Table of Contents

UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
Washington, DC 20549

FORM 10-K

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

For the fiscal year ended December 31, 2019

OR

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

For the transition period from _____ to _____

Commission File Number 001-33038

ZIOPHARM Oncology, Inc.

(Exact Name of Registrant as Specified in Its Charter)

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

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

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

Title of each class	**Trading Symbol**	**Name of each exchange on which registered**
Common Stock (par value $0.001 per share)	**ZIOP**	**The Nasdaq Stock Market LLC**

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

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

Indicate by check mark if the registrant is not required to file reports pursuant to Section 13 or 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 every Interactive Data File required to be submitted 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 such files). Yes ☒ No ☐

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

Large Accelerated Filer	☒	Accelerated Filer	☐
Non- Accelerated Filer	☐	Smaller Reporting Company	☐
		Emerging Growth Company	☐

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

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

The aggregate market value of the registrant's common stock held by non-affiliates was $834,869,811 as of June 28, 2019 (the last business day of the registrant's most recently completed second fiscal quarter), based on a total of 143,202,369 shares of common stock held by non-affiliates and a closing price of $5.83 as reported on the Nasdaq Capital Market on June 28, 2019. For purposes of this computation, all officers, directors, and 10% beneficial owners of the registrant are deemed to be affiliates. Such determination should not be deemed to be an admission that such officers, directors or 10% beneficial owners are, in fact, affiliates of the registrant.

As of February 14, 2020, there were 212,999,979 shares of the registrant's common stock, $0.001 par value per share, outstanding.

DOCUMENTS INCORPORATED BY REFERENCE:

Portions of the definitive proxy statement for the registrant's 2020 annual meeting of stockholders, which is to be filed within 120 days after the end of the fiscal year ended December 31, 2019, are incorporated by reference into Part III of this Form 10-K, to the extent described in Part III.

ZIOPHARM Oncology, Inc.
ANNUAL REPORT ON FORM 10-K
FOR THE FISCAL YEAR ENDED DECEMBER 31, 2018

TABLE OF CONTENTS

		Page
PART I		
Item 1.	Business	5
Item 1A.	Risk Factors	37
Item 1B.	Unresolved Staff Comments	69
Item 2.	Properties	69
Item 3.	Legal Proceedings	69
Item 4.	Mine Safety Disclosures	69
PART II		
Item 5.	Market for Registrant's Common Equity, Related Stockholder Matters and Issuer Purchases of Equity Securities	70
Item 6.	Selected Financial Data	72
Item 7.	Management's Discussion and Analysis of Financial Condition and Results of Operations	72
Item 7A.	Quantitative and Qualitative Disclosures About Market Risk	86
Item 8.	Financial Statements and Supplementary Data	86
Item 9.	Changes in and Disagreements with Accountants on Accounting and Financial Disclosures	86
Item 9A.	Controls and Procedures	86
Item 9B.	Other Information	87
PART III		
Item 10.	Directors, Executive Officers and Corporate Governance	88
Item 11.	Executive Compensation	88
Item 12.	Security Ownership of Certain Beneficial Owners and Management and Related Stockholder Matters	88
Item 13.	Certain Relationships and Related Transactions, and Director Independence	88
Item 14.	Principal Accountant Fees and Services	89
PART IV		
Item 15.	Exhibits and Financial Statement Schedules	90
	Signatures	95
	Financial Statements	F-1

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Special Note Regarding Forward-Looking Statements

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

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

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

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

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

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

PART I

Item 1. Business

BUSINESS OVERVIEW

We are a clinical-stage biopharmaceutical company focused on discovering, acquiring, developing and commercializing next generation immuno-oncology platforms that leverage cell- and gene-based therapies to treat patients with cancer. We are developing two immuno-oncology platform technologies that utilize the immune system by employing innovative cell engineering and novel, controlled gene expression technologies designed to deliver safe, effective, and scalable non-viral cell- and viral-based gene therapies for the treatment of multiple cancer types. Our first platform is referred to as *Sleeping Beauty* and is based on the genetic engineering of immune cells using a non-viral transposon/transposase system that is intended to stably reprogram T cells outside of the body for subsequent infusion. Our second platform is referred to as Controlled IL-12 and is designed to stimulate expression of interleukin 12, or IL-12, a master regulator of the immune system, in a controlled and safe manner to focus the patient's immune system to more effectively attack cancer cells. We intend to use both of our platforms to become a leading immuno-oncology company focused on developing innovative, cost-effective therapies primarily aimed at the large unmet needs in solid tumors.

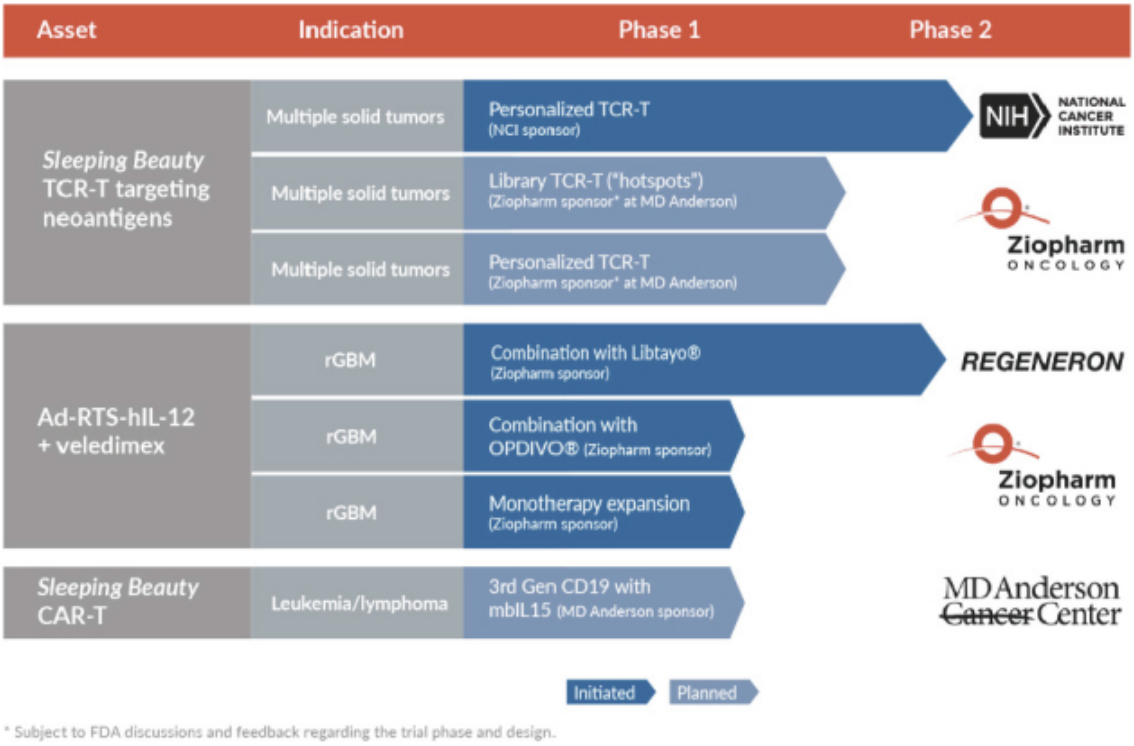
Using our *Sleeping Beauty* platform, we are developing T cell receptor, or TCR, T cell therapies to target solid tumors. Our program designs and manufactures T cells that are intended to target tumor-specific antigens, thereby delivering personalized therapy that can attack patients' malignancies. These genetic changes are referred to as neoantigens as they are only expressed by the tumor, reducing the potential for toxicity upon targeting normal cells. Under our Cooperative Research and Development Agreement, the National Cancer Institute, or NCI, is conducting a Phase 2 clinical trial to evaluate autologous peripheral blood lymphocytes genetically modified with the *Sleeping Beauty* system to express autologous (personalized) TCRs. The U.S. Food and Drug Administration, or FDA, has cleared the investigational new drug, or IND, application submitted by the NCI for this clinical trial. The trial was initiated in October 2019 and preparations to enable patient enrollment by the NCI are underway. We expect the trial will enroll patients with a broad range of solid tumors over the next several years. In addition, we are currently planning a clinical program to study our TCR approach with The University of Texas MD Anderson Cancer Center, or MD Anderson. Under this program, we expect to clinically evaluate both our Personalized TCR Approach and our Library TCR Approach.

Our Controlled IL-12 platform uses virotherapy based on an engineered replication-incompetent adenovirus, referred to as Ad-RTS-hIL-12, plus veledimex as a gene delivery system to conditionally produce IL-12, a potent, naturally occurring anti-cancer protein, to treat patients with solid tumors where a specific target is unknown. Our Controlled IL-12 platform allows us to deliver IL-12 in a tunable dose as the cytokine is under transcriptional control of the RheoSwitch Therapeutic System® (RTS®). We are currently studying our Controlled IL-12 Platform as a monotherapy in a Phase 1 clinical trial of patients with recurrent glioblastoma multiforme, or rGBM. Our substudy of this clinical trial is fully enrolled with 36 patients and is designed to encourage use of low-dose steroids and 20 mg veledimex to further understand the potential of Controlled IL-12 as a monotherapy. We are also developing our Controlled IL-12 platform in combination with immune checkpoint inhibitors. We have completed dosing in a Phase 1 dose-escalation clinical trial of Ad-RTS-hIL-12 plus veledimex in combination with PD-1 antibody OPDIVO® (nivolumab) in patients with rGBM. Dosing is ongoing in a Phase 2 clinical trial evaluating Ad-RTS-hIL-12 plus veledimex in combination with PD-1 antibody Libtayo® (cemiplimab-rwlc) for the treatment of recurrent or progressive glioblastoma multiforme in adults.

We are developing chimeric antigen receptor, or CAR, T cell, or CAR$^+$ T, therapies targeting CD19 on malignant B cells using our *Sleeping Beauty* platform in collaboration with MD Anderson. In a Phase 1 trial, we plan to infuse donor-derived T cells after allogeneic bone marrow transplantation, or BMT, for recipients who have relapsed with CD19$^+$ leukemias and lymphomas with our CD19-specific CAR$^+$ T therapies manufactured using our rapid personalized manufacture, or RPM, technology. RPM enables T cells to be infused as soon as the day

after gene transfer which is made possible by the genetic modification of resting T cells to express CAR and membrane bound IL-15, or mbIL15. We are also advancing our RPM technology in Greater China with Eden BioCell, Ltd., or Eden BioCell, our joint venture with TriArm Therapeutics, Ltd. Eden BioCell will lead the clinical development and commercialization of *Sleeping Beauty*-generated CD19-specific RPM CAR+ T therapies using patient-derived (autologous) T cells in order to treat patients with relapsed or refractory CD19+ leukemias and lymphomas.

Our Pipeline



OUR STRATEGY

Our goal is to become a leading immuno-oncology company focused on developing innovative, cost-effective therapies primarily aimed at the large unmet needs in solid tumors. Key elements of our strategy include:

- *Building an end-to-end TCR solution targeting solid tumors.* We believe our study with the NCI represents the first time a non-viral, genetically engineered TCR T cell, or TCR+ T cell, therapy will be administered to patients. We intend to strengthen our position in the field of T cell targeting solid tumors by investing significantly to optimize and expand our process development and manufacturing capabilities, creating an end-to-end, scalable solution. We intend to build this end-to-end solution to develop treatments using (i) TCR+ T cells expressing recipient-derived (autologous) TCRs, which we refer to as our Personalized TCR Approach and (ii) TCR+ T cells expressing third party (allogeneic) TCRs from a library, which we refer to as our Library TCR Approach. We plan to significantly expand our library of TCRs derived from third parties that are reactive to mutated KRAS, TP53 and EGFR as part of our commitment to advance clinical development for the treatment of patients whose solid tumors have driver mutations.
- *Executing on the clinical trials of our Controlled IL-12 platform as both a monotherapy and in combination with immune checkpoint inhibitors.* We intend to continue executing on several clinical

trials to treat rGBM with our Controlled IL-12 program as both a monotherapy and in combination with immune checkpoint inhibitors, such as PD-1 inhibitors. In our clinical trials, we have observed that Controlled IL-12 increases T cell activity in the tumor microenvironment in patients with rGBM and we expect to conduct trials of Controlled IL-12 in other tumor types as both a monotherapy and, potentially, in combination with immune checkpoint inhibitors.

