyte abnormalities (21%) each, LFTs increased (16%), leukopenia (13%) and pyrexia, hypotension, lymphopenia, anemia, and cytokine release syndrome (11%) each. Importantly, all TEAEs and SAEs ³ Grade 3 reversed rapidly upon discontinuation of veledimex oral dosing.

Also at the AACR 2014 Immunology and Immunotherapy Meeting in December 2014, together with Intrexon, we presented preclinical data supporting the potential for cytolytic activity against solid tumor targets with allogeneic, genetically-modified stem cells enabled for controlled release of cell-linking moieties, or CLMs, within the tumor micro-environment and preclinical data describing the development of a novel, high-throughput screening technology for rapidly identifying bi-specific antibodies capable of inducing targeted immunologic activity through the activation of T-cells or other immune cells against tumors. CLMs are small bi-specific antibody fragments capable of directing potent T-cell mediated tumor lysis by bridging the immunologic synapses of T-cells and surface targets on tumor cells. Previous studies have shown that the systemic distribution and pharmacokinetic profile of bi-specific antibodies limit their utility for many target/effector combinations. In

two preclinical studies, Intrexon and Ziopharm researchers interrogated a large number of CLM-based effectors for their ability to activate white blood cells from peripheral blood and lyse receptor target-positive tumor cells. Allogeneic, tumor targeting stem cells were then genetically modified to express CLMs within the tumor microenvironment using the RTS® platform as a mechanism for providing spatial and temporal control. The first study demonstrated the ability of Intrexon's proprietary image-based screening systems and rapid DNA assembly to screen a large number of EGFR and HER2 receptor-targeted CLM variants for their ability to recruit CD3+ T-cells and mediate selective cell killing against target positive cells in peripheral blood co-cultures. The image-based screening platform allowed for real time target cell killing information to be obtained, as well as kinetic cell morphologic analyses to understand the dynamics of killing activity, thereby shortening the developmental timeline to lead candidate selection. The second study validated these CLM candidates in scalable, allogeneic endometrial regenerative cells, or ERCs, genetically modified to express an anti-CD3-anti-EGFR CLM under RTS® ligand inducible control. Expression of CLMs under the RTS® inducible promoter provided effective control of CLM secretion and modulation of killing activity, with veledimex-dependent cytotoxicity of greater than 80% against an EGFR+ KRAS mutant lung cancer cell model. CLM-expressing ERCs were found to be effective in co-culture killing assays at cellular doses as low as 1% of target cells. These data supported the feasibility of localized cytolytic activity of CLM-secreting allogeneic cell therapy products against EGFR+ KRAS mutant solid tumor malignancies.

We have completed the Phase 2 monotherapy studies in melanoma and breast cancer using Ad-RTS-IL-12 + veledimex. Additionally, we expect a future trial with IL-12 in combination therapies with standard of care for breast cancer. As the treatment of advanced melanoma has undergone and continues to undergo a rapid evolution with the introduction and approval of highly promising new single and combination agents, the standard of care in this indication has become uncertain, resulting in a much more competitive and commercially unpredictable environment. As a result, we are pursuing intratumoral injection of Ad-RTS-IL-12 + veledimex in brain cancer and breast cancer, and will pause further development of Ad-RTS-IL-12 + veledimex in melanoma with intratumoral injection. However, through current strategic initiatives, we expect to utilize RTS-IL-12 + veledimex in cell based immunotherapy of melanoma and other cancers. We plan to initiate a Phase 1 trial to evaluate Ad-RTS-IL-12 + veledimex as a single agent in the treatment of patients with brain cancer in the first half of 2015.

CAR-T Cells

We are actively pursuing non-viral, genetic engineering technologies to develop novel CAR-T, NK and TCR cells. Combining this technology with Intrexon's industrialized synthetic biologic engineering and clinically tested and validated RTS IL-12 modules, represents a differentiated approach to genetically modified CAR-T cell and other immune cells. Employing novel cell engineering techniques and multigenic gene programs, we expect to implement next-generation non-viral adoptive cellular therapies based on designer cytokines and CARs under control of RTS® technology targeting both hematologic malignancies and solid tumors. We plan to leverage the synergy between the platforms to accelerate a promising synthetic immuno-oncology pipeline, with up to five CAR-T therapies expected to enter the clinic in 2015 and programs for the development of allogeneic CAR-T therapies that can be used off-the-shelf expected to be initiated in 2016.

Research suggests that T cells can be re-programmed to have a very strong anti-cancer therapeutic effect through the expression of CARs to redirect specificity to tumors without HLA restrictions. The signature event within this field has resulted from the infusion of T cells expressing CARs into patients with B cells leukemias and lymphomas. Many of these patients have responded to these new therapies with a durable and dramatic anti-tumor effect after infusing CD19-specific T cells. Despite the highly promising results that have been demonstrated by early researchers in the field, current technologies and approaches have shown a number of serious drawbacks, including toxicity, manufacturing complexity and expense. A particular problem is that infusions of T cells into patients with large amounts of disease have invariably led to significant issues of toxicity for recipient patients. These toxicities primarily involve three major, potentially catastrophic side-effects:

- The rapid killing of tumor cells releases a large number intracellular constituents that are very toxic to various organs and is called "tumor lysis syndrome" that can be fatal,

- the supra-physiologic release of cytokines ("cytokine storm") that causes fever, instability of blood pressure, mental status changes and on occasion, death, and
- on-target, and off-tissue toxicity represented by the concomitant damage of normal B cells and loss of humoral (antibody) immunity.

We expect to be able to tightly control expansion and activation of CAR-T cells in the body, which has the potential to alleviate or abrogate these toxicities.

MD Anderson's platform, which uses the exclusive Sleeping Beauty system, or SB system, generates and characterizes new CAR-T designs, which enables a high throughput approach to evaluate the CAR-T. This "EZ-CAR-T" non-viral system is used to fashion immuno-receptors that differ in specificity and ability to activate T cells. These CAR-T molecules are evaluated in a "go/no go" system based on serial killing and protection of T cells from activation-induced cell death. Non-viral gene transfer using the SB system is unique in the field of oncology. Examples of cell engineering techniques that we expect to employ with the SB system are induced pluripotent stem cell (iPSC) processing technologies combined with Laser-enabled Analysis and Processing, or LEAP®, which consists of computerized image-based selection and laser processing for very rapid cell identification and purification as well as AttSite® Recombinases, which involves stable, targeted gene integration and expression with proprietary serine recombinases. We believe the advanced DNA vectors derived from SB can be used to avoid the expense and manufacturing difficulty associated with creating CAR-T cells using viral vectors. After electroporation, the transposon/transposase improves the efficiency of integration of plasmids used to express CAR and other transgenes in T cells. Propagation of genetically modified T cells on activating and propagating cells, or AaPC, provide a competitive advantage over other non-viral methods of modification. The SB system combined with artificial antigen-presenting cells can selectively propagate and thus retrieve CAR+ T cells suitable for human application. T cells can also be genetically modified using these technologies to target a panel (several) cancer antigen targets. We are on the verge of implementing technology to manufacture "minimally-manipulated" T cells within days of gene transfer by electroporation.

We expect this platform will rapidly integrate with Intrexon's RTS® and multigenic control gene programs. The programs are also designed and built for rapid transition to universal donor products or minimally manipulated point of care products. Dr. Laurence Cooper and colleagues at MD Anderson recently published research which demonstrated that transformed, primary, and pluripotent stem cells can be permanently modified to eliminate HLA-A expression, demonstrating how to generate a priori cells from one allogeneic donor for infusion into multiple recipients representing a significant step towards our goal of on-demand therapy that can be pre-deployed at multiple sites and infused when needed. The primary factor limiting the development of a universal donor product is the existence of graft-vs-host response, or GVHD. GVHD occurs because the newly transplanted cells regard the recipient's body as foreign. When this happens, the newly transplanted cells attack the recipient's body. Additional research from Dr. Cooper and colleagues at MD Anderson suggests that "universal" allogeneic T cells generated from one donor could be administered to multiple recipients. This is achieved by genetically editing CD19-specific CAR+ T cells to eliminate expression of the endogenous a ß TCR, the gene responsible for triggering GVHD, without compromising CAR-dependent effector functions. Genetically modified T cells are generated using the SB system to stably introduce the CD19-specific CAR with subsequent permanent deletion of a or ß TCR chains with nucleases. The translation of the SB system and AaPC for use in clinical trials highlights how a nimble and cost-effective approach to developing genetically modified T cells can be used to implement clinical trials infusing next-generation T cells with improved therapeutic potential. We are expanding our initial trials targeting CD19 and planning to conduct additional trials with re-designed CAR-Ts expanding beyond CD19+ tumor cells.

Anticipated Milestones

We expect the following milestones to occur in 2015 and 2016:

- Intra-tumoral IL-12 RheoSwitch® programs:
  - Early data is expected in the fourth quarter of 2015 for our Phase 1/2 study in Breast Cancer with standard of care.

    - Early data is expected in the fourth quarter of 2015 for our Phase 1 study of Glioblastoma multiforme (GBM).
- CAR-T programs:
    - We expect to initiate two Phase 1 studies of next-generation CD19 CARs in the second quarter of 2015.
    - We expect to initiate a Phase 1 study of next-generation CAR with an inducible cytokine in the fourth quarter of 2015.
    - We expect to initiate a novel CAR for myeloid malignancies in the fourth quarter of 2015.
    - We expect to receive interim data on two Phase 1 CARs studies in advanced leukemia and lymphomas in the fourth quarter of 2015.
- We expect to initiate other leukemia and solid tumor CAR-T cell studies in 2016.
- We expect to initiate allogeneic, off-the-shelf T-cell studies in 2016.

Data from all programs is expected in 2015 and 2016. We are also evaluating additional potential preclinical candidates and continuing discovery efforts aimed at identifying other potential product candidates under our Channel Agreement with Intrexon. In addition, we may seek to enhance our pipeline in synthetic biology through focused strategic transactions, which may include acquisitions, partnerships and in-licensing activities. We are actively seeking to out-license some or all of our small molecule programs to further support our synthetic biology efforts.

Small Molecule Programs

In addition to our synthetic biology programs discussed above, we have certain rights to three small molecule programs, palifosfamide (or isophosphoramide mustard), darinaparsin and indibulin, all of which we are no longer actively pursuing. With respect to palifosfamide, in March 2013, we announced that the pivotal Phase 3 study, PICASSO 3, did not meet its primary endpoint of progression-free survival, and that we would terminate our development program in metastatic soft tissue sarcoma. In addition, we recently received the overall survival endpoint data from our study of palifosfamide in combination with carboplatin and etoposide chemotherapy versus carboplatin and etoposide alone in chemotherapy naïve patients with metastatic small cell lung cancer, which we refer to as MATISSE. This data will be submitted for presentation at a scientific forum during the first half of 2015.

We are seeking transactions with third parties for the possible out-license of palifosfamide. With respect to darinaparsin, we have entered into an amended and restated global licensing agreement with Solasia Pharma K.K., or Solasia, on July 31, 2014 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. During 2014, we determined to no longer pursue clinical development of indibulin.

Development Plans

As of December 31, 2014, we have approximately $42.8 million of cash and cash equivalents. Taking into account our receipt of approximately $94.6 million in net proceeds from our February 2015 public offering of common stock, and given our development plans, we anticipate cash resources will be sufficient to fund our operations into the first quarter of 2017. This 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, including the factors discussed in the “Risk Factors” section of this form 10-K and

the uncertainties applicable to our forecast for the overall sufficiency of our capital resources. 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. In particular, 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 Intrexon, agreed to enter into a research and development agreement pursuant to which we will 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 and $20 million per year. In addition, we also expect to enter into additional collaboration and technology transfer agreements with MD Anderson and Intrexon 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. Further, in light of our entry into the MD Anderson License, we expect to establish operations in Houston, Texas that will enable us to join and collaborate with the MD Anderson academic and medical community, which may require that we add headcount in the future, and which could add to our general and administrative expenses going forward. 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 was entered into on January 13, 2015 and is only beginning to be implemented, therefore the actual costs associated therewith may be significantly in excess of forecasted amounts.

Financial Overview

Overview of Results of Operations

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 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.

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 warrants.