- *Advancing our third generation CD19 CAR+ T program.* We believe our CD19 CAR+ T therapies may solve the manufacturing difficulties limiting the commercial potential of other CAR+ T programs. Our CAR+T program targeting CD19 on malignant B cells will be developed in collaboration with MD Anderson in the United States and with Eden BioCell in Greater China.
- *Selectively collaborating with third parties that provide complementary technologies or capabilities.* We expect to collaborate selectively with companies that have enabling technologies or other capabilities to accelerate the development of our programs. In any collaboration, we expect to retain development control or receive significant economic and commercial rights to our product candidates.
- *Creating a leading, fully integrated biotechnology company focused on advancing our oncology platforms through clinical trials.* In 2019, we supplemented our existing team with additional research and development depth. We expect to continue expanding our personnel and infrastructure, particularly focused on cell therapy, in order to accelerate the execution of our clinical programs. As part of this expansion, we expect to establish internal manufacturing facilities compliant with current good manufacturing practice, or GMP, to support the proposed clinical trials for our TCR program.

SLEEPING BEAUTY PLATFORM TECHNOLOGY

We are pursuing non-viral genetic engineering technologies to develop novel neoantigen-specific TCR+ T and CD19-specific CAR+ T therapies. The platform we have licensed from MD Anderson uses the *Sleeping Beauty* non-viral genetic modification system to generate and characterize TCR and CAR designs in T cells.

Limitations of Existing Approaches to Manufacturing T Cell Therapies

T cells are a type of white blood cell that play a central role in the immune system. T cells are involved in both detecting and killing infected or abnormal cells, such as cancer cells, as well as coordinating immune responses. In recent years, companies have begun developing therapies that include T cells engineered specifically for each patient. Manufacturing such products is separated into discrete steps and typically undertaken at a centralized facility. The production time varies from approximately two to four weeks with additional time needed for quality control requirements. Manufacturing based on viral transduction, propagation and shipping has many drawbacks:

- *Scalability*. The requirement to be able express a multitude of TCRs, whether to neoantigens unique to patients or neoantigens shared between patients, will be a challenge when the choice of gene transfer for TCR is based on virus.
- *Time to manufacture*. The need to propagate (numerically expand) T cells requires the product be in culture in compliance with cGMP during which the intended recipient may be unable to receive the genetically modified T cells.
- *Expense of production.* The need to generate virus and the production time with the associated logistical complications increase the cost of manufacturing the genetically modified T cells.
- *Required lymphodepletion*. The infusion of T cells that have been propagated *ex vivo*, or outside the body, tends to make them dependent on cytokines to survive and thrive after infusion. This has resulted in the use of chemotherapy and other approaches of immunosuppression to “free up” pro-survival cytokines, such as endogenous IL-15, in the recipient prior to the administration of T cells. Lymphodepletion facilitates the sustained persistence of genetically modified T cells in the patient, but it exposes the patient to medical complications, raises expense, and limits the ability of the technology to be scaled as the administration of chemotherapy requires specialized centers.

- *Toxicity*. Infusing large numbers of T cells recognizing a single antigen, such as CD19, commonly places the recipient at risk from the synchronous activation of these T cells resulting in cytokine release syndrome and other associated toxicities, which can be severe and life threatening.

We believe these disadvantages will restrict companies from commercializing effective TCR therapies and continue limiting the commercial potential of CAR-T therapies.

***Sleeping Beauty* Solution**

The *Sleeping Beauty* system is a gene transfer method that utilizes a transposase enzyme to "cut and paste" donor transposon DNA from introduced plasmid into chromosomes using a process called transposition. The system can be used to stably deliver genes to a variety of cell types including human T cells. *Sleeping Beauty* transposons appear to integrate in a random distribution at thymine-adenine, or TA, dinucleotide sites, making them less likely to cause off-target effects when compared to other transposons and viral gene delivery methods.

We use the *Sleeping Beauty* system to express TCRs that target patients' antigens as well as CARs that enable a T cell to recognize specific proteins or antigens that are present on the surface of other cells. Our RPM technology is used in our third generation CAR+ T therapy, which uses the *Sleeping Beauty* system to co-express our proprietary mbIL15 and a kill switch along with the CAR, and we may elect to incorporate our mbIL15 technology in our TCR therapies in the future. Interleukin 15 (IL-15) has a variety of apparently beneficial effects as it is considered a pro-survival cytokine that promotes survival of T cells. Our pre-clinical data suggest that incorporating mbIL15 into a TCR and CAR+ T therapies enhances *in vivo* persistence of the TCR and CAR+ T cells.

We believe our *Sleeping Beauty* platform has several advantages compared with the viral gene transfer technologies used by other TCR and CAR-T companies:

- *Reduced costs.* By using DNA plasmid and avoiding the time-consuming and laborious manufacture of virus, our *Sleeping Beauty* technology may reduce the manufacturing expense and challenges associated with viral gene transfer systems in creating T cells engineered to express TCR and CAR.
- *Shortened manufacturing.* We expect the T cell manufacturing process with *Sleeping Beauty* to significantly reduce virus-based manufacturing times. In the preclinical setting, the time to administration of third-generation *Sleeping Beauty*-modified T cells co-expressing mbIL15 and a kill switch has been shortened to two days or less from gene transfer. This reduction in time is primarily achieved through the elimination of *in vitro* T cell activation and propagation which avoids the need to culture T cells, which can take between approximately two and four weeks.
- *Customizable therapies.* Our *Sleeping Beauty* platform may allow us to manufacture more customizable therapies, thereby enabling us to provide personalized TCR+ T cell therapy against unique, and potentially multiple, patient-specific neoantigens.
- *Potential improved safety profile.* We expect that including mbIL15 will enable the T cells in our TCR+ T or CAR+ T therapies to engraft from low starting (infusion) numbers. We believe this reduced T cell dose may reduce the side effects caused by cytokine release syndrome, which is often experienced by patients receiving larger infusions of TCR+ T or CAR+ T or cells.
- *Potential to avoid lymphodepletion.* The addition of our proprietary mbIL15 may enable the administration of TCR- or CAR-expressing "younger" T cells with an ability to be long-lived after infusion. The ability of TCR or CAR+ T cells to signal via mbIL15 increases TCR or CAR persistence and has the potential to eliminate lymphodepletion as the T cells rely on their own source of this pro-survival cytokine rather than scavenging endogenous soluble IL-15 from the recipient.
- *Local Manufacturing.* Our *Sleeping Beauty* technology enables the potential for a hospital-based manufacturing model in addition to a centralized manufacturing approach currently being employed by other companies for their CAR+ T cell products.

SLEEPING BEAUTY TCR PROGRAM

Background

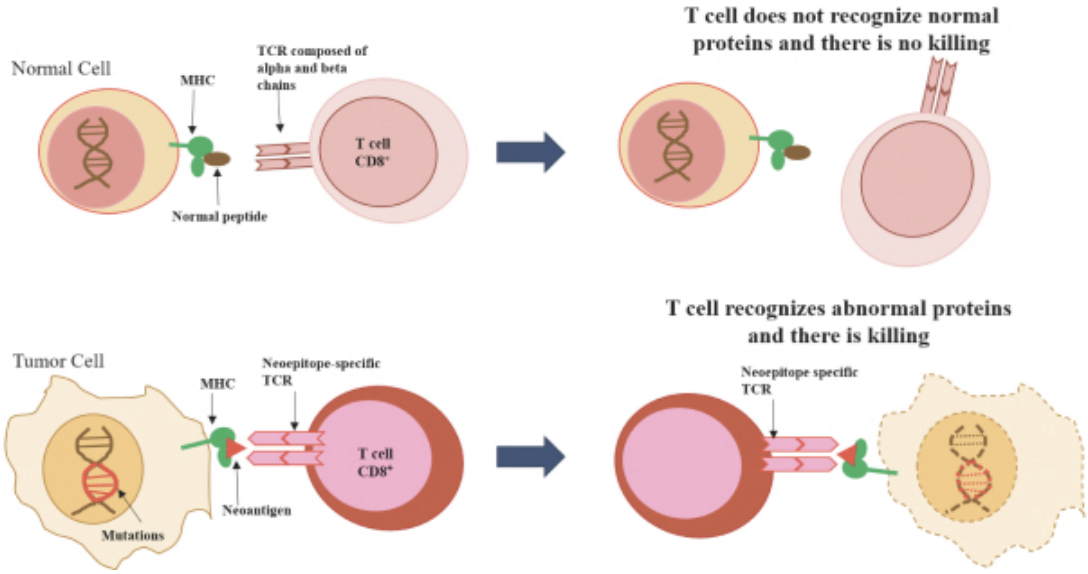
Each T cell has a unique alpha/beta TCR and an ability to rapidly increase in numbers when the TCR interrogates a target and detects a threat. A TCR can recognize cancer cells as a threat as the receptor docks with a specialized set of molecules on the cancer cell surface called the major histocompatibility complex, or MHC. The MHC reveals the health of a cell based on the loading of peptides (processed protein), which then await examination by unique TCRs on populations of T cells. Two types of MHC, Class I and Class II, are interrogated by TCRs on T cells. Class I molecules activate $CD8^+$ T cells which have evolved an ability to be efficient killers. Class II molecules activate $CD4^+$ T cells which help coordinate an efficient immune response. In each person, there are both many different TCR structures and many different MHC structures. TCRs within each person are adapted to work with their own MHC structures or alleles. For a T cell to recognize and destroy a tumor cell, the TCR must recognize the foreign antigen in the context of MHC and then be activated to deepen the engagement to kill the cell. This is different from CARs, which directly recognize antigens, such as CD19, on the surface of malignant B cells, without the need for presentation by MHC.

Genes in cancer cells can lead to the production of proteins, which are then processed by the cell into protein fragments known as peptides. When these peptides are presented to T cells by MHC, by either tumor cells or antigen presenting cells, and they result in T cell activation, they are known as antigens. When these immunogenic peptides are derived from proteins which are in turn expressed from genes that are mutated only in tumor cells (for example, within the cancer genome and not encoded in the germline), they are known as neoantigens. Tumor cells presenting neoantigens via MHC are targets for T cells. T cells can recognize and kill neoantigen-presenting cancer cells and effect a positive feedback loop to heighten the immune response.

The immune system avoids targeting the body’s own healthy cells principally through processes known as immune tolerance by which T cells do not respond to MHCs containing peptides from normal proteins and therefore avoid targeting healthy cells for destruction. The recognition by the TCR of peptide presented by the MHC is a vital immune mechanism that allows the body both to respond against foreign threats, including cancer, as well as to avoid targeting the body’s own healthy cells.

Tumors utilize a variety of strategies to evade and suppress the host immune system. This renders T cells residing within the tumor, referred to as tumor-infiltrating lymphocytes, or TIL, ineffective and, despite expressing tumor-specific TCRs, unable to recycle their effector functions to eliminate tumor. To overcome immune suppression, “young” T cells are needed, such as those found in the peripheral blood. However, these circulating T cells do not typically express tumor-specific TCRs in adequate numbers. We seek to address this problem by genetically modifying peripheral blood-derived T cells to express TCRs with specificity to tumor-derived antigens, especially neoantigens, and propagating them to sufficient numbers prior to administration.

The figure below describes how T cell recognition of genetic mutations leads to the killing of tumor cells.



Neoantigens are encoded by tumor-specific mutated genes that are often unique to each patient. Targeting these neoantigens requires TCRs that are generated on a patient-by-patient basis. During cancer initiation and progression, tumor cells acquire mutations in naturally-occurring genes that are responsible for transformation, known as driver mutations. Some of these driver mutations occur in “hotspots” and are a class of mutations shared between tumor types and between individuals. Since driver mutations can be anticipated, it is possible to prepare TCRs in a library in advance of a patient’s need.