Results of Operations for the fiscal year ended December 31, 2014 versus December 31, 2013

Revenues Revenues for the years ended December 31, 2014 and 2013 were as follows:

	Year ended December 31,		Change	
($ in thousands)	**2014**	**2013**		
Collaboration revenue	$1,373	$800	$573	72%

Revenue for the year ended December 31, 2014 increased in comparison to the year ended December 31, 2013. In connection with our March 7, 2011 collaboration agreement with Solasia Pharma K.K., we received $5.0 million in research and development funding which was being earned over the period of effort, originally estimated to be 75 months. In July 2014, we entered into an amended and restated License and Collaboration Agreement with Solasia (see Note 8 to the accompanying financial statements), resulting in the Company no longer being obligated to continue their research and development efforts in connection with the upfront

payment. However, there are certain deliverables, including the transition of clinical trial data, intellectual property, and completion of certain services that are included in the amended and restated License and Collaboration Agreement which are not separable from the agreement and have no stand-alone value. As a result, the Company determined that the estimated period for amortizing the upfront payment now coincides with the completion of the aforementioned deliverables which has been estimated to be December 31, 2015. Accordingly, the Company has recorded $1.4 million in revenue during the year ended December 31, 2014 while the remaining deferred revenue balance of $1.4 million at December 31, 2014 has been classified as current.

Research and Development Expenses Research and development expenses during the years ended December 31, 2014 and 2013 were as follows:

($ in thousands)	2014	2013	Change	
Research and development	$32,706	$42,852	$(10,146)	-24%

Research and development expenses for the year ended December 31, 2014 decreased by $10.1 million when compared to the year ended December 31, 2013. On March 26, 2013, we announced the decision to immediately terminate development of palifosfamide in first-line metastatic soft tissue sarcoma and during the quarter ended September 30, 2013, completed a workforce reduction plan to reduce costs (see Note 4 in the accompanying financial statements). This resulted in lower costs of $2.4 million related to the Phase 3 palifosfamide study in SCLC as the decision was made to suspend enrollment pending further data, lower costs related to the Phase 3 palifosfamide study in soft tissue sarcoma ("STS") of $11.2 million, lower other clinical costs of $0.9 million, lower employee-related costs of $2.0 million and lower manufacturing costs of $3.4 million. The decrease was offset by an increase of $5.6 million in discovery activities, $3.7 million in nonclinical activities, and $0.5 million of other costs all related to our synthetic biology program.

General and Administrative Expenses General and administrative expenses during the years ended December 31, 2014 and 2013 were as follows:

	Year ended December 31,			
($ in thousands)	2014	2013	Change	
General and administrative	$12,166	$15,661	$(3,495)	-22%

General and administrative expenses for the year ended December 31, 2014 decreased by $3.5 million when compared to the year ended December 31, 2013. The decrease was primarily due to lower employee-related costs of $1.8 million as a result of our workforce reduction plan (see Note 4 in the accompanying financial statements) and $1.7 million in non-employee contracted costs.

Other Income (Expense) Other income (expense) during the years ended December 31, 2014 and 2013 were as follows:

	Year ended December 31,			
($ in thousands)	2014	2013	Change	
Other income (expense), net	$ (5)	$ (579)	$ 574	-99%
Change in fair value of warrants	11,723	1,185	10,538	889%
Total	$11,718	$ 606	$11,112	

The decrease in other income (expense) from the year ended December 31, 2014 compared to the year ended December 31, 2013 was due primarily to the change in the fair value of liability-classified warrants, which yielded a gain of $11.7 million for the year ended December 31, 2014 as compared to a gain of $1.2 million for the year ended December 31, 2013. The liability-classified warrants are fully expired as of December 31, 2014.

Results of Operations for the fiscal year ended December 31, 2013 versus December 31, 2012

Revenues Revenues for the years ended December 31, 2013 and 2012 were as follows:

($ in thousands)	Year ended December 31, 2013	2012	Change	
Collaboration revenue	$800	$800	$—	0%

Revenue for the year ended December 31, 2013 was the same as the year ended December 31, 2012. This is due to the continued recognition of income related to our entry into the collaboration agreement with Solasia Pharma K.K. on March 7, 2011. Under this agreement we received $5.0 million in research and development funding which we are recognizing over the estimated period of performance under the agreement, currently 75 months.

Research and Development Expenses Research and development expenses during the years ended December 31, 2013 and 2012 were as follows:

($ in thousands)	2013	2012	Change	
Research and development	$42,852	$83,446	$(40,594)	-49%

Research and development expenses for year ended December 31, 2013 decreased by $40.6 million when compared to the year ended December 31, 2012. On March 26, 2013, we announced the decision to immediately terminate development of palifosfamide in first-line metastatic soft tissue sarcoma and during the quarter ended June 30, 2013, we completed a workforce reduction plan to reduce costs (see Note 4 in the accompanying financial statements). This resulted in lower costs of $7.2 million related to the Phase 3 palifosfamide study in SCLC as the decision was made to suspend enrollment pending further data, lower costs related to the Phase 3 palifosfamide study in STS of $3.1 million, lower clinical costs of $1.8 million, lower preclinical trial costs of $4.0 million, lower manufacturing costs of $5.3 million, lower employee-related costs of $4.2 million, and lower safety costs of $0.8 million. We also incurred an $18.7 million non-cash expense in 2012, related to our channel partnership arrangement with Intrexon, while we did not incur a similar expense in 2013. The decrease was partially offset by an increase of $4.5 million in discovery activities related to our synthetic biology program.

General and Administrative Expenses General and administrative expenses during the years ended December 31, 2013 and 2012 were as follows:

($ in thousands)	Year ended December 31, 2013	2012	Change	
General and administrative	$15,661	$19,523	$(3,862)	-20%

General and administrative expenses for the year ended December 31, 2013 decreased by $3.9 million when compared to the year ended December 31, 2012. The decrease was primarily due to lower employee-related costs of $1.9 million as a result of our workforce reduction plan (see Note 4 in the accompanying financial statements) as well as $1.9 million in non-employee contracted costs and other costs of $0.1 million.

Other Income (Expense) Other income (expense) during the years ended December 31, 2013 and 2012 were as follows:

($ in thousands)	Year ended December 31, 2013	2012	Change	
Other income, net	$ (579)	$ (13)	$ (566)	4354%
Change in fair value of warrants	1,185	6,050	(4,865)	-80%
Total	$ 606	$6,037	$(5,431)	

The decrease in other income (expense) from the year ended December 31, 2013 compared to the year ended December 31, 2012 was due primarily to the change in the fair value of liability-classified warrants, which yielded a gain of $1.2 million in 2013 as compared to a gain of $6.1 million in 2012. The change in liability-classified warrants is primarily attributable to the increase in our stock price, offset by a decrease in the remaining term and a decrease in volatility. Additional changes are attributable to increased state tax refunds and decreased interest rates on invested funds. This gain is offset by a loss on disposition of property, plant and equipment of $0.6 million. In addition, we recognized a loss on disposal of property, plant and equipment of $0.6 million in 2013.

Liquidity and Capital Resources

As of December 31, 2014, we had approximately $42.8 million in cash and cash equivalents, compared to $68.2 million in cash and cash equivalents as of December 31, 2013. Taking into account our receipt of approximately $94.6 million in net proceeds from our 2015 public offering of common stock, as described below, and given our development plans, we anticipate cash resources will be sufficient to fund our operations into the first quarter of 2017. However, changes may occur that would consume our existing capital prior to that time, including the scope and 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. We have estimated the sufficiency of our cash resources based in part on the anticipated advancement of our synthetic biology product candidates in the clinic under our exclusive channel partnership with Intrexon and our license agreement with The University of Texas M.D. Anderson Cancer Center, and we expect that the costs associated with these and additional product candidates will increase the level of our overall research and development expenses significantly going forward.

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 synthetic biology products are greater than the corresponding costs associated with clinical trials for small molecule candidates.

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 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, 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 effective registration statement on Form S-3 (Registration Statement 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 $94.2 million after deducting underwriting discounts and estimated offering expenses payable by the Company.

October 2013 Public Offering

On October 23, 2013, 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 14,300,000 shares of our common stock. The price to the public in the offering was $3.50 per share, and the underwriters agreed to purchase the shares from the Company pursuant to the underwriting agreement at a purchase price of $3.29 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 2,145,000 shares of common stock at a purchase price of $3.29 per share, and the underwriters elected to exercise such option in full. The offering was made pursuant to the Company's effective registration statement on Form S-3 (Registration Statement No. 333-177793) previously filed with the SEC, and a prospectus supplement thereunder. The underwriters purchased the 14,300,000 shares and the additional 2,145,000 shares on October 29, 2013. The net proceeds from the offering were approximately $53.9 million after deducting underwriting discounts and estimated offering expenses payable by the Company.

Cash Increases and (Decreases)

The following table summarizes our net increase (decrease) in cash and cash equivalents for the years ended December 31, 2014, 2013 and 2012:

	Year ended December 31,		
($ in thousands)	**2014**	**2013**	**2012**
Net cash provided by (used in):			
Operating activities	$(36,650)	$(59,509)	$(78,832)
Investing activities	(193)	(131)	(1,559)
Financing activities	11,442	54,538	48,984
Net increase (decrease) in cash and cash equivalents	$(25,401)	$ (5,102)	$(31,407)

Net cash used in operating activities was $36.7 million for the year ended December 31, 2014 compared to $59.5 million for the year ended December 31, 2013. The $22.8 million decrease in cash used was primarily due to a decrease in research and development expenses, in conjunction with our restructuring efforts.

Net cash used in investing activities was $193 thousand for year ended December 31, 2014 compared to $131 thousand for the year ended December 31, 2013. The change was due to increased spending on property, plant, and equipment.

Net cash provided by financing activities was $11.4 million for the year ended December 31, 2014 compared to $54.5 million for the year ended December 31, 2013. The change is due to $10.6 million proceeds from warrant exercises during the year ended December 31, 2014, as compared to $53.9 million received from a financing that occurred during the year ended December 31, 2013.

Operating capital and capital expenditure requirements

We anticipate that losses will continue for the foreseeable future. At December 31, 2014, our accumulated deficit was approximately $372.1 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 II – Item 1A. “Risk Factors.”

Working capital as of December 31, 2014 was $33.3 million, consisting of $44.1 million in current assets and $10.8 million in current liabilities. Working capital as of December 31, 2013 was $62.5 million, consisting of $70.3 million in current assets and $7.8 million in current liabilities.

Contractual obligations

The following table summarizes our outstanding obligations as of December 31, 2014 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	$3,157	$ 1,235	$ 1,498	$ 424	$ —
Royalty and license fees	1,850	1,275	550	25	—
Contract milestone payments	10	10	—	—	—
Total	$5,017	$ 2,520	$ 2,048	$ 449	$ —

Our commitments for operating leases relate to the lease for our corporate headquarters in Boston, MA, and office space in New York, NY. Our commitments for royalty and license fees relate to our royalty agreements with Southern Research Institute, requiring minimum royalty payments, as well as our license agreement with The University of Texas M. D. Anderson Cancer Center, requiring payment upon the first patient treated in a pivotal trial in darinaparsin, currently being developed under the amended and restated License and Collaboration Agreement with Solasia. As part of the amended and restated License and Collaboration agreement with Solasia (see Note 8 to the accompanying financial statements), we will receive full reimbursement of this license payment. The contract milestone and contract installment payments relate to our agreement with Baxter Healthcare Corporation for the purchase of the assets relating to indibulin, and to our CRO agreements with Novella Clinical, Inc. The remaining contract installment payments to Baxter are comprised of three separate $250 thousand payments on November 3, 2015-2017. However, for the purpose of the above table, we have assumed that the payment of the milestones will occur within five years of December 31, 2014. On July 16, 2012, we decided to close our Germanton, Maryland office. In June 2013, we paid off the remainder of the Germantown, Maryland lease obligation. Included in the above table are obligations for the subleased portion of

our Boston and New York offices as noted below and in Note 8 to the financial statements. We expect to receive a total of $306 thousand in the next year, $640 thousand in the next 2-3 years, and $278 thousand in the next 4-5 years from our subtenant in the New York office. The company is actively pursuing a subtenant to lease a portion of the space in the Boston Office that was vacated by a previous subtenant, in October 2014.

On January 13, 2015, subsequent to the balance sheet date, the Company entered into a license agreement with The University of Texas M.D. Anderson Cancer Center as detailed in note 3. The agreement includes quarterly payments of $3.75 million which would increase “Royalty and License Fees” in the above chart by $15 million in the column “Less than 1 Year” and by $30 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;
- Fair value measurements of stock based compensation and warrants; and
- Income taxes.

Clinical Trial Expenses

Clinical trial expenses include expenses associated with 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.

Fair Value Measurements of Stock Based Compensation and Warrants

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 liability classified warrants. In connection with valuing stock options and liability classified warrants we use the Black-Scholes model and the binomial model, respectively, 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 expected 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 warrants. Such changes may lead to a significant change in the expense we recognize in connection with share-based payments and warrants.

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, *Summary of Significant Accounting Principles* to our financial statements included in this report.

Off-Balance Sheet Arrangements

We currently do not have any special purpose entities or off-balance sheet financing arrangements.

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 clinical studies outside of the United States primarily in Western Europe. These business operations are not material at this time, therefore any currency fluctuations will not have a material impact on our financial position, results of operations or cash flows.

Item 8. Financial Statements and Supplementary Data

The information required by this Item 8 is contained on pages F-1 through F-31 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, 2014. 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, 2014, 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, 2014.

McGladrey LLP, an independent registered public accounting firm, has issued an attestation report on our internal control over financial reporting as of December 31, 2014. 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, 2014 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 entitled *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, 2014 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	2,451,362	$ 4.34	—
2012 Stock Option Plan	4,054,301	3.91	4,585,769
Total:	6,505,663	$ 4.07	4,585,769
Equity compensation plans not approved by stockholders:			
	—	$ —	—
Total:	—	$ —	—

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 entitled *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 entitled *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 entitled *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:

The exhibits which are filed or furnished with this report or which are incorporated herein by reference are set forth in the Exhibit Index beginning on page A-1, which is incorporated herein by reference.

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: February 26, 2015

By: /s/ Jonathan Lewis
Jonathan Lewis
Chief Executive Officer
(Principal Executive Officer)

Date: February 26, 2015

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

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/ Jonathan Lewis Jonathan Lewis	Director and Chief Executive Officer (Principal Executive Officer)	February 26, 2015
/s/ Kevin G. Lafond Kevin G. Lafond	Vice President, Chief Accounting Officer and Treasurer (Principal Financial and Accounting Officer)	February 26, 2015
/s/ Murray Brennan Murray Brennan	Director	February 26, 2015
/s/ James Cannon James Cannon	Director	February 26, 2015
/s/ Wyche Fowler, Jr. Wyche Fowler, Jr.	Director	February 26, 2015
/s/ Randal J. Kirk Randal J. Kirk	Director	February 26, 2015
/s/ Timothy McInerney Timothy McInerney	Director	February 26, 2015
/s/ Michael Weiser Michael Weiser	Director	February 26, 2015

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ZIOPHARM Oncology, Inc. *(a development stage enterprise)*

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REPORT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

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

We have audited the accompanying balance sheets of ZIOPHARM Oncology, Inc. as of December 31, 2014 and 2013, and the related statements of operations, changes in stockholders' equity, and cash flows for each of the three years in the period ended December 31, 2014. We also have audited ZIOPHARM Oncology, Inc's internal control over financial reporting as of December 31, 2014, based on criteria established in *Internal Control — Integrated Framework* issued by the Committee of Sponsoring Organizations of the Treadway Commission in 2013. ZIOPHARM Oncology, Inc.'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 report on internal control over financial reporting. Our responsibility is to express an opinion on these financial statements and an opinion on the Company's internal control over financial reporting based on our audits.

We conducted our audits in accordance with the standards of the Public Company Accounting Oversight Board (United States). Those standards require that we plan and perform the audits to obtain reasonable assurance about whether the financial statements are free of material misstatement and whether effective internal control over financial reporting was maintained in all material respects. Our audits of the financial statements included examining, on a test basis, evidence supporting the amounts and disclosures in the financial statements, assessing the accounting principles used and significant estimates made by management, and evaluating the overall financial statement presentation. 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.

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 *(a)* pertain to the maintenance of records that, in reasonable detail, accurately and fairly reflect the transactions and dispositions of the assets of the company; *(b)* 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 *(c)* provide reasonable assurance regarding prevention or timely detection of unauthorized acquisition, use, or disposition of the company's assets that could have a material effect on the financial statements.

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

In our opinion, the financial statements referred to above present fairly, in all material respects, the financial position of ZIOPHARM Oncology, Inc. as of December 31, 2014 and 2013, and the results of its operations and its cash flows for each of the years in the three-year period ended December 31, 2014, in conformity with accounting principles generally accepted in the United States of America. Also in our opinion, ZIOPHARM Oncology, Inc. maintained, in all material respects, effective internal control over financial reporting as of December 31, 2014, based on criteria established in *Internal Control — Integrated Framework* issued by the Committee of Sponsoring Organizations of the Treadway Commission of 2013.

/s/ McGladrey LLP

Boston, Massachusetts
February 26, 2015

ZIOPHARM Oncology, Inc.

BALANCE SHEETS

(in thousands, except share and per share data)

	December 31, 2014	December 31, 2013
ASSETS		
Current assets:		
Cash and cash equivalents	$ 42,803	$ 68,204
Receivables	145	145
Prepaid expenses and other current assets	1,139	1,948
Total current assets	44,087	70,297
Property and equipment, net	531	801
Deposits	128	128
Other non current assets	491	528
Total assets	$ 45,237	$ 71,754
LIABILITIES AND STOCKHOLDERS' EQUITY		
Current liabilities:		
Accounts payable	$ 2,004	$ 422
Accrued expenses	7,182	6,357
Deferred revenue - current portion	1,360	800
Deferred rent - current portion	280	212
Total current liabilities	10,826	7,791
Deferred revenue	—	1,933
Deferred rent	570	851
Warrant liabilities	—	11,776
Other long term liabilities	—	20
Total liabilities	$ 11,396	$ 22,371
Commitments and contingencies (note 8)		
Stockholders' equity:		
Common stock, $0.001 par value; 250,000,000 shares authorized; 104,452,105 and 100,159,618 shares issued and outstanding at December 31, 2014 and 2013, respectively	$ 104	$ 100
Additional paid-in capital - common stock	406,349	386,511
Additional paid-in capital - warrants issued	—	3,603
Accumulated Deficit	(372,612)	(340,831)
Total stockholders' equity	33,841	49,383
Total liabilities and stockholders' equity	$ 45,237	$ 71,754

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,		
	2014	2013	2012
Revenue	$ 1,373	$ 800	$ 800
Operating expenses:			
Research and development	32,706	42,852	83,446
General and administrative	12,166	15,661	19,523
Total operating expenses	44,872	58,513	102,969
Loss from operations	(43,499)	(57,713)	(102,169)
Other income (expense), net	(5)	(579)	(13)
Change in fair value of warrants	11,723	1,185	6,050
Net loss	$ (31,781)	$ (57,107)	$ (96,132)
Basic and diluted net loss per share	$ (0.31)	$ (0.66)	$ (1.22)
Weighted average common shares outstanding used to compute basic and diluted net loss per share	101,130,710	85,943,175	78,546,112

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

ZIOPHARM Oncology, Inc.

STATEMENTS OF CHANGES IN STOCKHOLDERS' EQUITY

(in thousands, except share and per share data)

	Stockholder's Equity					
	Common Stock		Additional Paid-in Capital Common Stock	Additional Paid-in Capital Warrants	Deficit Accumulated During the Development Stage	Total Stockholders' Equity
	Shares	Amount				
Balance at December 31, 2011	69,206,044	$ 69	$ 246,519	$ 12,611	$ (187,592)	$ 71,607
Stock-based compensation	—	—	4,880	—	—	4,880
Issuance of common stock in a securities offering, net of commission and expenses of $3,426	10,114,401	11	49,159	—	—	49,170
Exercise of warrants to purchase common stock	259,660	—	1,011	(269)	—	742
Exercise of employee stock options	8,300	—	30	—	—	30
Issuance of restricted common stock	258,032	—	—	—	—	—
Repurchase of shares of restricted common stock	(123,153)	—	(546)	—	—	(546)
Cancelled restricted stock	(123,370)	—	—	—	—	—
Expired warrants	—	—	5,433	(5,433)	—	—
Issuance of common stock in a collaboration agreeement	3,636,926	3	18,691	—	—	18,694
Net loss	—	—	—	—	(96,132)	(96,132)
Balance at December 31, 2012	83,236,840	$ 83	$ 325,177	$ 6,909	$ (283,724)	$ 48,445

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

ZIOPHARM Oncology, Inc.

STATEMENTS OF CHANGES IN STOCKHOLDERS' EQUITY (Cont.)

(in thousands, except share and per share data)

	Common Stock		Additional Paid-in Capital Common Stock	Additional Paid-in Capital Warrants	Deficit Accumulated During the Development Stage	Total Stockholders' Equity/
	Shares	Amount				
Stock-based compensation	—	—	3,507	—	—	3,507
Issuance of common stock, net of commission and expenses of $3,678	16,445,000	16	53,864	—	—	53,880
Exercise of warrants to purchase common stock	112,808	—	396	(196)	—	200
Exercise of employee stock options	570,168	1	955	—	—	956
Issuance of restricted common stock	75,272	—	—	—	—	—
Repurchase of shares of restricted common stock	(116,723)	—	(498)	—	—	(498)
Cancelled of restricted stock	(163,747)	—	—	—	—	—
Expired warrants	—	—	3,110	(3,110)	—	—
Net loss	—	—	—	—	(57,107)	(57,107)
Balance at December 31, 2013	100,159,618	$ 100	$ 386,511	$ 3,603	$ (340,831)	$ 49,383

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

ZIOPHARM Oncology, Inc.

STATEMENTS OF CHANGES IN STOCKHOLDERS' EQUITY (Cont.)

(in thousands, except share and per share data)

	Stockholder's Equity					
	Common Stock		Additional Paid-in Capital Common Stock	Additional Paid-in Capital Warrants	Deficit Accumulated During the Development Stage	Total Stockholders' Equity/
	Shares	Amount				
Stock-based compensation	—	—	4,743	—	—	4,743
Exercise of warrants to purchase common stock	3,747,254	4	13,963	(3,313)	—	10,654
Exercise of employee stock options	613,138	—	1,386	—	—	1,386
Issuance of restricted common stock	66,828	—	—	—	—	—
Repurchase of shares of restricted common stock	(112,333)	—	(544)	—	—	(544)
Cancelled of restricted stock	(22,400)	—	—	—	—	—
Expired warrants	—	—	290	(290)	—	—
Net loss	—	—	—	—	(31,781)	(31,781)
Balance at December 31, 2014	104,452,105	$ 104	$406,349	$ 0	$ (372,612)	$ 33,841

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

ZIOPHARM Oncology, Inc.

STATEMENTS OF CASH FLOWS
(in thousands)

	For the Year Ended December 31,		
	2014	2013	2012
Cash flows from operating activities:			
Net loss	$(31,781)	$(57,107)	$ (96,132)
Adjustments to reconcile net loss to net cash used in operating activities:			
Depreciation and amortization	462	738	658
Stock-based compensation	4,743	3,507	4,880
Change in fair value of warrants	(11,723)	(1,185)	(6,050)
Loss on disposal of fixed assets	—	585	48
Common stock issued in exchange for in-process research and development	—	—	18,694
Change in operating assets and liabilities:			
(Increase) decrease in:			
Receivables	—	(87)	21
Prepaid expenses and other current assets	809	4,964	(5,599)
Other noncurrent assets	37	473	(230)
Deposits	—	4	(43)
Increase (decrease) in:			
Accounts payable	1,582	(1,087)	(218)
Accrued expenses	827	(10,159)	5,695
Deferred revenue	(1,373)	(800)	(800)
Deferred rent	(213)	625	244
Other noncurrent liabilities	(20)	20	—
Net cash used in operating activities	(36,650)	(59,509)	(78,832)
Cash flows from investing activities:			
Purchases of property and equipment	(193)	(132)	(1,559)
Proceeds from sale of property and equipment	—	1	—
Net cash used in investing activities	(193)	(131)	(1,559)
Cash flows from financing activities:			
Proceeds from exercise of stock options	1,386	956	30
Payments to employees for repurchase of restricted common stock	(544)	(498)	(546)
Proceeds from exercise of warrants	10,600	200	330
Proceeds from issuance of common stock and warrants, net	—	53,880	49,170
Net cash provided by financing activities	11,442	54,538	48,984
Net decrease in cash and cash equivalents	(25,401)	(5,102)	(31,407)
Cash and cash equivalents, beginning of period	68,204	73,306	104,713
Cash and cash equivalents, end of period	$ 42,803	$ 68,204	$ 73,306
Supplementary disclosure of cash flow information:			
Cash paid for interest	$ —	$ —	$ —
Cash paid for income taxes	$ —	$ —	$ —
Supplementary disclosure of noncash investing and financing activities:			
Exercise of equity-classified warrants to common shares	$ 692	$ 196	$ 269
Exercise of liability-classified warrants to common shares	$ 54	$ —	$ 412

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

ZIOPHARM Oncology, Inc.