Other Approaches to Targeting Neoantigens

Several companies are pursuing “public” antigens that are encoded within a patient’s normal germline, such as cancer testes, PRAME, MAGE series, and NY-ESO-1. Targeting these antigens when they occur in tumors typically enables a library of pre-assembled TCRs to be created as proteins from these germline targets that can be shared within cancer types between patients. We believe there are several drawbacks to relying solely on this approach:

- Public antigens are not present in many tumors, which limits their appeal.
- Public antigens are often not homogeneously expressed throughout the tumor because they are typically not driver mutations, which increases the likelihood that the infused TCR-modified T cells will not deliver a complete response.
- Public antigens are, by definition, also coded within the germline, leading to endogenous TCRs used for cloning and re-expression having sub-optimal affinity and the native T cell unable to recognize the cancer due to immune tolerance. As a result, *ex vivo* genetic alteration of the alpha and beta chains of the TCR is likely required to improve affinity, which increases the likelihood of on-target but off-tissue toxicity resulting in adverse events.

We believe the superior approach is to genetically modify T cells to target neoantigens present in the cancer genome but not in the germline that are presented though MHC class I and II, which should increase the number of targets and improve the therapeutic potential of the product. This requires a “personal” approach to T cell therapy in which the introduced TCRs recognize neoantigens of a patient’s tumor. When targeting unique neoantigens it is likely that more than one mutated protein will need to be addressed by more than one TCR to

prevent relapse of tumors that fail to express the targeted neoantigens. Neoantigens that can be shared between patients and thus occur in "hotspots," may be driver mutations and, therefore, the cancer cell relies upon their presence rendering it less likely the tumor can escape and thus relapse when T cells are infused with a single specificity. We believe that neoantigen-targeted therapies will improve patient outcomes, particularly for patients with solid tumors and we believe we are the only company using non-viral gene transfer to develop TCR+T therapies that target neoantigens through both classes of MHC.

Our Approach to Targeting Neoantigens

Using our *Sleeping Beauty* platform, we are developing TCR+ T therapies initially to target solid tumors. Our TCR program designs and manufactures T cells that are intended to target tumor-specific neoantigens, thereby delivering personalized therapy that can attack an individual patient's cancer. The *Sleeping Beauty* system uses DNA plasmids to reprogram T cells to express introduced TCRs on a patient-by-patient basis, which addresses inter-tumor heterogeneity, and to express more than one TCR for each patient and/or to target driver mutations, which addresses intra-tumor heterogeneity.

The genetic modification using the *Sleeping Beauty* system of recipient-derived products enables us to target neoantigens in two ways, which we refer to as our Personalized TCR Approach and as our Library TCR Approach (**Figure 1**). We believe we are the only company that is using non-viral gene transfer to develop both personalized TCR+ T therapies and TCR+ T therapies from a library of TCRs derived from third parties. We believe using the *Sleeping Beauty* system to scale TCR-T to infuse multiple products per patient and develop a library of TCRs to facilitate the recruitment of patients is a competitive advantage.

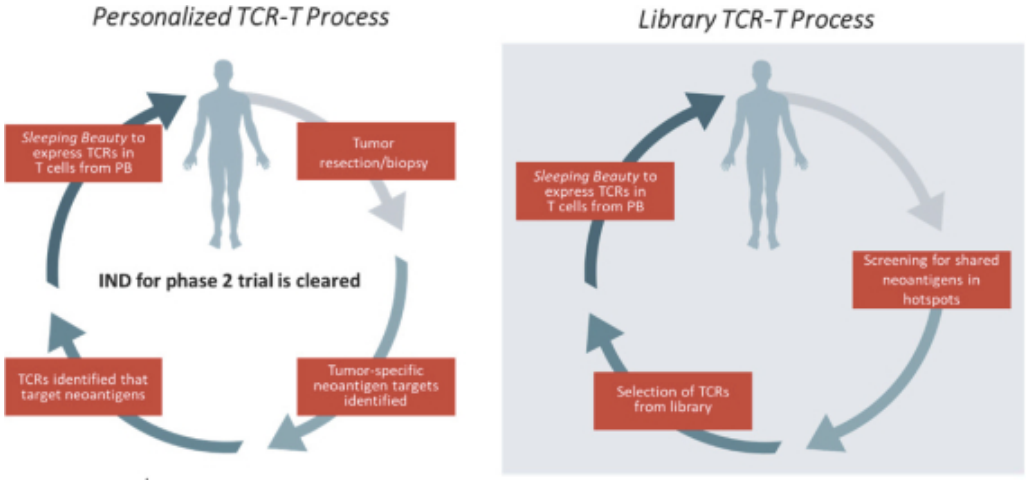


Figure 1: Our two approaches to TCR+ T therapies targeting neoantigens. Both approaches use the Sleeping Beauty system to genetically modify T cells from the patients' peripheral blood, or PB, to express one or more TCRs. The "Personalized TCR-T Process" (left) is based on the real-time identification of unique neoantigens and TCRs generated on a patient-by-patient basis. The "Library TCR-T Process" (right) is based on the science that some tumors share mutations in hotspots and TCRs can be prepared in anticipation of a patient's need.

Our Personalized TCR Approach

Most neoantigens are unique to each patient's tumor. We plan to address this uniqueness in our Personalized TCR Approach by infusing TCR+ T cells expressing recipient-derived TCRs. There are three essential steps in creating a T cell therapy targeting personalized neoantigens:

1. *Detecting and prioritizing neoantigens*. Detecting a patient's unique set of neoantigens requires one or more samples of the patient's malignant tissue(s) and sampling of normal cells, followed by

sequencing to reveal a catalog of candidate neoantigens that are found in the tumor cells, but not in normal cells. Bioinformatics can be used to identify and prioritize the candidate neoantigens that are driver mutations.

2. *Detecting and prioritizing TCRs*. Only a subset of candidate sequence changes are neoantigens as defined by their ability to stimulate a T cell response and thus are characterized as immunogenic. Validating targets requires the presentation of candidate neoantigens via MHC with T cells to be co-cultured with antigen presenting cells to efficiently identify the reactive T cells. One or more of the TCRs from individual reactive T cells are then sequenced.

3. *Manufacturing TCR$^+$ T cells*. The sequence of one or more TCRs recognizing one or more neoantigens are placed into DNA plasmids as *Sleeping Beauty* transposons. These DNA plasmids are inserted into T cells derived from peripheral blood using a process called electroporation. T cells stably expressing the introduced TCR(s) are then propagated to produce the TCR$^+$ T cells in clinically-sufficient numbers before they are released for administration into a patient (**Figure 2**).

The process for the production and infusion of *Sleeping Beauty* TCR-modified T cells is based on the electro-transfer of DNA plasmids containing coding for TCR(s) recognizing one or more neoantigens into T cells derived from a patient's peripheral blood. The TCRs are typically sequenced from TIL responding to the targeted neoantigens. Following electroporation, the genetically modified T cells are propagated to large numbers using the "rapid expansion protocol" which is a technology that has been shown by the NCI to generate T cells that can recognize solid tumors. We believe the use of circulating T cells as the source of effector cells, rather than TIL, will improve the T cell's ability to kill tumor cells because these circulating lymphocytes are generally "young" and can proliferate and survive *in vivo* to sustain anti-tumor effects.

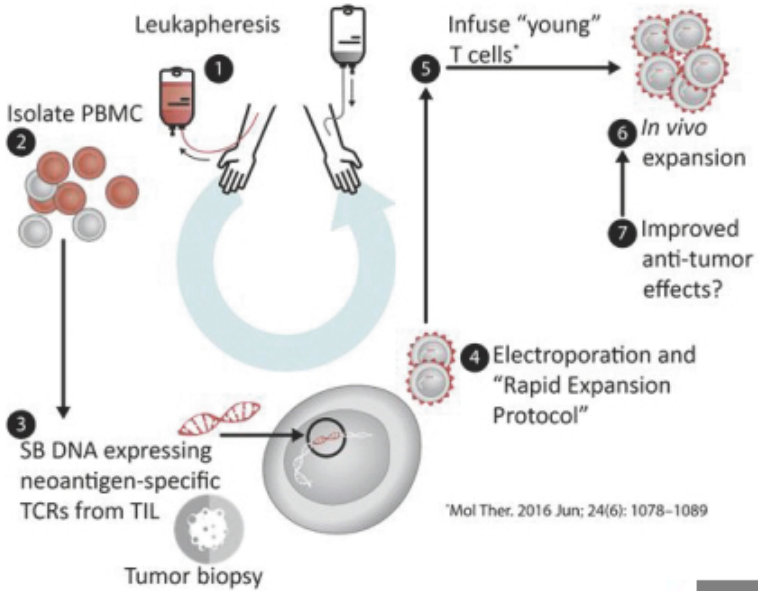


Figure 2: Overview of process to manufacture clinical-grade Sleeping Beauty TCR-modified T cells. Peripheral blood mononuclear cells, or PBMC, are obtained by apheresis and "young" T cells therein genetically modified by electroporation using the Sleeping Beauty system to insert TCRs. As needed, the gene transfer step is repeated to generate T-cell products with more than one specificity. The genetically modified T cells are numerically expanded using the rapid expansion protocol and then infused in the patient.

To be successful, genetically modified T cells targeting one or more neoantigens will need to address the fact that (1) among a population of patients, not all tumors express the targeted neoantigen, referred to as inter-tumor heterogeneity, and (2) within a single patient, not all tumor cells express the targeted antigen, referred to as intra-tumor heterogeneity. Inter-tumor heterogeneity limits the number of recipients that are eligible to receive a treatment and intra-tumor heterogeneity creates the risk of antigen-escape variants, increasing the likelihood of cancer relapse. As a result, we believe companies developing T cell therapies targeting neoantigens must address both inter- and intra-tumor heterogeneity.

Our Library TCR Approach

Our Library TCR Approach is based on the finding that a subset of neoantigens are shared between patients and between classes of tumors. These neoantigens are referred to as "hotspots" and their presence allows us to administer TCR+ T cells expressing TCRs from a library derived from third parties. The advantage of the Library TCR Approach is that a subset of patients with solid tumors may be rapidly treated based on screening them for target neoantigens, identifying MHC, and matching these two data sets to the TCRs in the library. Once a match has been identified, the TCR is introduced into peripheral blood-derived T cells using the *Sleeping Beauty* system, propagated to large numbers using the "rapid expansion protocol" and then infused into the patient in the same process employed by our Personalized TCR Approach.

We have in-licensed from the NCI multiple allogeneic TCRs derived from third parties that are reactive to mutated KRAS, TP53 and EGFR in hotspots and we plan to expand our TCR library as part of our commitment to advance clinical development for the treatment of patients whose solid tumors have driver mutations. These TCRs are typically obtained from TILs. Recent data published online in *Clinical Cancer Research* showed that TP53 mutation-reactive T cells circulating in peripheral blood are a source of neoantigen-specific TCRs for adoptive cell therapy.

Clinical Development of TCR Program

We believe that a non-viral platform represents the only commercially feasible way of manufacturing neoantigen therapies due to the obstacles presented by inter-tumor heterogeneity and intra-tumor heterogeneity. In 2017, we entered into a Cooperative Research and Development Agreement, or CRADA, with the NCI for the development of adoptive cell transfer-based immunotherapies to treat solid tumors under the direction of Steven A. Rosenberg, M.D., Ph.D., Chief of the Surgery Branch at the NCI. Under our CRADA, the NCI will perform clinical evaluations of *Sleeping Beauty*-engineered T cells to express TCRs that are typically reactive against unique neoantigens to mediate cancer regression in patients with refractory solid tumors for several tumor types, including gastrointestinal and genitourinary, breast, ovarian, non-small cell lung cancer and glioblastoma. We anticipate that patients will receive populations of T cells genetically modified to express more than one TCR so that more than one neoantigen can be targeted in the patient. We expect infusing multiple TCRs per patient will reduce the probability of leaving some cancer cells unaddressed, lowering the risk of cancer relapse. The primary objective of the clinical trial is to evaluate tumor response rate with secondary objective to evaluate the safety and tolerability of the therapy. The FDA has cleared the IND application submitted by the NCI for this clinical trial and the trial was initiated in early October. We expect the NCI to begin treating patients in the first half of 2020.