NOTES TO FINANCIAL STATEMENTS

1. Organization

ZIOPHARM Oncology, Inc., which we refer to as "ZIOPHARM" or the "Company", is a biopharmaceutical company that seeks to acquire, develop and commercialize, on its own or with commercial partners, a diverse portfolio of cancer therapies that can address unmet medical needs through synthetic biology.

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, 2014, the Company's accumulated deficit was approximately $372.6 million. Taking into account the receipt of approximately $94.6 million in net proceeds from the February 2015 public offering of common stock, and given the development plans, the Company anticipates cash resources will be sufficient to fund operations into the first quarter of 2017. 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. There can be no assurance that any such financing can be obtained by the Company, or if obtained, what the terms thereof may be, or that any amount that the Company is able to raise will be adequate to support the Company's working capital requirements until it achieves profitable operations.

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 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 effective registration statement on Form S-3 (Registration Statement 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 $94.2 million after deducting underwriting discounts and estimated offering expenses payable by the Company.

On October 23, 2013, 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 14,300,000 shares of our common stock. The price to the public in the offering was $3.50 per share, and the underwriters agreed to purchase the shares from the Company pursuant to the underwriting agreement at a purchase price of $3.29 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 2,145,000 shares of common stock at a purchase price of $3.29 per share, and the underwriters elected to exercise such option in full. The offering was made pursuant to the Company's effective registration statement on Form S-3 (Registration Statement No. 333-177793) previously filed with the SEC, and a prospectus supplement thereunder. The underwriters purchased the 14,300,000 shares and the additional 2,145,000 shares on October 29, 2013. The net proceeds from the offering were approximately $53.9 million after deducting underwriting discounts and estimated offering expenses payable by the Company.

ZIOPHARM Oncology, Inc.

NOTES TO FINANCIAL STATEMENTS

2. Financings (Continued)

On January 20, 2012, 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 9,650,000 shares of our common stock. The price to the public in the offering was $5.20 per share, and the underwriters agreed to purchase the shares from the Company pursuant to the underwriting agreement at a purchase price of $4.888 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 1,447,500 shares of common stock at a purchase price of $4.888 per share. The offering was made pursuant to the Company's effective registration statement on Form S-3 (Registration Statement No. 333-177793) previously filed with the SEC, and a prospectus supplement thereunder. The underwriters purchased the 9,650,000 shares on January 25, 2012 and purchased an additional 464,401 shares on January 31, 2012 pursuant to the partial exercise of their option to purchase additional shares, resulting in our issuing a total of 10,114,401 shares. The net proceeds from the offering were approximately $49.2 million after deducting underwriting discounts 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 ("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;
- Fair value measurements for stock based compensation and warrants; and
- Income taxes.

Subsequent Events

On January 13, 2015, the Company, together with Intrexon, entered into a license agreement, or the License, with The University of Texas M.D. Anderson Cancer Center ("MD Anderson"). Pursuant to the License, the Company and Intrexon hold an exclusive, worldwide license to certain technologies owned and licensed by MD Anderson including technologies relating to novel chimeric antigen receptor (CAR) T-cell therapies arising from the laboratory of Laurence Cooper, M.D., Ph.D., professor of pediatrics at MD Anderson, as well as either co-exclusive or non-exclusive licenses under certain related technologies.

Pursuant to the terms of the License, MD Anderson will receive, within sixty days of the date of the License, consideration of $50 million in shares of our common stock (or 10,124,561 shares), and $50 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

ZIOPHARM Oncology, Inc.

NOTES TO FINANCIAL STATEMENTS

3. Summary of Significant Accounting Policies (Continued)

the Company's and Intrexon's common stock ending on the date prior to the announcement of the entry into the License, collectively referred to as the License Shares, pursuant to the terms of the License Shares Securities Issuance Agreement described below. The Company and Intrexon also agreed to reimburse MD Anderson for out of pocket expenses for maintaining patents covering the licensed technologies.

In addition, pursuant to the License, MD Anderson has agreed to transfer to us certain existing research programs described in the License and to grant to Intrexon and us certain additional technology rights related thereto. In connection with such transfer, the terms of the License also require us and Intrexon to enter into a research and development agreement with MD Anderson pursuant to which the Company will provide funding for certain research and development activities of MD Anderson for a period of three years, in an amount between $15 and $20 million per year. The first quarterly payment of $3.75 million due under this arrangement is required to be made by us within 60 days of the date of the License.

The term of the 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 License; provided, however, that following the expiration of the term, the Company and Intrexon 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 License and subject to a 90 day cure period, MD Anderson will have the right to convert the License into a non-exclusive license if the Company and Intrexon 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 License and subject to a 180 day cure period, MD Anderson will have the right to terminate the License with respect to specific technology(ies) funded by the government or subject to a third party contract if the Company and Intrexon 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 License if the Company and Intrexon fail to timely deliver the shares due in consideration for the License. MD Anderson may also terminate the agreement with written notice upon material breach by us and Intrexon, if such breach has not been cured within 60 days of receiving such notice. In addition, the License will terminate upon the occurrence of certain insolvency events for both us and Intrexon and may be terminated by the mutual written agreement of us, Intrexon and MD Anderson.

On January 9, 2015, in order to induce MD Anderson to enter into the License on an accelerated schedule, the Company and Intrexon entered into a letter agreement, or the Letter Agreement, pursuant to which MD Anderson will receive consideration of $7.5 million in shares of the 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 the our and Intrexon's common stock ending on the date prior to the Letter Agreement, collectively referred to as the Incentive Shares, in the event that the License was entered into on or prior to 8:00 am pacific time on January 14, 2015, referred to as the Accelerated Closing Deadline. The Incentive Shares will be issued to MD Anderson within sixty days of the date of the License pursuant to the terms of the Incentive Shares Securities Issuance Agreement described below.

In connection with the entry into the License, on January 13, 2015, the Company entered into a Securities Issuance Agreement with MD Anderson, or the License Shares Securities Issuance Agreement, pursuant to which the Company agreed to issue and sell the License Shares to MD Anderson in consideration for the License. The closing of the issuance and sale of the License Shares under the License Shares Securities Issuance Agreement will occur within sixty days of the date of the License, subject to customary closing conditions.

In connection with the entry into the Letter Agreement, on January 13, 2015, the Company entered into a Securities Issuance Agreement with MD Anderson, or the Incentive Shares Securities Issuance Agreement,

ZIOPHARM Oncology, Inc.

NOTES TO FINANCIAL STATEMENTS

3. Summary of Significant Accounting Policies (Continued)

pursuant to which the Company agreed to issue and sell the Incentive Shares to MD Anderson in consideration for the execution and delivery of the License on or prior to the Accelerated Closing Deadline in connection with the Letter Agreement. The closing of the issuance and sale of the Incentive Shares under the Incentive Shares Securities Issuance Agreement will occur within sixty days of the date of the License, subject to customary closing conditions.

Also in connection with the License and the issuance of the License Shares and the Incentive Shares, on January 13, 2015, the Company and 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 our common stock held by MD Anderson on the date that the Registration Statement is filed, within 15 days of the closing under the License Shares Securities Issuance Agreement. Under the Registration Rights Agreement, the Company is obligated to use our reasonable best efforts to cause the Registration Statement to be declared effective as promptly as practicable after filing and in no event later than 120 days of the closing under the License Shares Securities Issuance Agreement and 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.

Our director, Randall J. Kirk, is the CEO, a director, and the largest stockholder of Intrexon, which is a party to the License. Mr. Kirk is also one of our principal stockholders.

On February 3, 2015, the Company entered into an underwriting agreement with J.P. Morgan Securities LLC (see Note 2 above).

The Company evaluated all other events and transactions that occurred after the balance sheet date through the date of this filing. Except as disclosed above, the Company did not have any other 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.

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.

ZIOPHARM Oncology, Inc.

NOTES TO FINANCIAL STATEMENTS

3. Summary of Significant Accounting Policies (Continued)

Restricted Cash

Other assets include $388 thousand that is restricted as collateral for the Company's facility leases and $103 thousand that is restricted as collateral for a line of credit.

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.

Warrants

The Company applies the accounting standard which provides guidance in assessing whether an equity-based financial instrument is indexed to an entity's own stock for purposes of determining whether a financial instrument should be treated as a derivative. In applying the methodology the Company concluded that certain warrants issued by the Company have terms that do not meet the criteria to be considered indexed to the Company's own stock and therefore are classified as liabilities in the Company's balance sheet. The liability classified warrants are subject to re-measurement at each balance sheet date and any change in fair value is recognized as a component of "Other income, net" in the accompanying Statement of Operations. Fair value is measured using the binomial valuation model. In December 2011, the Company switched from the Black-Scholes valuation model to the binomial valuation model as it provides a better evaluation of the fair market value of the Company's liability-classified warrants.

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.

Assets and liabilities measured at fair value on a recurring basis as of December 31, 2014 and 2013 are as follows:

($ in thousands)	Fair Value Measurements at Reporting Date Using			
Description	Balance as of December 31, 2014	Quoted Prices in Active Markets for Identical Assets/Liabilities (Level 1)	Significant Other Observable Inputs (Level 2)	Significant Unobservable Inputs (Level 3)
Cash equivalents	$ 37,290	$ 37,290	$ —	$ —
Warrant liability	$ —	$ —	$ —	$ —

ZIOPHARM Oncology, Inc.

NOTES TO FINANCIAL STATEMENTS

3. Summary of Significant Accounting Policies (Continued)

($ in thousands)

Description	Balance as of December 31, 2013	Fair Value Measurements at Reporting Date Using: Quoted Prices in Active Markets for Identical Assets/Liabilities (Level 1)	Significant Other Observable Inputs (Level 2)	Significant Unobservable Inputs (Level 3)
Cash equivalents	$ 66,794	$ 66,794	$ —	$ —
Warrant liability	$ 11,776	$ —	$ 11,776	$ —

The cash equivalents consist primarily of short term U.S. treasury money market mutual funds which are actively traded. The warrants were valued using a binomial valuation model. As of December 31, 2014, all liability classified warrants had expired. See Note 9 to the financial statements, Warrants, for additional disclosure on the valuation methodology and significant assumptions.

Revenue Recognition

The Company receives revenue from a collaboration agreement (see Note 8 to the financial statements, Commitments and Contingencies). Collaboration arrangements typically include payments for one or more of the following: non-refundable, upfront license fees, funding of research and development efforts, milestone payments if specified objectives are achieved and/or profit-sharing or royalties on product sales. Arrangements containing multiple elements are divided into separate units of accounting if certain criteria are met, including whether the delivered element has stand-alone value to the collaborative partner. The consideration received is then allocated among the separate units based on their respective fair values and the applicable revenue recognition criteria are applied to each of the separate units.

Revenue from non-refundable, upfront research and development fees is reported as research and development revenue and is recognized on a straight-line basis over the contracted or estimated period of performance, which is typically the development term. Research and development funding is earned over the period of effort.

Milestone payments are recognized as research and development revenue upon achievement of the milestone only if (1) the milestone payment is non-refundable, (2) substantive effort is involved in achieving the milestone and (3) the amount of the milestone is reasonable in relation to the effort expended or the risk associated with achievement of the milestone. If any of these conditions are not met, the milestone payment is deferred and recognized as revenue over the estimated remaining period of performance under the contract as the Company completes its performance obligations.

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

ZIOPHARM Oncology, Inc.

NOTES TO FINANCIAL STATEMENTS

3. Summary of Significant Accounting Policies (Continued)

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 10 to the financial statements, Income Taxes).

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, 2014, 2013, and 2012 and did not capitalize any such costs on the balance sheets. The Company recognized $3.7 million, $2.3 million, and $3.1 million of compensation expense related to vesting of employee stock options during the years ended December 31, 2014, 2013, and 2012, respectively. In the years ended December 31, 2014, 2013, and 2012, the Company recognized $1.0 million, $1.2 million, and $1.7 million of compensation expense, respectively, related to vesting of restricted stock (see Note 12 to the financial statements, Stock Option Plan). In the years ended December 31, 2014, 2013, and 2012, the Company recognized $4.7 million, $3.5 million, and $4.9 million of compensation expense, respectively, related to vesting of all employee and director awards. The following table presents share-based compensation expense included in the Company's Statements of Operations:

	Year ended December 31,		
(in thousands)	**2014**	**2013**	**2012**
Research and development	$1,416	$ 792	$1,917
General and administrative	3,327	2,715	2,963
Share based employee compensation expense before tax	4,743	3,507	4,880
Income tax benefit	—	—	—
Net share based employee compensation expense	$4,743	$3,507	$4,880

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 2014, 2013, and 2012 was approximately $3.58, $2.51, and $3.06 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

ZIOPHARM Oncology, Inc.