We are also planning a clinical program to study our TCR approach with MD Anderson. We are engaging with the FDA regarding the trial design for this program that will evaluate both our Personalized TCR Approach and our Library TCR Approach.

Solid Tumor Malignancy Prevalence

Cancer is the second most common cause of death in the United States, accounting for nearly one of every four deaths. Approximately 1,762,450 new cancer cases were expected to be diagnosed, and 606,880 cancer deaths expected to occur, in the United States in 2019 according to the American Cancer Society. Of these, the majority were caused by solid tumors. Invasive cancer, such as malignancies of epithelial tissue represent 80% to 90% of

all cancer cases according to the Surveillance, Epidemiology, and End Results Program of the National Cancer Institute. These diseases include colorectal, lung, ovarian, skin, bladder, head and neck cancers, among others.

CONTROLLED IL-12 PLATFORM TECHNOLOGY

Background

Ad-RTS-hIL-12 plus veledimex is our gene delivery system to regulate production of IL-12, a potent, naturally occurring anti-cancer protein which functions as a master regulator of the immune system. We control the generation of recombinant IL-12 using a replication-incompetent adenoviral, or Ad, vector administered via a single injection of virus into the brain tumor and engineered to conditionally express human IL-12, or hIL-12 (**Figure 3**). The conditional expression of hIL-12 is modulated with the RheoSwitch Therapeutic System® (RTS®) by the small molecule veledimex, an activator ligand orally administered that has been shown to cross the blood-brain barrier.

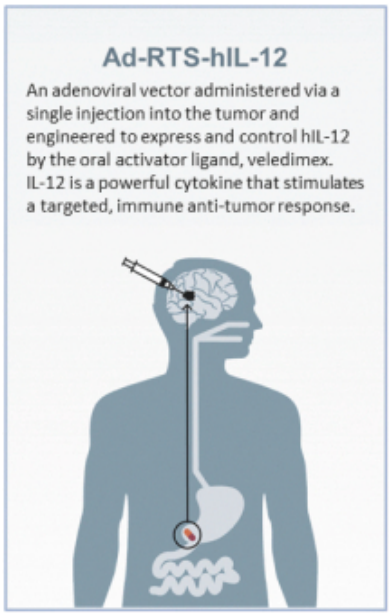


Figure 3: Schematic of the vector system to conditionally express IL-12 after intra-tumor injection of replication incompetent adenovirus and oral administration of veledimex capsule that activates transcription via the RTS.

In this way, Ad-RTS-hIL-12 is administered within the tumor under the control of the RTS "switch". Activation of the switch, and therefore conditional gene expression and subsequent IL-12 protein production, is tightly controlled by the activator ligand, veledimex, delivered to the patient as a daily oral capsule, typically over 14 days. When veledimex is administered to a patient, the switch is turned "on" and IL-12 is produced; when veledimex is withdrawn, the switch is turned "off" and production of recombinant IL-12 ceases. The amount of IL-12 produced is proportional to the dosing of veledimex which further enhances control of this cytokine. We believe the ability regulate production of IL-12 after administration of the virus is critical for the development of this potent cytokine.

The recombinant IL-12 has been shown to be biologically active as, for example, it can stimulate production of the body's own interferon-gamma, or IFN-g. IL-12 is a potent pro-inflammatory cytokine capable of reversing immune escape mechanisms and improving the function of tumor fighting natural killer, or NK, cells and T cells.

Controlled IL-12 has been shown to biologically turn "cold tumors hot." In our clinical trials, we have seen deep and sustained infiltration of activated T cells (i.e., "hot" tumors) where previously there had been very little T cell infiltration (i.e., "cold" tumors). Data from repeat biopsies obtained four to six months following administration of Ad-RTS-hIL-12 plus veledimex has shown an increased and sustained infiltration of activated T cells producing IFN-g within the brain-tumor lesion as reported in *Science Translation Medicine*. Data from our Phase 1 monotherapy clinical trial provided compelling evidence from biopsies, taken more than four months after administration of Ad-RTS-hIL-12 plus veledimex, demonstrating that Controlled IL-12 causes a sustained influx of activated killer ($CD8^+$) T cells into brain tumors. These data also show upregulated expression of PD-1/PDL-1 biomarkers, suggesting that the combination of Ad-RTS-hIL-12 plus veledimex with an immune checkpoint inhibitor, such as targeting PD-1, may improve patient outcomes.

Clinical Development of Controlled IL-12

We have tested Ad-RTS-IL-12 plus veledimex in several Phase 1 and 2 clinical trials for the treatment of patients with metastatic melanoma, breast cancer and brain cancer. We have focused much of our efforts in developing Ad-RTS-IL-12 plus veledimex, as both a monotherapy and in combination with immune checkpoint inhibitors, for adults and children with recurrent brain tumors. We believe Controlled IL-12 may have broad applicability potentially across many tumor times and we expect to initiate clinical trials of Ad-RTS-IL-12 plus veledimex in additional oncology indications as a monotherapy and, potentially, in combination with checkpoint inhibitors.

Monotherapy: Clinical Development Ad-RTS-IL-12 plus Veledimex for Adult rGBM

We previously conducted a Phase 1 clinical trial of patients with rGBM, referred to as the Main Study, in patients with rGBM. The primary objective of the trial is to determine the safety and tolerability of a single intra-tumoral Ad-RTS-hIL-12 injection activated upon dosing with oral veledimex. Secondary objectives are to determine the maximum tolerated dose, the immune responses elicited, and assessment of biologic response.

A subset of patients in the Main Study (n=6) with unifocal disease who received single administration of Ad-RTS-hIL-12 with 20 mg daily dosing (15 total planned doses) of veledimex along with low-dose steroids, achieved 17.8 months median overall survival, or mOS. Based on this result, we initiated a substudy, referred to as the Expansion Substudy, designed to encourage use of low-dose steroids and 20 mg veledimex to further understand the potential of Controlled IL-12 as a monotherapy.

Thirty-six additional patients with rGBM were recruited into the Expansion Substudy and at the 2019 Society for Neuro-Oncology, or SNO, Annual Meeting, we announced the following interim results from the Expansion Substudy:

- We observed a decrease in tumor from baseline resulted in a patient’s lesion being too small to measure, assessed as a partial response (per iRANO), with follow up ongoing.
- We provided an analysis of MRI findings of pseudoprogression in subjects with initial increases and subsequent decreases in tumor size, which was consistent with immune-mediated anti-tumor effects.
- We observed that subjects in the Expansion Substudy were comparable to the subjects in the Main Study, except a higher percentage of subjects enrolled in the Expansion Substudy had multifocal disease (as compared with unifocal disease) and fewer previous recurrences of disease.
- Subjects receiving 20 mg of veledimex in both the Main Study and Expansion Substudy (n=20) with unifocal disease at entry, receiving low-dose steroids (defined as <20 mg cumulative dosing of dexamethasone during the time of veledimex dosing) had a mOS of 16.2 months. The mOS for these subjects in the Expansion Substudy alone (n=14) had not been reached at a mean follow up of 9.7 months.
- We observed subjects with multifocal disease at initial enrollment that received 20mg of veledimex and low-dose steroids (n=13) had a mOS of 10.1 months. We believe this is consistent with literature, which shows that multifocal glioblastoma is associated with worse prognosis compared to unifocal disease.
- Adverse reactions that we observed in the Expansion Substudy as of the data cut-off date were consistent with prior studies of Controlled IL-12 and were predictable, dose-related, and promptly reversible upon discontinuation of veledimex.
- Drug-related toxicities we observed as of the data cut-off date were comparable to the Main Study, and were predictable, dose-related, and promptly reversible upon discontinuation of veledimex. There were no drug-related deaths reported.

Interim Results from Expansion Substudy Presented at 2019 SNO Annual Meeting

Cohort	Cumulative Steroids (Days 0-14)	No. of Subjects	No. of Subjects Alive	Median Survival (95% CI) (mons)	Mean Follow-up (mons)
Unifocal	≤20 mg	20	7	16.2 (8.9, 18.5)	12.3
	>20 mg	16	4	9.8 (4.6, 30.2)	9.7
Multifocal	≤20 mg	13	5	10.1 (2.6, -)	7.5
	>20 mg	2	0	10.9 (9.4, 12.5)	10.9

Combination Therapy

We have completed enrollment in a Phase 1 clinical trial to evaluate Ad-RTS-hIL-12 plus veledimex in combination with Bristol-Myers Squibb Company's OPDIVO® (nivolumab), an immune checkpoint inhibitor, or PD-1 inhibitor, in adult patients with rGBM. This trial was initiated in 2018 and is exploring the potentially synergistic effect of this combination in 21 patients, which have been enrolled. This multi-center, open-label, single-arm trial is being conducted at four sites. Patients with rGBM scheduled for resection who had not been treated previously with inhibitors of immune-checkpoint pathways received Ad-RTS-hIL-12 intratumorally at the time of surgical resection plus a dose of veledimex (10 or 20mg), daily for 14 days. Patients receive nivolumab intravenously (1 or 3 mg/kg) every two weeks until documented progression or withdrawal from the clinical trial and an expansion cohort at the full dose of 20 mg veledimex and 3mg/kg of nivolumab was included. We provided an interim update for this trial at the 2019 SNO Annual Meeting where we announced that:

- We observed a decrease of approximately 64% in a patient's tumor from baseline resulting in a partial response (per iRANO), with follow up ongoing.
- We provided an analysis of MRI findings of pseudoprogression in subjects, which was consistent with immune-mediated anti-tumor effects.
- Active dosing is ongoing in the trial and mOS had not been reached, with a mean follow up for these subjects of 4.8 months.
- No dose limiting toxicities, no serious adverse events that were considered related to the combination with nivolumab and no clinically significant overlapping toxicities had been observed in the trial as of the data cut-off date.

In November 2018, we announced a clinical supply agreement with Regeneron to evaluate Ad-RTS-hIL-12 plus veledimex in combination with Regeneron's PD-1 antibody Libtayo® (cemiplimab-rwlc) to treat patients with rGBM. Libtayo has been approved in the United States for the treatment of patients with metastatic cutaneous squamous cell carcinoma, or CSCC, or locally advanced CSCC who are not candidates for curative surgery or curative radiation. We are currently enrolling subjects in a Phase 2 clinical trial of Ad-RTS-hIL-12 plus veledimex in combination with Libtayo. This multi-center, open-label, single-arm trial will be conducted at approximately 10 hospitals and will enroll approximately 36 patients with rGBM, with the primary endpoints being safety and efficacy. Patients with rGBM scheduled for resection who have not been treated previously with inhibitors of immune-checkpoint pathways will receive Ad-RTS-hIL-12 intratumorally at the time of surgical resection plus a dose of veledimex (20mg), daily for 14 days. Patients will receive cemiplimab intravenously (350 mg) every three weeks until documented progression or withdrawal from the clinical trial. Under the terms of our agreement with Regeneron, we will be responsible for the conduct and costs of the clinical trial, and Regeneron will supply Libtayo for the trial.

Expansion of Controlled IL-12 Program

In our clinical trials, we have observed that Controlled IL-12 increases T cell activity in the tumor microenvironment including the compelling mOS of patients with rGBM with unifocal disease at entry, the decrease in a patient's tumor from baseline (after pseudo-progression), and the increased infiltration of T cells consistent with pseudo-progression. These data suggest that our Controlled IL-12 may be effective in other tumor types as both a monotherapy and in combination with immune checkpoint inhibitors. We expect to evaluate

Controlled IL-12 in multiple tumor types in smaller clinical trials. The first such clinical trial is a Phase 1 clinical trial of Ad-RTS-hIL-12 plus veledimex for the treatment of glioma in the pontine region of the brain, known as diffuse intrinsic pontine glioma, or DIPG.

Glioblastoma Prevalence

We are currently developing Controlled IL-12 to treat patients with rGBM. Glioblastoma is an aggressive primary brain tumor affecting approximately 74,000 people worldwide each year; it is a fast-growing, aggressive type of central nervous system tumor, with an estimated 12,760 new adult cases predicted in the United States for 2018 according to the American Brain Tumor Association. Recurrence rates for this type of cancer are near 90 percent, and prognosis for adult patients is poor with treatment often combining multiple approaches including surgery, radiation and chemotherapy.