NOTES TO FINANCIAL STATEMENTS

3. Summary of Significant Accounting Policies (Continued)

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 Staff Accounting Bulletin No. 110. The assumptions for volatility, expected life, dividend yield and risk-free interest rate are presented in the table below:

	2014	2013	2012
Weighted average risk-free interest rate	1.74 - 2.11%	1.00 - 2.10%	0.79 - 1.13%
Expected life in years	6	6	6
Expected volatility	85.22 - 94.55%	83.40 - 95.96%	83.36 - 83.53%
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 potential dilutive shares, which include outstanding common stock options, unvested restricted stock and warrants, 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, 2014, 2013, and 2012 consist of the following:

	December 31,		
	2014	2013	2012
Stock options	6,505,664	6,747,303	7,147,303
Unvested restricted stock	144,508	352,865	733,739
Warrants	—	10,539,767	11,197,454
	6,650,172	17,639,935	19,078,496

New Accounting Pronouncements

In August 2014, the FASB issued ASU 2014-15, Presentation of Financial Statements—Going Concern (Subtopic 205-40) in which management should evaluate whether there are conditions or events, considered in the aggregate, that raise substantial doubt about the entity's ability to continue as a going concern within one year after the date that the financial statements are issued (or within one year after the date that the financial statements are available to be issued when applicable). When management identifies conditions or events that raise substantial doubt about an entity's ability to continue as a going concern, management should consider whether its plans that are intended to mitigate those relevant conditions or events will alleviate the substantial doubt. This update is effective for annual periods beginning after December 15, 2016, and early application is permitted for any annual or interim period thereafter.

On June 10, 2014, the FASB issued ASU 2014-10, Development Stage Entities (Topic 915), which simplifies financial reporting for development stage entities by eliminating requirements specific to development stage entities. As a result, entities in a development stage will no longer need to present inception-to-date information about income statement line items, cash flows, and equity transactions. Instead, the new guidance clarifies how these entities should tailor existing disclosures to explain the risks and uncertainties related to their activities. This update is effective for annual periods beginning after December 15, 2014, and early application is permitted

ZIOPHARM Oncology, Inc.

NOTES TO FINANCIAL STATEMENTS

3. Summary of Significant Accounting Policies (Continued)

for any annual or interim period for which the entity's financial statements have not yet been issued. The Company adopted this guidance prior to issuing the financial statements in this Quarterly Report on Form 10-Q. The adoption of ASU 2014-10 impacted presentation and disclosure only and did not have any impact on financial position or results of operations.

In May 2014, the FASB issued ASU 2014-09, Revenue from Contracts with Customers (Topic 606), which clarifies the principles for recognizing revenue and develops a common revenue standard for U.S. GAAP and 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, 2016, including interim periods within that reporting period and early application is not permitted. The company believes that the adoption of this standard will not have an impact on our financial position or results of operations.

4. Restructuring

The Company underwent restructuring activities during the year ended December 31, 2013 which included a reduction in workforce and office space, resulting in sublease agreements in Boston and New York. As a result, the Company incurred restructuring charges of $1.7 million, $0.6 million was included in general and administrative expenses and $1.1 million was included in research and development expenses. The Company also incurred charges for exit and disposal activities from the Boston and New York sublease agreements which resulted in an aggregate loss of $0.8 million recorded in general and administrative expenses, and a loss on the disposal of fixed assets of $0.6 million, recorded in Other income in the Statement of Operations for the year ended December 31, 2013.

On October 17, 2013, the Company entered into a sublease agreement to lease 7,259 square feet in our New York office to a subtenant. The Company remains primarily liable to pay rent on the original lease. Accordingly, 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 our subtenant. The Company retired assets in this subleased area as a result of this sublease with a net book value of $392 thousand, and recorded a loss on disposal of fixed assets for the same amount for the year ended December 31, 2013.

On August 30, 2013, the Company entered into a sublease agreement to lease 5,249 square feet in our Boston office 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 $42 thousand for the year ended December 31, 2013, representing the remaining contractual obligation of $367 thousand, less $325 thousand in payments from our subtenant. The Company retired assets in this subleased area as a result of this sublease with a net book value of $194 thousand, and recorded a loss on disposal of fixed assets. The company previously held a security deposit of $20 thousand in accordance with the sublease, which was recorded in other non-current assets and other liabilities on the balance sheet for the year ended December 31, 2013. This sublease tenant vacated the lease in October 2014. As of December 31, 2014, the company applied the $20 thousand deposit against outstanding rent. The company is actively pursuing a subtenant to lease a portion of the space in the Boston Office that was vacated by a previous subtenant.

On July 16, 2012, the Company announced that it restructured its management team and closed its Germantown, MD office. As a result of this action, the Company recorded a restructuring charge, consisting primarily of

ZIOPHARM Oncology, Inc.

NOTES TO FINANCIAL STATEMENTS

4. Restructuring (Continued)

severance, stock based compensation associated with stock option modifications (see Note 12 to the financial statements, Stock Option Plan) and health benefit continuation costs of approximately $1.3 million. These costs are included in general and administrative expense for the year ended December 31, 2012.

5. Property and Equipment, net

Property and equipment, net, consists of the following:

	December 31,	
(in thousands)	**2014**	**2013**
Office and computer equipment	$ 1,094	$ 1,076
Software	874	884
Leasehold improvements	927	841
Manufacturing equipment	251	153
	3,146	2,954
Less: accumulated depreciation	(2,615)	(2,153)
Property and equipment, net	$ 531	$ 801

Depreciation and amortization charged to the Statement of Operations for the years ended December 31, 2014, 2013, and 2012 was: $462 thousand, $738 thousand and, $658 thousand, respectively.

6. Accrued Expenses

Accrued expenses consist of the following:

	December 31,	
(in thousands)	**2014**	**2013**
Clinical consulting services	$2,802	$3,751
Preclinical services	2,027	513
Employee compensation	768	252
Professional services	422	582
Payroll taxes and benefits	417	255
Manufacturing services	308	547
Other consulting services	226	230
Accrued vacation	212	227
Accrued expenses	$7,182	$6,357

7. Related Party Transactions

On January 6, 2011, the Company entered into an Exclusive Channel Partner Agreement, or Channel Agreement, with Intrexon Corporation, or Intrexon (see Note 8 to the financial statements, Commitments and Contingencies, for additional disclosure relating to the Channel Agreement). Our director, Randall J. Kirk, is the CEO, a director, and the largest stockholder of Intrexon. During the year ended December 31, 2012, the Company paid Intrexon approximately $11.4 million, of which $6.6 million was for preclinical and clinical research services already incurred and the remaining $4.8 million was for services expected to be incurred within a year. This amount was included as part of prepaid expenses and other current assets on the balance sheet as of December 31, 2012. During the year ended December 31, 2013, the Company expensed $7.8 million for services performed by Intrexon, of which $4.8 million was applied to the prepaid balance in other current assets, $2.4 million was paid to Intrexon and $0.6 million was recorded in accrued expenses. As of December 31, 2013, the prepaid balance in other current assets on the accompanying balance sheet has been reduced to $0. During the

ZIOPHARM Oncology, Inc.

NOTES TO FINANCIAL STATEMENTS

7. Related Party Transactions (Continued)

year ended December 31, 2014, the Company expensed $12.0 million for services performed by Intrexon, of which $10.1 million was paid to Intrexon and $1.9 million was recorded in accounts payable and accrued expenses. As of December 31, 2014, the prepaid balance in other current assets on the accompanying balance sheet has been reduced to $0.

On January 25, 2012, Intrexon purchased 1,923,075 shares of common stock in the Company's public offering (see Note 2 to the financial statements, Financings).

On November 7, 2012, the Company issued 3,636,926 shares of common stock to Intrexon (see Note 11 to the financial statements, Preferred Stock and Stockholders' Equity).

On October 29, 2013, Intrexon purchased 2,857,143 shares of common stock in the Company's public offering (see Note 2 to the financial statements, Financings).

On February 2, 2015, Intrexon purchased 1,440,000 shares of common stock in the Company's public offering (see Note 2 to the financial statements, Financings).

Intrexon's purchases were made on terms that were the same as others participating in the above financings.

8. Commitments and Contingencies

Operating Leases

Prior to December 31, 2012, the Company entered into an operating lease in New York, NY, consisting of 6,251 square feet of 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 1,008 square feet of office space. As of December 31, 2012, the Company occupied 7,259 square feet of space in New York, NY, and maintained a $388 thousand letter of credit. The collateral for the letter of credit is recorded in other non-current assets on the balance sheet as of December 31, 2014. 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 7,259 square feet in our New York office 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 our subtenant. The Company retired assets in this subleased area as a result of this sublease with a net book value of $392 thousand, and recorded a loss on disposal of fixed assets for the same amount for the year ended December 31, 2013. The Company continues to maintain a $388 thousand letter of credit. The collateral for the letter of credit is recorded in other non-current assets on the balance sheet as of December 31, 2014. The lease for office space in New York, NY expires in October 2018.

Prior to December 31, 2012, the Company entered into separate operating lease agreements for various spaces in a building in Boston, MA. That space consisted of 5,249 square feet on the first floor, 8,538 square feet on the second floor, and 6,959 square feet on the third floor. In June 2012, the Company re-negotiated a master lease for the entire Boston office space, added 9,800 square feet of office space on the fourth floor, surrendered 4,113 square feet from the second floor, and incorporated all floors' lease agreements under the same master agreement expiring in August 2016. The Company provided an additional $41 thousand security deposit for the additional space on the fourth floor. As of December 31, 2012, a total security deposit of $127 thousand was paid to its landlord for security deposits for these agreements.

ZIOPHARM Oncology, Inc.

NOTES TO FINANCIAL STATEMENTS

8. Commitments and Contingencies (Continued)

On August 30, 2013, the Company entered into a sublease agreement to lease 5,249 square feet in our Boston office 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 $42 thousand for the year ended December 31, 2013, representing the remaining contractual obligation of $367 thousand, less $325 thousand in payments from our subtenant. The Company retired assets in this subleased area as a result of this sublease with a net book value of $194 thousand, and recorded a loss on disposal of fixed assets. The company previously held a security deposit of $20 thousand in accordance with the sublease, which was recorded in other non-current assets and other liabilities on the balance sheet for the year ended December 31, 2013. This sublease tenant vacated the lease in October 2014. As of December 31, 2014, the company applied the $20 thousand deposit against outstanding rent. The company is actively pursuing a subtenant to lease a portion of the space in the Boston Office that was vacated by a previous subtenant.

As of December 31, 2014, the Company occupies 21,184 square feet of space in its Boston, MA office and has paid a total of $127 thousand for security deposits, which are recorded in other non-current assets on the balance sheet.

In April 2011, the Company entered into an operating lease for office space in Germantown, MD, consisting of 2,227 square feet. As of December 31, 2011, the Company recorded the $4 thousand security deposit in other non-current assets on the balance sheet. The lease would have expired in March 2014; however, on July 16, 2012, the Germantown, Maryland office was closed. In June 2013, the Company paid off the remainder of the Germantown, Maryland lease obligation.

Future net minimum lease payments under operating leases as of December 31, 2014 are as follows (in thousands):

2015	$ 1,235
2016	997
2017	501
2018	424
2019	—
	3,157
Less: contractual sublease income	(1,224)
Future minimum lease payments, net	$ 1,933

Total rent expense was approximately $1.2 million, $1.0 million, and $1.1 million for the years ended December 31, 2014, 2013, and 2012. 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, 2014 and 2013 of $850 thousand ($280 thousand current and $570 long-term) and $1.1 million ($212 thousand current and $851 long-term) respectively, which is recorded in deferred rent on the balance sheet.

License Agreements

Exclusive Channel Partner Agreement with Intrexon Corporation

On January 6, 2011, the Company entered into an Exclusive Channel Partner Agreement, or the Channel Agreement, with Intrexon that governs a “channel partnering” arrangement in which the Company uses

ZIOPHARM Oncology, Inc.

NOTES TO FINANCIAL STATEMENTS

8. Commitments and Contingencies (Continued)

Intrexon's technology directed towards *in vivo* expression of effectors in connection with the development of Ad-RTS-IL-12 + veledimex and DC-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 the Company collectively refer to as the Cancer Program. The Channel Agreement establishes committees comprised of representatives of us and Intrexon 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 Intrexon 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 collectively refer 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 the rights described without Intrexon'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 development, commercialization and certain aspects of manufacturing of ZIOPHARM Products. Intrexon is responsible for the costs of 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 Intrexon's patents.

Subject to certain expense allocations and other offsets provided in the Channel Agreement, the Company will pay Intrexon on a quarterly basis 50% of net profits derived in that quarter from the sale of ZIOPHARM Products, calculated on a ZIOPHARM Product-by- ZIOPHARM Product basis. The Company has likewise agreed to pay Intrexon 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 Intrexon.

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 Intrexon 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 Intrexon following an unconsented assignment by us or our election not to pursue development of a Superior Therapy).

ZIOPHARM Oncology, Inc.

NOTES TO FINANCIAL STATEMENTS

8. Commitments and Contingencies (Continued)

Our obligation to pay 50% of net profits or revenue described above with respect to these "retained" products will survive termination of the Channel Agreement.

License Agreement—The University of Texas M. D. Anderson Cancer Center

On January 13, 2015, the Company, together with Intrexon, entered into a license agreement, or the License, with MD Anderson. Pursuant to the License, the Company and Intrexon hold an exclusive, worldwide license to certain technologies owned and licensed by MD Anderson including technologies relating to novel chimeric antigen receptor (CAR) T-cell therapies arising from the laboratory of Laurence Cooper, M.D., Ph.D., professor of pediatrics at MD Anderson, as well as either co-exclusive or non-exclusive licenses under certain related technologies.

Pursuant to the terms of the License, MD Anderson will receive, within sixty days of the date of the License, consideration of $50 million in shares of our common stock (or 10,124,561 shares), and $50 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 announcement of the entry into the License, collectively referred to as the License Shares, pursuant to the terms of the License Shares Securities Issuance Agreement described below. The Company and Intrexon also agreed to reimburse MD Anderson for out of pocket expenses for maintaining patents covering the licensed technologies.

In addition, pursuant to the License, MD Anderson has agreed to transfer to us certain existing research programs described in the License and to grant to Intrexon and us certain additional technology rights related thereto. In connection with such transfer, the terms of the License also require us and Intrexon to enter into a research and development agreement with MD Anderson pursuant to which the Company will provide funding for certain research and development activities of MD Anderson for a period of three years, in an amount between $15 and $20 million per year. The first quarterly payment of $3.75 million due under this arrangement is required to be made by us within 60 days of the date of the License.

The term of the 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 License; provided, however, that following the expiration of the term, the Company and Intrexon 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 License and subject to a 90 day cure period, MD Anderson will have the right to convert the License into a non-exclusive license if the Company and Intrexon 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 License and subject to a 180 day cure period, MD Anderson will have the right to terminate the License with respect to specific technology(ies) funded by the government or subject to a third party contract if the Company and Intrexon 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 License if the Company and Intrexon fail to timely deliver the shares due in consideration for the License. MD Anderson may also terminate the agreement with written notice upon material breach by us and Intrexon, if such breach has not been cured within 60 days of receiving such notice. In addition, the License will terminate upon the occurrence of certain insolvency events for both us and Intrexon and may be terminated by the mutual written agreement of us, Intrexon and MD Anderson.

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

ZIOPHARM Oncology, Inc.

NOTES TO FINANCIAL STATEMENTS

8. Commitments and Contingencies (Continued)

shares of Intrexon's common stock in each case based on a trailing 20 day volume weighted average of the closing price of the our and Intrexon's common stock ending on the date prior to the Letter Agreement, collectively referred to as the Incentive Shares, in the event that the License was entered into on or prior to 8:00 am pacific time on January 14, 2015, referred to as the Accelerated Closing Deadline. The Incentive Shares will be issued to MD Anderson within sixty days of the date of the License pursuant to the terms of the Incentive Shares Securities Issuance Agreement described below.

In connection with the entry into the License, on January 13, 2015, the Company entered into a Securities Issuance Agreement with MD Anderson, or the License Shares Securities Issuance Agreement, pursuant to which the Company agreed to issue and sell the License Shares to MD Anderson in consideration for the License. The closing of the issuance and sale of the License Shares under the License Shares Securities Issuance Agreement will occur within sixty days of the date of the License, subject to customary closing conditions.

In connection with the entry into the Letter Agreement, on January 13, 2015, the Company entered into a Securities Issuance Agreement with MD Anderson, or the Incentive Shares Securities Issuance Agreement, pursuant to which the Company agreed to issue and sell the Incentive Shares to MD Anderson in consideration for the execution and delivery of the License on or prior to the Accelerated Closing Deadline in connection with the Letter Agreement. The closing of the issuance and sale of the Incentive Shares under the Incentive Shares Securities Issuance Agreement will occur within sixty days of the date of the License, subject to customary closing conditions.

Also in connection with the License and the issuance of the License Shares and the Incentive Shares, on January 13, 2015, the Company and 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 our common stock held by MD Anderson on the date that the Registration Statement is filed, within 15 days of the closing under the License Shares Securities Issuance Agreement. Under the Registration Rights Agreement, the Company is obligated to use our reasonable best efforts to cause the Registration Statement to be declared effective as promptly as practicable after filing and in no event later than 120 days of the closing under the License Shares Securities Issuance Agreement and 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.

License Agreement with DEKK-Tec, Inc.

On October 15, 2004, the Company entered into a license agreement with DEKK-Tec, Inc., pursuant to which it was granted an exclusive, worldwide license for palifosfamide.

In consideration for the license rights, DEKK-Tec is entitled to receive payments upon achieving certain milestones in varying amounts which on a cumulative basis may total $4.0 million. Of the aggregate milestone payments, most will be creditable against future royalty payments as referenced below. Additionally, the Company issued DEKK-Tec an option to purchase 27,616 shares of the Company's common stock for $0.02 per share, of which 13,808 options are still outstanding. DEKK-Tec is entitled to receive single digit percentage royalty payments on the sales of palifosfamide should it be approved for commercial sale. The Company's obligation to pay royalties will terminate on a country-by-country basis upon the expiration of all valid claims of patents in such country covering licensed product, subject to earlier termination in the event of defaults by the parties under the license agreement. No milestones under the license agreement have been reached or expensed since 2010.

ZIOPHARM Oncology, Inc.

NOTES TO FINANCIAL STATEMENTS

8. Commitments and Contingencies (Continued)

License Agreement with Southern Research Institute

On December 22, 2004, the Company entered into an Option Agreement with the Southern Research Institute, or SRI, pursuant to which the Company was granted an exclusive option to obtain an exclusive license to SRI's interest in certain intellectual property, including exclusive rights related to certain isophosphoramide mustard analogs. On February 5, 2007, the Company exercised its option and entered into the exclusive license agreement. Under the license agreement, the Company is required to remit minimum annual royalty payments of $25 thousand until the first commercial sale of a licensed product. These payments were made for the years ended December 31, 2014, 2013, and 2012. The Company may be required to make payments upon achievement of certain milestones in varying amounts which on a cumulative basis could total up to $775 thousand. In addition, SRI will be entitled to receive single digit percentage royalty payments on the sales of a licensed product in any country until all licensed patents rights in that country which are utilized in the product have expired. No milestones under the license agreement were reached or expensed since the agreement's inception.

Patent and Technology License Agreement—The University of Texas M. D. 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 The Board of Regents of the University of Texas System, acting on behalf of The University of Texas M. D. Anderson Cancer Center and the Texas A&M University System, which the Company refers to, collectively, as the Licensors. Under this agreement, the Company was 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 the 2003 Stock Option Plan for $0.002 per share following the successful completion of certain clinical milestones, of which 37,666 have vested. The remaining 12,556 shares will vest 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. In addition, the Licensors are entitled to receive certain milestone payments. The Company may be required to make additional payments 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.

The license agreement also contains other provisions customary and common in similar agreements within the industry, such as the right to sublicense the Company rights under the agreement. On July 31, 2014, the Company amended and restated the License and Collaboration Agreement between the Company and Solasia Pharma K.K. or Solasia, granting to 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. Solasia will be responsible for all costs related to the development, manufacturing and commercialization of darinaparsin. The Licensors will receive a portion of all milestone and royalty payments made by Solasia to the Company in accordance with the terms of the Company's license agreement with the Licensors.

Collaboration Agreement with Solasia Pharma K.K.

On March 7, 2011, the Company entered into a License and Collaboration Agreement with Solasia Pharma K.K., or Solasia.

ZIOPHARM Oncology, Inc.

NOTES TO FINANCIAL STATEMENTS

8. Commitments and Contingencies (Continued)

Pursuant to the License and Collaboration Agreement, the Company granted Solasia an exclusive license to develop and commercialize darinaparsin in both IV and oral forms and related organic arsenic molecules, in all indications for human use in a pan- Asian/Pacific territory comprised of 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. Under the License and Collaboration Agreement, the Company provided Solasia with drug product to conduct clinical trials. These transfers were accounted for as a reduction of research and development costs and an increase in collaboration receivables. The agreement provides that Solasia will be responsible for the development and commercialization of darinaparsin in the pan-Asian/Pacific territory.

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

The $5.0 million upfront payment received in March 2011 is being amortized over the period of the Company's research and development effort. The Company originally estimated this period to be 75 months. In accordance with the amended and restated License and Collaboration Agreement with Solasia, the Company is no longer obligated to continue their research and development efforts in connection with the upfront payment. However, there are certain deliverables that are included in the amended and restated License and Collaboration Agreement including transfer of intellectual property and prior research and development results, which were originally estimated by management to be completed by March 31, 2015 when the amended and restated License and Collaboration Agreement was signed in July 2014. Management reassessed the period of performance related to the remaining transitional services to be completed under the agreement and determined that the services are now expected to be completed by December 31, 2015. As a result, the Company has determined that the estimated remaining period for delivering the transitional services at September 30, 2014 was 15 months through December 31, 2015. Accordingly, the Company has recorded $1.4 million in revenue during the twelve months ended December 31, 2014 while the remaining deferred revenue balance of $1.4 million at December 31, 2014 has been classified as current.

License Agreement with Baxter Healthcare Corporation

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.

ZIOPHARM Oncology, Inc.

NOTES TO FINANCIAL STATEMENTS

8. Commitments and Contingencies (Continued)

During each of the years ended December 31, 2014, 2013, and 2012, the installment payments of $250 thousand were met and expensed.

Collaboration Agreement with Harmon Hill, LLC

On April 8, 2008, the Company signed a collaboration agreement for Harmon Hill, LLC, or Harmon Hill, to provide consulting and other services for the development and commercialization of oncology therapeutics by ZIOPHARM.

The Company expensed $200 thousand during the year ended December 31, 2012 under this agreement. This agreement expired on November 8, 2012.

On June 27, 2013, the Company signed a new collaboration agreement with Harmon Hill to provide consulting and other services for the development and commercialization of oncology therapeutics by ZIOPHARM, effective April 1, 2013. Under the agreement the Company has agreed to pay Harmon Hill $15 thousand per month for the consulting services. Subject to renewal or extension by the parties, the term of the agreement is for a one year period. The Company expensed $135 thousand and $180 thousand for the years ended December 31, 2013 and 2014, respectively.

CRO Services Agreement with Novella Clinical, Inc.

On December 4, 2008, the Company entered into a Master Clinical Research Organization Services Agreement with Novella Clinical, Inc., or Novella, under which Novella provides CRO services in support of our clinical trials. The work order for the newest trial being conducted by Novella was signed on November 2, 2012. Novella was entitled to cumulative payments of up to $790 thousand under these arrangements, which is payable in varying amounts upon Novella achieving specified milestones. During the year ended December 31, 2012, the Company expensed $256 thousand upon the achievement of various milestones. During the year ended December 31, 2013, two database related milestones and one site activation related milestone were met and expensed totaling $136 thousand.

On August 18, 2014 and November 6, 2014, the Company signed two amendments of the Master Clinical Research Organization Services Agreement with Novella. The amendments reflect the removal of data management, statistical and clinical study report services, as well as a change in the timeline and scope of clinical trial support. During the year ended December 31, 2014, three clinical milestones were met and expensed totaling $236 thousand.

CRO Services Agreement with MS Clinical Services, LLC.