Recurrent glioblastoma is an aggressive cancer with one of the lowest 3-year survival rates, at 3%, among all cancers. For patients who have experienced multiple recurrences, the prognosis is particularly poor, with an OS of six to seven months, while overall survival in patients who have failed temozolomide and bevacizumab, or equivalent salvage chemotherapy, is approximately three to five months.

In children, the incidence of brain cancer is approximately 4.84 per 100,000, according to the NCI. DIPG accounts for approximately 15 percent of all cases of pediatric brain tumors, with a median survival time of less than one year. Because of where these tumors are situated, DIPG is inaccessible to surgery and there are no known curative options.

SLEEPING BEAUTY CAR+ T PROGRAM

Background

We are developing CAR+ T cell therapies targeting CD19 for hematologic malignancies using our *Sleeping Beauty* platform. Our CAR+ T program is focused on (1) shortening the time the patient must wait for treatment with engineered T cells, (2) increasing the access of hospitals to deliver, and patients to receive, this therapy, and (3) providing safe and efficacious T cell therapies to patients.

CARs are engineered molecules that, when present on the surface of a T cell, enable the T cell to directly recognize specific proteins or antigens that are present on the surface of other cells. CAR+ T cell therapies are manufactured individually for the recipient's use by modifying T cells outside the body, causing the T cells to stably express CARs. Our CAR+ T program is focused on CD19, which is a protein expressed on the cell surface of B cells and a validated target for B cell driven hematological malignancies.

Two autologous anti-CD19 CAR+ T cell therapies have been approved by the FDA for the treatment of relapsed/refractory (R/R) B-cell precursor acute lymphoblastic leukemia (Kymriah®) and R/R large B-cell lymphoma (Kymriah® and Yescarta®). These approaches have been successful in helping patients fight cancer, in particular CD19-positive cancers, resulting in significant remission rates. However, we believe the viral manufacturing approaches used to manufacture these therapies will limit their commercial success.

We believe our *Sleeping Beauty* CAR+ T therapy will offer distinct advantages to the approach used by other CAR-T cell companies. In particular, the ability of the DNA plasmids from the *Sleeping Beauty* system to integrate into resting T cells, coupled with expression of mbIL15 and CAR, will enable infused T cells to propagate within the patient to target leukemias and lymphoma, thereby avoiding the need to numerically expand T cells for weeks in bioreactors before administration. The reduced cost associated with using DNA plasmids, instead of virus and avoiding lengthy *ex vivo* manufacturing, and the flexibility to insert industry leading CAR technology in a "cassette" based approach, provides a solution to the cost and complexity of the current approach to manufacturing CAR+ T cells.

Clinical Development of CAR+ T

In the preclinical setting, the time to manufacture and administer third-generation *Sleeping Beauty*-modified CAR+ T cells co-expressing mbIL15 has been reduced to two days or less from gene transfer. This very rapid manufacturing process may deliver genetically modified T cells with superior therapeutic potential *in vivo*. Preclinical studies of our third-generation *Sleeping Beauty* CAR+ T cells, presented at the 2017 Annual Meeting of ASH, demonstrated that a single dose of T cells co-expressing a CD19-specific CAR, mbIL15, and kill switch resulted in sustained *in vivo* persistence that produced potent anti-tumor effects and superior leukemia-free survival in mice. We are advancing our CAR+ T technology in the United States in collaboration with MD Anderson in a Phase 1 clinical trial in the United States infusing CD19-specific CAR+ T therapies manufactured using our RPM technology. In this trial, we plan to infuse donor-derived T cells after allogeneic BMT for recipients who have relapsed with CD19+ leukemias and lymphomas. We announced the FDA cleared the IND application submitted by MD Anderson for this clinical trial in early October and we expect MD Anderson to initiate the trial in the first half of 2020.

This trial will build upon the results seen in our second generation CAR+ T clinical trial, which employed a revised CAR design and shortened manufacturing process advancement, with culturing times as short as two weeks. This clinical trial enrolled 26 patients with advanced lymphoid malignancies at MD Anderson. A summary of this trial was presented by Dr. Partow Kebriaei of MD Anderson in a presentation at the 2017 Annual Meeting of ASH in December 2017. Interim data from the trial demonstrated that autologous T cells infused after lymphodepleting chemotherapy could be detected and exhibited anti-tumor effects and had an encouraging safety profile in patients with relapsed/refractory CD19+ malignancies. Complete responses at one month were reported in four of eight patients with either ALL (n=5), chronic lymphocytic leukemia (n=1), or diffuse large B-cell lymphoma (n=2), with two morphologic complete responses at three months. Follow-up blood tests demonstrated sustained persistence of infused T cells and targeting of malignant and normal B cells. A letter published in *Blood*, the journal of the American Society of Hematology, discussed long-term outcomes of seven patients with relapsed or refractory B-cell lymphoid malignancies that received first generation CD19-specific CAR-T cells infused after autologous hematopoietic stem-cell transplantation (HSCT). The letter reported that four of the seven patients demonstrated sustained persistence of CAR+ T (median time of persistence duration was 4.5 years, range 2-5 years) and that five-year progression-free survival and overall survival were 71% and 86%, respectively. There were no dose limiting toxicities with only grade 1 or 2 adverse events being reported.

Joint Venture with Eden BioCell Limited

In conjunction with TriArm Therapeutics, Ltd., or TriArm, we have launched Eden BioCell to lead clinical development and commercialization of *Sleeping Beauty*-generated CAR-T therapies in the People's Republic of China (including Macau and Hong Kong), Taiwan and Korea. Eden BioCell is focused on advancing our RPM technology using patient-derived (autologous) T cells in order to treat patients with relapsed or refractory CD19+ leukemias and lymphomas. TriArm is a privately-owned cell therapy company with operations in Germany, China and the United States that was formed by Panacea Venture Healthcare, a fund co-founded and managed by James Huang, Managing Partner of Kleiner Perkins Caufield & Byers China.

We licensed the rights to Eden BioCell for our third-generation *Sleeping Beauty*-generated CAR-T therapies targeting the CD19 antigen. Eden BioCell is owned equally by us and TriArm and the parties share decision-making authority. TriArm has committed up to $35.0 million to this joint venture and will manage all clinical development to execute trials in the territory.

Hematologic Tumor Malignancy Prevalence

According to the Leukemia and Lymphoma Society, an estimated 176,200 people are expected to be diagnosed with leukemia, lymphoma, or myeloma in 2019. New diagnoses for such hematologic malignancies in the United States represented approximately 10% of the new cancer cases in the United States in 2019.

License Agreements, Intellectual Property and Other Agreements

Our goal is to obtain, maintain, and enforce patent protection for our products, formulations, processes, methods, and other proprietary technologies to preserve our trade secrets and other confidential information and to operate without infringing 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 License Agreement with PGEN Therapeutics

On October 5, 2018, we entered into an exclusive license agreement, or the License Agreement, with PGEN Therapeutics, or PGEN, a wholly owned subsidiary of Precigen Inc., or Precigen, which was formerly known as Intrexon Corporation. As between us and PGEN, the terms of the License Agreement replace and supersede the terms of: (a) that certain Exclusive Channel Partner Agreement by and between us and Precigen, dated January 6, 2011, as amended by the First Amendment to Exclusive Channel Partner Agreement effective September 13, 2011, the Second Amendment to the Exclusive Channel Partner Agreement effective March 27, 2015, and the Third Amendment to Exclusive Channel Partner Agreement effective June 29, 2016, which was subsequently assigned by Precigen to PGEN; (b) certain rights and obligations pursuant to that certain License and Collaboration Agreement effective March 27, 2015 between us, Precigen and ARES TRADING Trading S.A., or Ares Trading, a subsidiary of Merck KGaA, or Merck, as assigned by Precigen to PGEN, or the Ares Trading Agreement; (c) that certain License Agreement between us, Precigen, and MD Anderson, with an effective date of January 13, 2015, or the MD Anderson License, which was subsequently assigned by Precigen and assumed by PGEN effective as of January 1, 2018; and (d) that certain Research and Development Agreement between us, Precigen and MD Anderson with an effective date of August 17, 2015, or the Research and Development Agreement, and any amendments or statements of work thereto.

Pursuant to the terms of the License Agreement, we have exclusive, worldwide rights to research, develop and commercialize (i) products utilizing Precigen's RheoSwitch® gene switch, or RTS, for the treatment of cancer, referred to as IL-12 Products, (ii) CAR products directed to (A) CD19 for the treatment of cancer, referred to as CD19 Products, and (B) a second target for the treatment of cancer, subject to the rights of Merck to pursue such target under the Ares Trading Agreement, and (iii) TCR products designed for neoantigens for the treatment of cancer. Under the License Agreement, we also have exclusive, worldwide rights for certain patents relating to the *Sleeping Beauty* technology to research, develop and commercialize TCR products for both neoantigens and shared antigens for the treatment of cancer, referred to as TCR Products.

We will be solely responsible for all aspects of the research, development and commercialization of the exclusively licensed products for the treatment of cancer. We are required to use commercially reasonable efforts to develop and commercialize IL-12 products and CD19 products and after a two-year period, the TCR Products.

PGEN has also granted us an exclusive, worldwide, royalty-bearing, sub-licensable license to research, develop and commercialize products utilizing an additional construct that expresses RTS IL-12 for the treatment of cancer, referred to as Gorilla IL-12 Products.

In consideration of the licenses and other rights granted by PGEN, we will pay PGEN an annual license fee of $100 thousand and we have agreed to reimburse PGEN for certain historical costs of the licensed programs up to $1.0 million, payable quarterly.

We will make milestone payments totaling up to an additional $52.5 million for each exclusively licensed program upon the initiation of later stage clinical trials and upon the approval of exclusively licensed products in various jurisdictions. In addition, we will pay PGEN tiered royalties ranging from low-single digit to high-single digit on the net sales derived from the sales of any approved IL-12 products and CAR products. We will also pay PGEN royalties ranging from low-single digit to mid-single digit on the net sales derived from the sales of any approved TCR products, up to a maximum royalty amount of $100.0 million in the aggregate. We will also pay PGEN 20% of any sublicensing income received by us relating to the licensed products.

We are responsible for all development costs associated with each of the licensed products, other than Gorilla IL-12 products. We and PGEN will share the development costs and operating profits for Gorilla IL-12 products, and we are responsible for 80% of the development costs and receiving 80% of the operating profits, and PGEN responsible for the remaining 20% of the development costs and receiving 20% of the operating profits.

PGEN will pay us royalties ranging from low-single digits to mid-single digits on the net sales derived from the sale of PGEN's CAR products, up to $50.0 million.

In consideration of our entry into the License Agreement, Precigen has forfeited and returned to us all shares of our Series 1 preferred stock held by or payable to Precigen as of the date of the License Agreement.

We determined that this transaction represented a capital transaction between related parties. We fair valued the preferred stock and the derivative liability on the date of the transaction, noting a total fair value of $163.3 million. The relinquishment of our obligation under the Ares Trading Agreement was also considered part of the overall capital transaction. We recognized an additional credit to accumulated deficit of $49.5 million as a result of the relief of the obligation under the Ares Trading Agreement (Note 7). The total amount of the settlement was $212.8 million.

We incurred approximately $7.4 million of transaction advisory costs with third-party vendors, of which $5.4 million was considered a direct cost associated with the Series 1 preferred stock extinguishment and is also included as part of the consideration transferred. The remaining $2.0 million of transaction costs were recognized as an expense during the year ended December 31, 2018.

We recognized a net credit to accumulated deficit of $207.3 million, calculated as the difference in the carrying value of the Series 1 preferred stock, derivative liability, and contract liability, and the consideration transferred of $5.4 million, in connection with the transaction. This amount is included in net income available to common shareholders in the calculation of earnings per share (Note 3).