On July 24, 2014, the Company entered into a Master Clinical Research Organization Services Agreement with MS Clinical Services, LLC., or Medsource, under which Medsource provides CRO services in support of our clinical trials. There are no milestones associated with this agreement.

ZIOPHARM Oncology, Inc.

NOTES TO FINANCIAL STATEMENTS

8. Commitments and Contingencies (Continued)

CRO Services Agreement with PPD Development, L. P.

The Company was party to a Master Clinical Research Organization Services Agreement with PPD Development, L. P., or PPD, dated January 29, 2010, a related work order dated June 25, 2010 and a related work order dated April 8, 2011 under which PPD provides clinical research organization, or CRO, services in support of the Company's clinical trials. During the years ended December 31, 2012 and 2013, the Company expensed $3.8 million and $9.2 million respectively. There are no remaining milestones related to this agreement.

CRO Services Agreement with Pharmaceutical Research Associates, Inc.

On December 13, 2011, the Company entered into a Master Clinical Research Organization Services Agreement with Pharmaceutical Research Associates, Inc., or PRA, under which PRA provides CRO services in support of our clinical trials. During the years ended December 31, 2012 and 2013, the Company expensed $7.3 million and $2.2 million, respectively. There are no remaining milestones related to this agreement.

9. Warrants

The Company has issued both warrants that are accounted for as liabilities and warrants that are accounted for as equity instruments.

The Company follows accounting standards that provide guidance in assessing whether an equity-issued financial instrument is indexed to an entity's own stock for purposes of determining whether a financial instrument should be treated as a derivative and classified as a liability. Accounting standards require that liability classified warrants be recorded at their fair value at each financial reporting period and the resulting gain or loss be recorded as other income (expense) in the Statements of Operations. Fair value is measured using the binomial valuation model.

In connection with the December 2009 public offering, the Company issued warrants to purchase an aggregate of 8,206,520 shares of common stock (including the investor warrants and 464,520 warrants issued to the Underwriters). The investor warrants were exercisable immediately and the underwriter warrants exercisable six months after the date of issuance. The warrants had an exercise price of $4.02 per share and a 5 year term. The fair value of the warrants was estimated at $22.9 million using a Black-Scholes model with the following assumptions: expected volatility of 105%, risk free interest rate of 2.14%, expected life of 5 years and no dividends.

Subject to certain exceptions, these warrants provide for anti-dilution protection should common stock or common stock equivalents be subsequently issued at a price less than the exercise price of the warrants then in effect, which was initially $4.02 per share. This provision was triggered in 2013 when stock was sold at $3.50 per share in our 2013 public offering. Accordingly, the outstanding warrants were increased by 184,367 warrants to 8,235,076 warrants.

The Company assessed whether the 2009 Warrants required accounting as derivatives. The Company determined that the warrants were not indexed to the Company's own stock in accordance with accounting standards codification Topic 815, *Derivatives and Hedging*. As such, the Company concluded the warrants did not meet the scope exception for determining whether the instruments required accounting as derivatives and should be classified in liabilities.

On December 31, 2013, the liability-classified warrants were valued at $11.8 million using a Binomial/Monte Carlo valuation model. The decrease in the fair value of the warrant liabilities of $1.2 million for the year ended December 31, 2013 was recorded as Other income, net in the Statements of Operations.

ZIOPHARM Oncology, Inc.

NOTES TO FINANCIAL STATEMENTS

9. Warrants (Continued)

On December 31, 2012, the liability-classified warrants were valued at $13.0 million using a Binomial/Monte Carlo valuation model. The decrease in the fair value of the warrant liabilities of $6.1 million for the year ended December 31, 2012 was recorded as Other income, net in the Statements of Operations.

The following pricing assumptions were used in the Binomial/Monte Carlo valuation model at December 31, 2013 and 2012:

	December 31, 2013	December 31, 2012
Risk-free interest rate	0.13%	0.25%
Expected life in years	0.94	1.94
Expected volatility	80%	70%
Expected dividend yield	0	0

Warrants accounted for as equity instruments include the following issuances:

In connection with its 2009 private placement, the Company issued warrants to purchase an aggregate of 2,910,954 shares of common stock (including 138,617 warrants issued to the placement agents) which were exercisable immediately. The warrants have an exercise price of $2.04 per share and have a 5 year term. The fair value of the warrants was estimated at $4.2 million using a Black-Scholes model with the following assumptions: expected volatility of 105%, risk free interest rate of 2.41%, expected life of 5 years and no dividends. The fair value of the warrants was recorded in the equity section of the balance sheet. In October 2009, 136,986 of these warrants were exercised.

During 2012, no new warrants were issued. However, 553,914 warrants were exercised for 259,660 shares of common stock. Of these warrants, 186,297 were equity-classified and 373,617 were liability-classified. Additionally, 1,359,317 equity-classified warrants and 579 liability-classified warrants expired without being exercised.

During 2013, no new warrants were issued. However 135,346 warrants were exercised for 112,808 shares of common stock. Of these warrants, all 135,346 were equity-classified; there were no liability-classified warrants exercised. Additionally, 706,708 equity-classified warrants expired without being exercised.

During 2014, no new warrants were issued. However 4,004,907 warrants were exercised for 3,725,277 shares of common stock. Of these warrants, 2,249,062 were equity-classified and 1,755,845 were liability-classified warrants. Additionally, 12,329 equity-classified warrants and 6,479,231 liability-classified warrants expired without being exercised.

All warrants have expired and none are outstanding as of December 31, 2014.

ZIOPHARM Oncology, Inc.

NOTES TO FINANCIAL STATEMENTS

10. 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, 2014 and 2013 are as follows:

	December 31,	
(in thousands)	**2014**	**2013**
Net operating loss carryforwards	$ 79,050	$ 66,209
Start-up and organizational costs	38,562	41,529
Research and development credit carryforwards	26,112	25,058
Stock compensation	1,181	1,028
Capitalized acquisition costs	11,376	12,323
Deferred revenue	534	1,074
Depreciation	208	129
Other	1,547	1,254
	158,570	148,604
Less valuation allowance	(158,570)	(148,604)
Net deferred tax assets	$ —	$ —

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, 2014, the Company has aggregate net operating loss carryforwards for federal tax purposes of approximately $206.9 million available to offset future federal taxable income to the extent permitted under the Internal Revenue Code of 1986, as amended, or IRC, expiring in varying amounts through 2033. Additionally, the Company has approximately $26.0 million of research and development credits at December 31, 2014, expiring in varying amounts through 2033, which may be available to reduce future taxes.

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. The net operating loss carryforwards for the year ended December 31, 2014 includes approximately $4.4 million resulting from excess tax deductions from stock options. Pursuant to ASC 740, the deferred tax asset relating to excess tax benefits generated from exercises of stock options was not recognized for financial statement purposes.

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 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

ZIOPHARM Oncology, Inc.

NOTES TO FINANCIAL STATEMENTS

10. Income Taxes (Continued)

available to offset future income tax liabilities and expenses. The valuation allowance increased by $10.0 million primarily due to net operating loss carryforwards, start-up and organizational costs, and the increase in research and development credits.

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)	**2014**	**2013**	**2012**
Federal income tax at statutory rates	34%	34%	34%
State income tax, net of federal tax benefit	2%	4%	5%
Research and development credits	3%	9%	10%
Stock compensation	-4%	-2%	-1%
Uncertain tax position adjustment	0%	0%	0%
Federal R&D tax grant	0%	0%	0%
Other	-4%	1%	2%
Increase in valuation allowance	-31%	-46%	-49%
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, 2014, 2013, and 2012 are as follows:

(in thousands)	
Balance at December 31, 2011	$275
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	—
Decreases for lapses of statute of limitations	—
Balance at December 31, 2012	$275
Increase/Decrease for tax positions related to the current year	—
Increase/Decrease for tax positions related to prior years	(37)
Decreases for settlements with applicable taxing authorities	—
Decreases for lapses of statute of limitations	—
Balance at December 31, 2013	$238
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	—
Decreases for lapses of statute of limitations	—
Balance at December 31, 2014	$238

ZIOPHARM Oncology, Inc.

NOTES TO FINANCIAL STATEMENTS

10. Income Taxes (Continued)

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 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 2014.

11. Preferred Stock and Stockholders' Equity

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), which the Company refers to as the Preferred Stock.

Common Stock

On January 6, 2011, and in conjunction with the Company's execution and delivery of a Channel Agreement, the Company entered into a Stock Purchase Agreement and Registration Rights Agreement. On January 12, 2011, and pursuant to that Stock Purchase Agreement, the Company sold 2,426,235 shares of the Company's common stock in a private placement for a total purchase price of $11.6 million, or $4.80 per share. The Company simultaneously issued an additional 3,636,926 shares of its common stock for a cash purchase price equal to the $0.001 par value of such shares, which price was deemed paid in partial consideration for the execution and delivery of the Channel Agreement.

On January 20, 2012, pursuant to an underwriting agreement between the Company and J. P. Morgan Securities LLC, as representative of the several underwriters named therein, the Company completed the sale of an aggregate 10,114,401 shares of the Company's common stock at a price of $5.20 per share in a public offering. The total gross proceeds resulting from the 2012 public offering were approximately $52.6 million, before deducting selling commissions and expenses (see Note 2 to the financial statements, Financings).

On November 7, 2012, the Company issued 3,636,926 shares of our common stock, which we refer to as the Milestone Shares, to Intrexon under the terms of its Stock Purchase Agreement with Intrexon dated January 6, 2011. Under the terms of the Stock Purchase Agreement with Intrexon, the Company agreed to issue the Milestone Shares under certain conditions upon dosing of the first patient in a ZIOPHARM-conducted Phase 2 clinical trial in the Unites States, or similar study as the parties may agree in a country other than the United States, of a product candidate that is created, produced, developed or identified directly or indirectly by us during the term of the Channel Agreement and that, subject to certain exceptions, involves DNA administered to humans for expression of anti-cancer effectors for the purpose of treatment or prophylaxis of cancer. On October 24, 2012, the Company initiated dosing in a Phase 2 study of Ad-RTS-IL-12 + veledimex for unresectable Stage III or IV melanoma, triggering the issuance of the Milestone Shares.

On October 29, 2013, pursuant to an underwriting agreement between the Company and J. P. Morgan Securities LLC, as representative of the several underwriters named therein, the Company completed the sale of an

ZIOPHARM Oncology, Inc.

NOTES TO FINANCIAL STATEMENTS

11. Preferred Stock and Stockholders' Equity (Continued)

aggregate 16,445,000 shares of the Company's common stock at a price of $3.50 per share in a public offering. The total gross proceeds resulting from this public offering were approximately $57.6 million, before deducting selling commissions and expenses (see Note 2 to the financial statements, Financings).

As of December 31, 2014, the Company had 104,452,105 shares of common stock issued and outstanding and no shares of Preferred Stock issued and outstanding.

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 effective registration statement on Form S-3 (Registration Statement 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 $94.2 million after deducting underwriting discounts 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.

12. Stock Option Plan

The Company adopted the 2003 Stock Option Plan, or the 2003 Plan, in 2003, and it was approved by the Company's stockholders on December 21, 2004. Upon approval of the 2012 Equity Incentive Plan, no additional stock awards may be granted under the 2003 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, 2014, the Company had outstanding options issued to its employees to purchase up to 5,112,800 shares of the Company's common stock, to its directors to purchase up to 902,529 shares of the Company's common stock, as well as options to consultants in connection with services rendered to purchase up to 490,334 shares of the Company's common stock.

Stock options to employees generally vest ratably over three years and have contractual terms of ten years. Stock options to directors generally vest ratably over two 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 26,364 additional shares for issuance under options granted outside of the 2003 Stock Option Plan. The options were granted to The University of Texas M. D. Anderson Cancer Center and DEKK-Tec, Inc. (see Note 8 to the financial statements, Commitments and Contingencies).

ZIOPHARM Oncology, Inc.

NOTES TO FINANCIAL STATEMENTS

12. Stock Option Plan (Continued)

Proceeds from the option exercises during the years ended December 31, 2014, 2013, and 2012 amounted to $1.4 million, $956 thousand, and $30 thousand, respectively. The intrinsic value of these options amounted to $2.6 million, $1.4 million and $11 thousand for years ended December 31, 2014, 2013 and 2012, respectively.