License Agreement and 2015 Research and Development Agreement—The University of Texas MD Anderson Cancer Center

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

On August 17, 2015, we, Precigen and MD Anderson entered into the Research and Development Agreement, or the 2015 R&D Agreement, to formalize the scope and process for the transfer by MD Anderson, pursuant to the terms of the MD Anderson License, of certain existing research programs and related technology rights, as well as the terms and conditions for future collaborative research and development of new and ongoing research programs. The rights and obligations of Precigen under the 2015 R&D Agreement were assigned to us pursuant to the Fourth Amendment to Research and Development Agreement which was entered into on September 18, 2019 (the "Fourth Amendment") with an effective date of October 5, 2018.

Pursuant to the 2015 R&D Agreement, we, Precigen and MD Anderson formed a joint steering committee to oversee and manage the ongoing research programs. Under our License Agreement with Precigen, we and Precigen agreed that Precigen would no longer participate on the joint steering committee after the date of the License Agreement. As provided under the MD Anderson License, we provided funding for research and development

activities in support of the research programs under the 2015 R&D Agreement for a period of three years and in an amount of no less than $15.0 million and no greater than $20.0 million per year. On November 14, 2017, we entered into an amendment to the 2015 R&D Agreement extending its term until April 15, 2021. During the year ended December 31, 2019, we made no payments to MD Anderson compared to $2.7 million during the year ended December 31, 2018. The decrease in cash paid to MD Anderson during the year ended December 31, 2019 as compared to the same period in the prior year is a result of the final quarterly payment being made to MD Anderson in January 2018 and the result of approved expenditures incurred by us being deducted from the January 2018 quarterly payment. The net balance of cash resources on hand at MD Anderson available to offset expenses and future costs is $20.3 million, which is included in other current assets on our balance sheet at December 31, 2019.

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

In connection with the execution of the 2019 R&D Agreement described below, on October 22, 2019, we amended the 2015 R&D Agreement to extend the term of the 2015 R&D Agreement until December 31, 2026 and to allow cash resources on hand at MD Anderson under the 2015 R&D Agreement to be used for development costs under the 2019 R&D Agreement.

2019 Research and Development Agreement—The University of Texas MD Anderson Cancer Center

On October 22, 2019, we entered into the 2019 Research and Development Agreement, or the 2019 R&D Agreement, with MD Anderson pursuant to which the parties agreed to collaborate with respect to the TCR program. Under the 2019 R&D Agreement, the parties will, among other things, collaborate on programs to expand our TCR library and conduct clinical trials. The activities under the 2019 R&D Agreement will be directed by a joint steering committee comprised of two members from our company and one member from MD Anderson.

We will own all intellectual property developed under the 2019 R&D Agreement and we will retain all rights to intellectual property for oncology products manufactured using non-viral gene transfer technologies under the 2019 R&D Agreement, including our *Sleeping Beauty* technology. We have granted MD Anderson an exclusive license for such intellectual property outside the field of oncology and to develop and commercialize autologous TCR products manufactured using viral gene transfer technologies, and a non-exclusive license for allogeneic TCR products manufactured using viral-based technologies.

Under the 2019 R&D Agreement, we agreed, beginning on January 1, 2021, to reimburse MD Anderson up to a total of $20 million for development costs under the 2019 R&D Agreement. In addition, we will pay MD Anderson royalties on net sales of its TCR products at rates in the low single digits. We are required to make performance-based payments upon the successful completion of clinical and regulatory benchmarks relating to

its TCR products. The aggregate potential benchmark payments are $36.5 million, of which only $3.0 million will be due prior to the first marketing approval of our TCR products. The royalty rates and benchmark payments owed to MD Anderson may be reduced upon the occurrence of certain events. We also agreed to sell our TCR products to MD Anderson at preferential prices and will sell our TCR products in Texas exclusively to MD Anderson for a limited period of time following the first commercial sale of our TCR products.

The 2019 R&D Agreement will terminate on December 31, 2026 and either party may terminate the 2019 R&D Agreement following written notice of a material breach. The 2019 R&D Agreement also contains customary provisions related to indemnification obligations, confidentiality and other matters.

In connection with the execution of the 2019 R&D Agreement, on October 22, 2019, we issued MD Anderson a warrant to purchase 3,333,333 shares of our common stock, which is referred to as the MD Anderson Warrant. The MD Anderson Warrant has an initial exercise price of $0.001 per share, expires on December 31, 2026 and vests upon the occurrence of certain clinical milestones.

The MD Anderson Warrant and the shares of our common stock to be issued upon exercise of the MD Anderson Warrant have not been registered under the Securities Act of 1933, as amended, and may not be offered or sold in the United States absent registration or an applicable exemption from registration requirements.

License Agreement with the National Cancer Institute

On May 28, 2019, we entered into a patent license agreement, or the Patent License, with the National Cancer Institute, or the NCI. Pursuant to the Patent License, we hold an exclusive, worldwide license to certain intellectual property to develop and commercialize patient-derived (autologous), peripheral blood T-cell therapy products engineered by transposon-mediated gene transfer to express TCRs reactive to mutated KRAS, p53 and EGFR neoantigens. In addition, pursuant to the Patent License, we hold an exclusive, worldwide license to certain intellectual property for manufacturing technologies to develop and commercialize autologous, peripheral blood T-cell therapy products engineered by non-viral gene transfer to express TCRs, as well as a non-exclusive, worldwide license to certain additional manufacturing technologies. On January 8, 2020, we amended the Patent License to expand the TCR library licensed from the NCI to include additional TCRs reactive to mutated KRAS and TP53 neoantigens.

Pursuant to the terms of the Patent License, we are required to pay the NCI a cash payment in the aggregate amount of $1.5 million payable in $0.5 million installments within sixty days, six-months, and the twelve-month anniversary of the effective date of the agreement for the Patent License. We also reimbursed the NCI for past patent expenses in the aggregate amount of approximately $46 thousand. Under the amendment to the patent license signed in January of 2020, we agreed to pay the NCI a cash payment of $600,000 within sixty days of the amendment.

The terms of the Patent License also require us to pay the NCI minimum annual royalties in the amount of $0.3 million, which amount will be reduced to $0.1 million once the aggregate minimum annual royalties paid by us equals $1.5 million.

We are also required to make performance-based payments upon successful completion of clinical and regulatory benchmarks relating to the licensed products. The aggregate potential benchmark payments are $4.3 million, of which aggregate payments of $3.0 million are due only after marketing approval in the United States or in Europe, Japan, Australia, China or India. The first benchmark payment of $0.1 million will be due upon the initiation of our first sponsored phase 1 clinical trial of a licensed product or licensed process in the field of use licensed under the Patent License.

In addition, we are required to pay the NCI one-time benchmark payments following aggregate net sales of licensed products at certain net sales up to $1.0 billion. The aggregate potential amount of these benchmark payments is $12.0 million. We must also pay the NCI royalties on net sales of products covered by the Patent

License at rates in the low to mid-single digits depending upon the technology included in a licensed product. To the extent we enter into a sublicensing agreement relating to a licensed product, we are required to pay the NCI a percentage of all consideration received from a sublicensee, which percentage will decrease based on the stage of development of the licensed product at the time of the sublicense.

The Patent License will expire upon expiration of the last patent contained in the licensed patent rights, unless terminated earlier. The NCI may terminate or modify the Patent License in the event of a material breach, including if we do not meet certain milestones by certain dates, or upon certain insolvency events that remain uncured following the date that is 90 days following written notice of such breach or insolvency event. We may terminate the Patent License, or any portion thereof, in our sole discretion at any time upon 60 days' written notice to the NCI. In addition, the NCI has the right to: (i) require us to sublicense the rights to the product candidates covered by the Patent License upon certain conditions, including if we are not reasonably satisfying required health and safety needs and (ii) terminate or modify the Patent License, including if we are not satisfying requirements for public use as specified by federal regulations.

Cooperative Research and Development Agreement (CRADA) with the National Cancer Institute

On January 10, 2017, we announced the signing of the CRADA with the NCI for the development of adoptive cell transfer, or ACT,-based immunotherapies genetically modified using the *Sleeping Beauty* transposon/transposase system to express TCRs for the treatment of solid tumors. The principal goal of the CRADA is to develop and evaluate ACT for patients with advanced cancers using autologous peripheral blood lymphocytes, or PBL, genetically modified using the non-viral *Sleeping Beauty* system to express TCRs that recognize neoantigens expressed within a patient's cancer. Research conducted under the CRADA will be at the direction of Steven A. Rosenberg, M.D., Ph.D., Chief of the Surgery Branch at the NCI, in collaboration with our researchers and PGEN researchers. During the year ended December 31, 2019 and 2018, the Company made payments of $2.5 million, each year. In February of 2019, the Company extended the CRADA with the NCI for two years, committing an additional $5.0 million to this program.

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 may be patentable. To help protect unpatentable proprietary know-how, and for inventions for which patents may be difficult to enforce, we currently rely, and in the future, will continue to rely, on trade secret protection and confidentiality agreements to protect our interests. To this end, we generally require employees, consultants, advisors and other contractors to enter into

confidentiality agreements that prohibit the disclosure of confidential information and, where applicable, require disclosure and assignment to us of the ideas, developments, discoveries and inventions important to our business.

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

Additional information as of December 31, 2019 about material patents and other proprietary rights covering our product candidates is set forth below.

Ad-RTS-IL-12 plus veledimex

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

CAR+ T

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

TCR+ T

In May 2019, we in-licensed from NCI a technology portfolio that includes intellectual property directed to certain TCR+ T cell therapy and manufacturing technology. Under the terms of the agreement, we hold an exclusive, worldwide license to certain intellectual property to develop and commercialize patient-derived (autologous), peripheral blood T-cell therapy products engineered by transposon-mediated gene transfer to express TCRs reactive to mutated KRAS, TP53 and EGFR neoantigens. In addition, we hold an exclusive, worldwide license to certain intellectual property for manufacturing technologies to develop and commercialize autologous, peripheral blood T-cell therapy products engineered by non-viral gene transfer to express TCRs, as well as a non-exclusive, worldwide license to certain additional manufacturing technologies.

Governmental Regulation and Product Approval

As a biopharmaceutical company, we are subject to extensive regulation. Our programmed T-cell product candidates are regulated as biologics. With this classification, commercial production of our products will need to occur in registered and licensed facilities in compliance with current Good Manufacturing Practices, or cGMPs, for biologics.

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

Government authorities in the United States (at the federal, state and local level) and in other countries and jurisdictions, extensively regulate, among other things, the research, development, preclinical and clinical testing, manufacturing, quality control, labeling, packaging, storage, record-keeping, promotion, advertising, sale,

distribution, post-approval monitoring and reporting, marketing and export and import of biopharmaceutical products such as those we are developing. Our product candidates must be approved by the FDA before they may be legally marketed in the United States and by the appropriate foreign regulatory agency before they may be legally marketed in foreign countries. Generally, our activities in other countries will be subject to regulation that is similar in nature and scope as that imposed in the United States, although there can be important differences. The process for obtaining regulatory marketing approvals and the subsequent compliance with applicable federal, state, local and foreign statutes and regulations require the expenditure of substantial time and financial resources.

U.S. Product Development Process

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

- completion of preclinical laboratory tests and animal studies according to Good Laboratory Practices, or GLPs, and applicable requirements for the humane use of laboratory animals or other applicable regulations;
- submission to the FDA of an Investigational New Drug Application, or IND, which must become effective before human clinical trials may begin;
- performance of adequate and well-controlled human clinical trials according to the FDA's regulations commonly referred to as Good Clinical Practices, or GCPs, and any additional requirements for the protection of human research subjects and their health information, to establish the safety and efficacy of the proposed biological product for its intended use;
- preparation and submission to the FDA of a Biologics License Application, or BLA, for marketing approval that includes substantive evidence of safety, purity, and potency from results of nonclinical testing and clinical trials;
- satisfactory completion of one or more FDA inspections of the manufacturing facility or facilities where the biological product is produced to assess compliance with cGMP to assure that the facilities, methods and controls used in product manufacture are adequate to preserve the biological product's identity, strength, quality and purity and, if applicable, the FDA's current Good Tissue Practices, or GTPs, for the use of human cellular and tissue products;
- potential FDA audit of the nonclinical study and clinical trial sites that generated the data in support of the BLA;
- payment of user fees for FDA review of the BLA; and

FDA acceptance, review and approval, or licensure, of the BLA, which might include review by an advisory committee, a panel typically consisting of independent clinicians and other experts who provide recommendations as to whether the application should be approved and under what conditions.

Before testing any biological product candidate, including our product candidates, in humans, the product candidate must undergo rigorous preclinical testing. Preclinical tests, also referred to as nonclinical studies,

include laboratory evaluations as well as *in vitro* and animal studies to assess the potential safety and efficacy of the product candidate. The clinical trial sponsor must submit an IND to the FDA before clinical testing can begin in the United States. An IND must contain the results of the preclinical tests, manufacturing information, analytical data, any available clinical data or literature, a proposed clinical protocol, an investigator's brochure, a sample informed consent form, and other materials. Clinical trial protocols detail, among other things, the objectives of the clinical trial, dosing procedures, subject selection and exclusion criteria, and the parameters to be used to monitor subject safety, including stopping rules that assure a clinical trial will be stopped if certain adverse events should occur. Each protocol and any amendments to the protocol must be submitted to the FDA as part of the IND. Some preclinical testing, such as toxicity studies, may continue even after the IND is submitted.

The IND automatically becomes effective 30 days after receipt by the FDA, unless the FDA raises concerns or questions regarding the proposed clinical trials or places the trial on a clinical hold within that 30-day time period. In such a case, the IND sponsor and the FDA must resolve any outstanding concerns before the clinical trial can begin. The FDA may also impose clinical holds on a biological product candidate at any time before or during clinical trials due to safety concerns or non-compliance. If the FDA imposes a clinical hold, trials may not recommence without FDA authorization and then only under terms authorized by the FDA.

Further, each clinical trial must be reviewed and approved by an independent institutional review board, or IRB, at or servicing each institution at which the clinical trial will be conducted. An IRB is charged with protecting the welfare and rights of trial participants and considers such items as whether the risks to individuals participating in the clinical trials are minimized and are reasonable in relation to anticipated benefits. The IRB also approves the form and content of the informed consent that must be signed by each clinical trial subject or his or her legal representative and must monitor the clinical trial until completed. Clinical trials involving recombinant or synthetic nucleic acid molecules also must be reviewed by an institutional biosafety committee, or IBC, a local institutional committee that reviews and oversees basic and clinical research conducted at that institution. The IBC assesses the safety of the research and identifies any potential risk to public health or the environment.

Clinical trials involve the administration of the biological product candidate to healthy volunteers or patients under the supervision of qualified investigators, generally physicians not employed by or under the trial sponsor's control. Clinical trials must be conducted and monitored in accordance with the FDA's regulations comprising the GCP requirements.

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

- *Phase 1*. The biological product is initially introduced into healthy human subjects and tested for safety. In the case of some products for severe or life-threatening diseases, especially when the product may be too inherently toxic to ethically administer to healthy volunteers, the initial human testing is often conducted in patients with the target disease or condition.
- *Phase 2*. The biological product is evaluated in a limited patient population to identify possible adverse effects and safety risks, to preliminarily evaluate the efficacy of the product for specific targeted diseases and to determine dosage tolerance, optimal dosage and dosing schedule.
- *Phase 3*. Clinical trials are undertaken to further evaluate dosage, clinical efficacy, potency, and safety in an expanded patient population, generally at geographically dispersed clinical trial sites. These clinical trials are intended to generate enough data to statistically evaluate the efficacy and safety of the product for approval, to establish the overall risk to benefit profile of the product and to provide an adequate basis for product labeling.

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

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

During all phases of clinical development, regulatory agencies require extensive monitoring and auditing of all clinical activities, clinical data, and clinical trial investigators. Annual progress reports detailing the results of the clinical trials must be submitted to the FDA. Written IND safety reports must be promptly submitted to the FDA, the NIH and the investigators for serious and unexpected adverse events, any findings from other studies, tests in laboratory animals or *in vitro* testing that suggest a significant risk for human patients, or any clinically important increase in the rate of a serious suspected adverse reaction over that listed in the protocol or investigator brochure. The sponsor must submit an IND safety report within 15 calendar days after the sponsor determines that the information qualifies for reporting. The sponsor also must notify the FDA of any unexpected fatal or life-threatening suspected adverse reaction within seven calendar days after the sponsor's initial receipt of the information. The FDA or the sponsor or its data safety monitoring board, an independent group of experts that evaluates study data for safety and makes recommendations concerning continuation, modification, or termination of clinical trials, may suspend or terminate a clinical trial at any time on various grounds, including a finding that the research patients are being exposed to an unacceptable health risk, including risks inferred from other unrelated immunotherapy trials. Similarly, an IRB can suspend or terminate approval of a clinical trial at its institution if the clinical trial is not being conducted in accordance with the IRB's requirements or if the biological product has been associated with unexpected serious harm to patients.

Concurrently with clinical trials, companies usually complete additional nonclinical studies and must also develop additional information about the physical characteristics of the biological product as well as finalize a process for manufacturing the product in commercial quantities in accordance with cGMP requirements. To help reduce the risk of the introduction of adventitious agents with use of biological products, the PHSA emphasizes the importance of manufacturing control for products whose attributes cannot be precisely defined. The manufacturing process must be capable of consistently producing quality batches of the product candidate and, among other things, the sponsor must develop methods for testing the identity, strength, quality, potency and purity of the final biological product. Additionally, appropriate packaging must be selected and tested, and stability studies must be conducted to demonstrate that the biological product candidate does not undergo unacceptable deterioration over its shelf life.

The FDA has a fast track designation program that is intended to expedite or facilitate the process for reviewing new drug or biologic products that meet certain criteria. Specifically, new drugs or biologics are eligible for Fast Track designation if they are intended to treat a serious or life-threatening disease or condition and demonstrate the potential to address unmet medical needs for the disease or condition. Unique to a fast track product, the FDA may consider for review sections of the BLA on a rolling basis before the complete application is submitted, if the sponsor provides a schedule for the submission of the sections of the BLA, the FDA agrees to accept sections of the BLA and determines that the schedule is acceptable, and the sponsor pays any required user fees upon submission of the first section of the BLA.

U.S. Review and Approval Processes

After the completion of clinical trials of a biological product, FDA approval of a BLA must be obtained before commercial marketing of the biological product. The BLA must include results of product development, laboratory and animal studies, human trials, information on the manufacture and composition of the product, proposed labeling and other relevant information.

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

Within 60 days following submission of the application, the FDA reviews a BLA submitted to determine if it is substantially complete before the agency accepts it for filing. The FDA may refuse to file any BLA that it deems incomplete or not properly reviewable at the time of submission and may request additional information. In this event, the BLA must be resubmitted with the additional information. The resubmitted application also is subject to review before the FDA accepts it for filing. Once the submission is accepted for filing, the FDA begins an in-depth substantive review of the BLA. The FDA reviews the BLA to determine, among other things, whether the proposed product is safe, potent, and/or effective for its intended use, and has an acceptable purity profile, and whether the product is being manufactured in accordance with cGMP to assure and preserve the product's identity, safety, strength, quality, potency and purity. The FDA may refer applications for novel biological products or biological products that present difficult questions of safety or efficacy to an advisory committee, typically a panel that includes clinicians and other experts, for review, evaluation and a recommendation as to whether the application should be approved and under what conditions. The FDA is not bound by the recommendations of an advisory committee, but it considers such recommendations carefully when making decisions. During the biological product approval process, the FDA also will determine whether a Risk Evaluation and Mitigation Strategy, or REMS, is necessary to ensure that the benefits of the product outweigh its risks and to assure the safe use of the biological product, which could include medication guides, physician communication plans, or elements to assure safe use, such as restricted distribution methods, patient registries and other risk minimization tools. FDA determines the requirement for a REMS, as well as the specific REMS provisions, on a case-by-case basis. If the FDA concludes a REMS is needed, the sponsor of the BLA must submit a proposed REMS. The FDA will not approve a BLA without a REMS, if required.

Before approving a BLA, the FDA will inspect the facilities at which the product is manufactured. The FDA will not approve the product unless it determines that the manufacturing processes and facilities are in compliance with cGMP requirements and adequate to assure consistent production of the product within required specifications. For immunotherapy products, the FDA also will not approve the product if the manufacturer is not in compliance with the GTPs, to the extent applicable. These are FDA regulations and guidance documents that govern the methods used in, and the facilities and controls used for, the manufacture of human cells, tissues, and cellular and tissue-based products, or HCT/Ps, which are human cells or tissue intended for implantation, transplant, infusion, or transfer into a human recipient. The primary intent of the GTP requirements is to ensure that cell and tissue-based products are manufactured in a manner designed to prevent the introduction, transmission and spread of communicable disease. FDA GTP regulations also require tissue establishments to register and list their HCT/Ps with the FDA and, when applicable, to evaluate donors through screening and testing. Additionally, before approving a BLA, the FDA will typically inspect one or more clinical sites to assure that the clinical trials were conducted in compliance with IND trial requirements and GCP requirements.

Notwithstanding the submission of relevant data and information, the FDA may ultimately decide that the BLA does not satisfy its regulatory criteria for approval. If the agency decides not to approve the BLA in its present form, the FDA will issue a Complete Response Letter, which generally outlines the specific deficiencies in the BLA identified by the FDA and may require additional clinical or other data or impose other conditions that must be met in order to secure final approval of the application. The deficiencies identified may be minor, for example, requiring labeling changes, or major, for example, requiring additional clinical trials. Even with the submission of additional information, the FDA may ultimately decide that the application does not satisfy the regulatory criteria for approval. If a Complete Response Letter is issued, the applicant may either resubmit the BLA, addressing all of the deficiencies identified in the letter, or withdraw the application.

The FDA may require that certain contraindications, warnings or precautions be included in the product labeling, or otherwise limit the scope of any approval. In addition, the FDA may require post marketing clinical trials, sometimes referred to as Phase 4 clinical trials, designed to further assess a biological product's safety and effectiveness, and testing and surveillance programs to monitor the safety of approved products that have been commercialized. After approval, many types of changes to the approved product, such as adding new indications, manufacturing changes and additional labeling claims, are subject to further testing requirements and FDA review and approval.

In addition, under the Pediatric Research Equity Act, or PREA, a BLA or supplement to a BLA must contain data to assess the safety and effectiveness of the product for the claimed indications in all relevant pediatric subpopulations and to support dosing and administration for each pediatric subpopulation for which the product is safe and effective. The FDA may grant deferrals for submission of data or full or partial waivers.

Post-Approval Requirements

Any products for which we receive FDA approvals are subject to continuing regulation by the FDA, including, among other things, record-keeping requirements, reporting of adverse experiences with the product, providing the FDA with updated safety and efficacy information, product sampling and distribution requirements, and complying with FDA promotion and advertising requirements.

In addition, quality control and manufacturing procedures must continue to conform to applicable manufacturing requirements after approval to ensure the long-term stability of the product. We rely, and expect to continue to rely, on third parties for the production of clinical and commercial quantities of our products in accordance with cGMP regulations. cGMP regulations require among other things, quality control and quality assurance as well as the corresponding maintenance of records and documentation and the obligation to investigate and correct any deviations from cGMP. Manufacturers and other entities involved in the manufacture and distribution of approved products are required to register their establishments with the FDA and certain state agencies, and are subject to periodic unannounced inspections by the FDA and certain state agencies for compliance with cGMP and other laws. Accordingly, manufacturers must continue to expend time, money, and effort in the area of production and quality control to maintain cGMP compliance. Discovery of problems with a product after approval may result in restrictions on a product, manufacturer, or holder of an approved BLA, including, among other things, recall or withdrawal of the product from the market.

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

Moreover, the FDA strictly regulates marketing, labeling, advertising and promotion of products. Drugs may be promoted only for the approved indications and in accordance with the provisions of the approved label, although physicians, in the practice of medicine, may prescribe approved drugs for unapproved indications. However, companies may share truthful and not misleading information that is otherwise consistent with the labeling. The FDA and other agencies actively enforce the laws and regulations prohibiting the promotion of off-label uses, and a company that is found to have improperly promoted off-label uses may be subject to significant liability.