Transactions under the Plan for the years ending December 31, 2014, 2013, and 2012 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, 2011	5,138,486	4.08		
Granted	2,309,650	4.36		
Exercised	(8,300)	3.61		
Cancelled	(292,533)	5.70		
Outstanding, December 31, 2012	7,147,303	4.11		
Granted	2,649,900	3.28		
Exercised	(570,168)	1.68		
Cancelled	(2,479,732)	4.58		
Outstanding, December 31, 2013	6,747,303	3.81		
Granted	1,099,300	4.95		
Exercised	(613,138)	2.26		
Cancelled	(727,801)	4.54		
Outstanding, December 31, 2014	6,505,664	$ 4.07	7.19	$9,084
Vested and unvested expected to vest at December 31, 2014	6,485,430	$ 4.10	5.80	$9,056
Options exercisable, December 31, 2014	3,781,162	$ 4.10	5.80	$4,130
Options exercisable, December 31, 2013	3,471,935	$ 4.01	5.03	$2,654
Options available for future grant	4,585,769			

At December 31, 2014, total unrecognized compensation costs related to non-vested stock options outstanding amounted to $7.9 million. The cost is expected to be recognized over a weighted-average period of 1.62 years.

Restricted Stock

In December 2014, the Company issued 66,828 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 2013, the Company issued 75,272 shares of restricted stock to its non-employee directors, which vested in their entirety on the one year anniversary of the grant date. In January, February and May 2012, the Company issued 101,500, 43,802 and 25,000 shares of restricted stock to employees, which vested ratably in annual installments over three years, respectively, commencing on the first anniversary of the grant date. In December 2012, the Company also issued 87,730 shares of restricted stock to its non-employee directors, which vested ratably in annual installments over three years, commencing on the first anniversary of the grant date.

In January, February and December 2014, the Company repurchased 16,031, 14,600 and 81,702 shares at average prices of $4.37, $4.40 and $5.04 per share, respectively, to cover payroll taxes. In January, March, May

ZIOPHARM Oncology, Inc.

NOTES TO FINANCIAL STATEMENTS

12. Stock Option Plan (Continued)

and December 2013, the Company repurchased 52,018, 5,400, 2,623, and 56,683 shares at average prices of $4.28, $4.50, $1.65 and $4.37 per share, respectively, to cover payroll taxes. In July and December 2012, the Company repurchased 15,740 and 107,413 shares at $6.06 and $4.19 per share, respectively, to cover payroll taxes. A summary of the status of non-vested restricted stock as of December 31, 2014, 2013 and 2012 is as follows:

	Number of Shares	Weighted-Average Grant Date Fair Value
Non-vested, December 31, 2011	950,906	$ 4.34
Granted	258,032	4.39
Vested	(351,829)	4.32
Cancelled	(123,370)	4.34
Non-vested, December 31, 2012	733,739	4.37
Granted	75,272	4.34
Vested	(292,399)	4.31
Cancelled	(163,747)	4.42
Non-vested, December 31, 2013	352,865	4.38
Granted	66,828	5.07
Vested	(253,835)	4.38
Cancelled	(21,350)	4.41
Non-vested, December 31, 2014	144,508	$ 4.70

As of December 31, 2014, there was $471 thousand 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 1.00 years.

13. 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 $79 thousand, $139 thousand, and $266 thousand to this plan during the years ended December 31, 2014, 2013, and 2012, respectively.

ZIOPHARM Oncology, Inc.

NOTES TO FINANCIAL STATEMENTS

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

Year Ended December 31, 2014	First Quarter	Second Quarter	Third Quarter	Fourth Quarter
Revenue	$ 200	$ 200	$ 633	$ 340
Total operating expenses	9,984	11,377	12,575	10,936
Loss from operations	(9,784)	(11,177)	(11,942)	(10,596)
Change in fair value of warrants	82	5,600	5,847	194
Net (loss)	(9,711)	(5,576)	(6,093)	(10,401)
Loss per share, basic and diluted	$ (0.10)	$ (0.06)	$ (0.06)	$ (0.09)

Year Ended December 31, 2013	First Quarter	Second Quarter	Third Quarter	Fourth Quarter
Revenue	$ 200	$ 200	$ 200	$ 200
Total operating expenses	23,783	18,496	9,315	6,919
Loss from operations	(23,583)	(18,296)	(9,115)	(6,719)
Change in fair value of warrants	10,788	(403)	(7,407)	(1,793)
Net (loss)	(12,799)	(18,692)	(16,713)	(8,903)
Loss per share, basic and diluted	$ (0.15)	$ (0.22)	$ (0.20)	$ (0.09)

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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	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 Warrant issued to placement agents in connection with ZIOPHARM, Inc. 2005 private placement (incorporated by reference to Exhibit 4.2 to the Registrant's Registration Statement on Form SB-2, SEC File No. 333-129020, filed October 14, 2005).
4.3	Schedule identifying holders of Warrants in the form filed as Exhibit 4.2 to this Report (incorporated by reference to Exhibit 4.3 to the Registrant's Registration Statement on Form SB-2, SEC File No. 333-129020, filed October 14, 2005).
4.4	Warrant for the Purchase of Shares of common stock dated December 23, 2004 (incorporated by reference to Exhibit 4.4 to the Registrant's Registration Statement on Form SB-2, SEC File No. 333-129020, filed October 14, 2005).
4.5	Option for the Purchase of common stock dated October 15, 2004 and issued to DEKK-Tec, Inc. (incorporated by reference to Exhibit 4.5 to the Registrant's Annual Report on Form 10-KSB, SEC File No. 000-32353, filed March 20, 2006).
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 in the form filed as Exhibit 4.6 to this Report. (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).
4.8	Form of common stock Purchase Warrant issued to placement agents in connection with the Registrant's 2006 private placement (incorporated by reference to Exhibit 4.2 to the Registrant's Current Report on Form 8-K, SEC File No. 000-32353, filed May 3, 2006).

Exhibit No.	Description of Document
4.9	Form of Warrant to Purchase Common Stock issued to investors in connection the Registrant's September 2009 private placement (incorporated by reference to Exhibit 4.1 to the Registrant's Current Report on Form 8-K filed September 15, 2009).
4.10	Form of Warrant to Purchase Common Stock issued to placement agents in connection with the Registrant's September 2009 private placement (incorporated by reference to Exhibit 4.2 to the Registrant's Current Report on Form 8-K filed September 15, 2009).
4.11	Form of Warrant to Purchase Common Stock issued to investors in connection with the Registrant's December 2009 public offering (incorporated by reference to Exhibit 4.1 to the Registrant's Current Report on Form 8-K filed December 8, 2009).
4.12	Form of Warrant to Purchase Common Stock issued to underwriters in connection with the Registrant's December 2009 public offering (incorporated by reference to Exhibit 4.1 to the Registrant's Current Report on Form 8-K filed December 8, 2009).
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 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 10.7 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 10.8 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 10.9 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 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 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 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 filed June 26, 2012).
10.9	Employment Agreement dated as of January 8, 2008 by and between the Registrant and Dr. Jonathan Lewis (incorporated by reference to Exhibit 10.6 to the Registrant's Annual Report on Form 10-KSB filed February 21, 2008).
10.10	Extension of Employment Agreement dated as of December 28, 2010 by and between the Registrant and Dr. Jonathan Lewis (incorporated by reference to Exhibit 10.1 to the Registrant's Current Report on Form 8-K filed December 28, 2010).
10.11	Extension of Employment Agreement dated as of January 8, 2013 by and between the Registrant and Dr. Jonathan Lewis (incorporated by reference to Exhibit 10.1 to the Registrant's Current Report on Form 8-K filed January 8, 2013).

Exhibit No.	Description of Document
10.12	Amendment and Extension to Employment Agreement dated January 8, 2014 by and between ZIOPHARM Oncology, Inc. and Jonathan Lewis, M.D., Ph.D. (incorporated by reference to Exhibit 10.1 to the Registrant's Current Report on Form 8-K filed January 8, 2014).
10.13	Employment Agreement dated July 8, 2011 by and between ZIOPHARM Oncology, Inc. and Hagop Youssoufian, MD, MSc (incorporated by reference to Exhibit 10.1 to the Registrant's Current Report on 8-K filed July 15, 2011).
10.14	Amendment No. 1 to Employment Agreement dated July 8, 2011 by and between the Company and Hagop Youssoufian, M.D., M.Sc. (incorporated by reference to Exhibit 10.1 to the Company's Current Report on Form 8-K filed April 3, 2012).
10.15	Employment Agreement effective September 6, 2011 by and between ZIOPHARM Oncology, Inc. and Caesar J. Belbel (incorporated by reference to Exhibit 10.1 to the Registrant's Current Report on Form 8-K filed September 6, 2011).
10.16	Amendment to Employment Agreement dated January 7, 2014 by and between ZIOPHARM Oncology, Inc. and Caesar J. Belbel (incorporated by reference to Exhibit 10.2 to the Registrant's Current Report on Form 8-K filed January 8, 2014).
10.17	Employment Agreement dated May 8, 2012 by and between the Company and Jason A. Amello (incorporated by reference to Exhibit 10.1 to the Registrant's Current Report on Form 8-K filed May 10, 2012).
10.18	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). +
10.19	License Agreement dated October 15, 2004, between ZIOPHARM, Inc. (predecessor to the Registrant) and DEKK-Tec, Inc. (incorporated by reference to Exhibit 10.6 to the Registrant's Registration Statement on Form SB-2, SEC File No. 333-129020, filed October 14, 2005). +
10.20	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). +
10.21	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). +
10.22	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 filed March 17, 2010).
10.23	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 filed January 12, 2011). +
10.24	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 filed May 3, 2012)
10.25	Form of subscription agreement between the ZIOPHARM, Inc. and the investors in the Registrant's 2005 private placement (incorporated by reference to Exhibit 10.7 to the Registrant's Registration Statement on Form SB-2, SEC File No. 333-129020, filed October 14, 2005).

Exhibit No.	Description of Document
10.26	Form of Subscription Agreement by and between the Registrant and investors in the Registrant's 2006 private placement (incorporated by reference to Exhibit 10.1 to the Registrant's Current Report on Form 8-K, SEC File No. 000-32353, filed May 3, 2006).
10.27	Form of Securities Purchase Agreement dated September 9, 2009 by and between the Registrant and investors in the Registrant's September 2009 private placement (incorporated by reference to Exhibit 10.1 to the Registrant's Current Report on Form 8-K filed September 15, 2009).
10.28	Form of Registration Rights Agreement dated September 9, 2009 by and between the Registrant and investors in the Registrant's September 2009 private placement (incorporated by reference to Exhibit 10.2 to the Registrant's Current Report on Form 8-K filed September 15, 2009).
10.29	Engagement Letter dated August 7, 2009 by and between the Registrant and Rodman & Renshaw, LLC (incorporated by reference to Exhibit 10.21 to the Registrant's Annual Report on Form 10-K filed March 1, 2011).
10.30	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 filed January 12, 2011).
10.31	Amendment 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 filed February 7, 2011).
10.32	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 filed March 1, 2011).
10.33	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 filed January 31, 2013).
23.1	Consent of Independent Registered Public Accounting Firm – McGladrey LLP
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.
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

+ Confidential treatment has been granted as to certain portions of this exhibit pursuant to Rule 406 of the Securities Act of 1933, as amended, or Rule 24b-2 of the Securities Exchange Act of 1934, as amended.

CONSENT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

We consent to the incorporation by reference in the Registration Statements on Forms S-8 (File Nos. 333-129884, 333-134280, 333-142701, 333-160496, 333-167925, 333-185433 and 333-199304) and Forms S-3 (File Nos. 333-134279, 333-141014, 333-161453, 333-162160, 333-163517, 333-166444, 333-174292, 333-177793 and 333-201826) of ZIOPHARM Oncology, Inc. of our report dated February 26, 2015 relating to our audit of the financial statements and the effectiveness of internal control over financial reporting, which appears in this Annual Report on Form 10-K of ZIOPHARM Oncology, Inc. for the year ended December 31, 2014.

/s/McGladrey LLP

Boston, Massachusetts
February 26, 2015

CERTIFICATION OF PRINCIPAL EXECUTIVE OFFICER

I, Jonathan Lewis, 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: February 26, 2015

/s/ Jonathan Lewis

Jonathan Lewis, 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: February 26, 2015

/s/ Kevin G. Lafond

Kevin G. Lafond, 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, 2014, as filed with the Securities and Exchange Commission on the date hereof (the "Report"), I, Jonathan Lewis, 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/ Jonathan Lewis

Jonathan Lewis, Chief Executive Officer
(Principal Executive Officer)
February 26, 2015

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, 2014, 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, Vice President, Chief Accounting Officer
and Treasurer (Principal Financial and Accounting Officer)
February 26, 2015