U.S. Marketing Exclusivity

The Biologics Price Competition and Innovation Act, or BPCIA, amended the PHSA to authorize the FDA to approve similar versions of innovative biologics, commonly known as biosimilars. Biosimilars are approved pursuant to an abbreviated pathway whereby applicants need not submit the full slate of preclinical and clinical data, and approval is based in part on the FDA's findings of safety, purity, and potency for the original biologic (i.e., the reference product). Reference products are eligible to receive 12 years of exclusivity from the time of first licensure of the product, which prevents the FDA from approving any biosimilars to the reference product

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

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

Orphan Drug Designation

Under the Orphan Drug Act, the FDA may grant orphan designation to a drug or biologic intended to treat a rare disease or condition, which is a disease or condition that affects fewer than 200,000 individuals in the United States or, if it affects more than 200,000 individuals in the United States, there is no reasonable expectation that the cost of developing and making a drug or biologic product available in the United States for this type of disease or condition will be recovered from sales of the product. Orphan designation must be requested before submitting a marketing application. After the FDA grants orphan designation, the identity of the therapeutic agent and its potential orphan use are disclosed publicly by the FDA. Orphan designation does not convey any advantage in or shorten the duration of the regulatory review and approval process.

If a product that has orphan designation subsequently receives the first FDA approval for the disease or condition for which it has such designation, the product is entitled to orphan product exclusivity, which means that the FDA may not approve any other applications to market the same drug or biological product for the same indication for seven years, except in limited circumstances, such as a showing of clinical superiority to the product with orphan exclusivity or inability to manufacture the product in sufficient quantities. The designation of such drug also entitles a party to financial incentives such as opportunities for grant funding towards clinical trial costs, tax advantages and user fee waivers. Competitors, however, may receive approval of different products for the indication for which the orphan product has exclusivity or obtain approval for the same product but for a different indication for which the orphan product has exclusivity. Orphan exclusivity also could block the approval of one of our products for seven years if a competitor obtains approval of the same product as defined by the FDA or if our product candidate is determined to be contained within the competitor's product for the same indication or disease. If an orphan designated product receives marketing approval for an indication broader than what is designated, it may not be entitled to orphan exclusivity. Orphan drug status in the European Union has similar but not identical benefits in that jurisdiction.

Coverage, Pricing and Reimbursement

Significant uncertainty exists as to the coverage and reimbursement status of any product candidates for which we obtain regulatory approval. In the United States and markets in other countries, sales of any products for which we receive regulatory approval for commercial sale will depend, in significant part, on the extent to which third-party payors provide coverage, and establish adequate reimbursement levels for such products. In the United States, third-party payors include federal and state healthcare programs, private managed care providers, health insurers and other organizations. The process for determining whether a third-party payor will provide coverage for a product may be separate from the process for setting the price of a product or for establishing the reimbursement rate that such a payor will pay for the product. Third-party payors may limit coverage to specific products on an approved list, also known as a formulary, which might not include all of the FDA-approved products for a particular indication. 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. Third-party payors are increasingly challenging the price, examining the medical necessity of and reviewing the cost-effectiveness of medical products, therapies and services, in addition to questioning their safety and efficacy.

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

The downward pressure on health care costs in general, particularly prescription drugs and biologics, has become very intense. Governments have shown significant interest in implementing cost-containment programs, including price controls, restrictions on reimbursement and requirements for substitution of generic products. As a result, increasingly high barriers are being erected to the entry of new products. The marketability of any product candidates for which we receive regulatory approval for commercial sale may suffer if the government and third-party payors fail to provide favorable coverage and adequate reimbursement. In addition, emphasis on managed care in the United States has increased and we expect will continue to increase the pressure on healthcare pricing. Coverage policies and third-party reimbursement rates may change at any time. Even if favorable coverage and reimbursement status is attained for one or more products for which we receive regulatory approval, less favorable coverage policies and reimbursement rates may be implemented in the future.

Health Care Laws Governing Interactions with Healthcare Providers

Healthcare providers, physicians and third-party payors in the United States play a primary role in the recommendation and prescription of drug products. Arrangements with healthcare providers, physicians, third-party payors and customers can expose pharmaceutical manufactures to broadly applicable fraud and abuse and other healthcare laws, including false claims, privacy and security, price reporting, and physician sunshine laws or regulations. Some of our pre-commercial activities are subject to some of these laws. The applicable federal, state and foreign healthcare laws and regulations laws that may affect a pharmaceutical manufacture's ability to operate include, but are not limited to:

- The federal Anti-Kickback Statute, which regulates our business activities, including our marketing practices, educational programs, pricing policies, and relationships with healthcare providers or other entities, by prohibiting, among other things, soliciting, receiving, offering or paying remuneration, directly or indirectly, to induce, or in return for, either the referral of an individual or the purchase or recommendation of an item or service reimbursable under a federal healthcare program, such as the Medicare and Medicaid programs;
- Federal civil and criminal false claims laws and civil monetary penalty laws, including the False Claims Act which permits a private individual acting as a "whistleblower" to bring actions on behalf of the federal government alleging violations of the False Claims Act, 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 civil and criminal statutes that prohibit, among other things, executing a scheme to defraud any healthcare benefit program or making false statements relating to healthcare matters;
- HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act of 2009, or HITECH, and their implementing regulations, which imposes certain requirements relating to the privacy, security and transmission of individually identifiable health information on entities and individuals subject to the law including certain healthcare providers, health plans, and healthcare clearinghouses, known as covered entities, as well as individuals and entities that perform services for them which involve the use, or disclosure of, individually identifiable health information, known as business associates;

- Requirements to report annually to CMS certain financial arrangements with physicians and teaching hospitals, as defined in the ACA and its implementing regulations, including reporting any "transfer of value" made or distributed to teaching hospitals, prescribers, and other healthcare providers and reporting any ownership and investment interests held by physicians and their immediate family members and applicable group purchasing organizations during the preceding calendar year; and
- State and foreign law equivalents of each of the above federal laws, such as anti-kickback and false claims laws which may apply to items or services reimbursed by any third-party payor, including commercial insurers; state laws that require pharmaceutical companies to comply with the industry's voluntary compliance guidelines and the applicable compliance guidance promulgated by the federal government that otherwise restricts certain payments that may be made to healthcare providers and entities; state laws that require drug manufacturers to report information related to payments and other transfer of value to physicians and other healthcare providers and entities; state laws that require the reporting of information related to drug pricing; state and local laws that require the registration of pharmaceutical sales representatives; 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.

Efforts to ensure that business arrangements comply with applicable healthcare laws involve substantial costs. It is possible that governmental and enforcement authorities will conclude that a pharmaceutical manufacturer's business practices do not comply with current or future statutes, regulations or case law interpreting applicable fraud and abuse or other healthcare laws and regulations. If any such actions are instituted against a pharmaceutical manufacturer, and it is not successful in defending itself or asserting its rights, it may be subject to the imposition of significant civil, criminal and administrative penalties, damages, disgorgement, monetary fines, imprisonment, possible exclusion from participation in Medicare, Medicaid and other federal healthcare programs, contractual damages, reputational harm, diminished profits and future earnings, and curtailment of operations, as well as additional reporting obligations and oversight if subject to a corporate integrity agreement or other agreement to resolve allegations of non-compliance with these laws. In addition, the approval and commercialization of drug products outside the United States may also subject a pharmaceutical manufacturer to foreign equivalents of the healthcare laws mentioned above, among other foreign laws.

Healthcare Reform Efforts

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

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

- created an annual, nondeductible fee on any entity that manufactures or imports certain branded prescription drug agents or biologic agents, which is apportioned among these entities according to their market share in certain government healthcare programs;
- increased the rebates a manufacturer must pay under the Medicaid Drug Rebate Program to 23.1% and 13% of the average manufacturer price for branded and generic drugs, respectively;
- created a new Medicare Part D coverage gap discount program, in which manufacturers must now agree to offer 70% point-of-sale discounts to negotiated prices of applicable brand drugs to eligible beneficiaries during their coverage gap period, as a condition for the manufacturer's outpatient drugs to be covered under Medicare Part D;

- extended manufacturers' Medicaid rebate liability to covered drugs dispensed to individuals who are enrolled in Medicaid managed care organizations, unless the drug is subject to discounts under the 340B drug discount program;
- created a new methodology by which rebates owed by manufacturers under the Medicaid Drug Rebate Program are calculated for drugs that are inhaled, infused, instilled, implanted or injected;
- expanded eligibility criteria for Medicaid programs by, among other things, allowing states to offer Medicaid coverage to additional individuals and by adding new mandatory eligibility categories for certain individuals with income at or below 133% of the federal poverty level, thereby potentially increasing manufacturers' Medicaid rebate liability;
- expanded the entities eligible for discounts under the Public Health Service pharmaceutical pricing program;
- created a new requirement to annually report drug samples that certain manufacturers and authorized distributors provide to physicians;
- expanded healthcare fraud and abuse laws, including the False Claims Act and the federal Anti-Kickback Statute, new government investigative powers, and enhanced penalties for noncompliance;
- created new requirements under the federal Physician Payments Sunshine Act for drug manufacturers to annually report information related to payments and other transfers of value made to physicians and teaching hospitals as well as ownership or investment interests held by physicians and their immediate family members;
- created a Patient-Centered Outcomes Research Institute to oversee, identify priorities in, and conduct comparative clinical effectiveness research, along with funding for such research;
- established a Center for Medicare & Medicaid Innovation at CMS to test innovative payment and service delivery models to lower Medicare and Medicaid spending, potentially including prescription drug spending; and
- created a licensure framework for follow on biologic products.

There remain legal and political challenges to certain aspects of the ACA. Since January 2017, President Trump has signed two executive orders and other directives designed to delay, circumvent or loosen certain requirements mandated by the ACA. Concurrently, Congress has considered legislation that would repeal or repeal and replace all or part of the ACA. While Congress has not passed repeal legislation, several bills affecting the implementation of certain taxes under the ACA have been signed into law. The Tax Cuts and Jobs Act of 2017, or Tax Act, includes a provision which repealed, effective January 1, 2019, the tax-based shared responsibility payment imposed by the ACA on certain individuals who fail to maintain qualifying health coverage for all or part of a year that is commonly referred to as the "individual mandate". Further, the 2020 federal spending package permanently eliminated, effective January 1, 2020, the PPACA-mandated "Cadillac" tax on high-cost employer-sponsored health coverage and medical device tax and, effective January 1, 2021, also eliminates the health insurer tax. The Bipartisan Budget Act of 2018, or the BBA, among other things, amended the ACA, effective January 1, 2019, to increase from 50 percent to 70 percent the point-of-sale discount that is owed by pharmaceutical manufacturers who participate in Medicare Part D and to close the coverage gap in most Medicare drug plans, commonly referred to as the "donut hole". In December 2018, CMS published a new final rule permitting further collections and payments to and from certain ACA qualified health plans and health insurance issuers under ACA risk adjustment program in response to the outcome of federal district court litigation regarding the method CMS uses to determine this risk adjustment. On December 14, 2018, a Texas U.S. District Court Judge ruled that ACA is unconstitutional in its entirety because the "individual mandate" was repealed by Congress as part of the Tax Act. Additionally, on December 18, 2019, the U.S. Court of Appeals for the 5th Circuit upheld the District Court ruling that the individual mandate was unconstitutional and remanded the case back to the District Court to determine whether the remaining provisions of the ACA are invalid as well.

It is unclear how this decision, future decisions, subsequent appeals, and other efforts to repeal and replace ACA will impact ACA.

In addition, other federal health reform measures have been proposed and adopted in the United States since the ACA was enacted. For example, as a result of the Budget Control Act of 2011, providers are subject to Medicare payment reductions of 2% per fiscal year, which went into effect on April 1, 2013 and, due to subsequent legislative amendments to the statute, including the BBA, will remain in effect through 2029 unless additional Congressional action is taken. Further, the American Taxpayer Relief Act of 2012 reduced Medicare payments to several providers and increased the statute of limitations period for the government to recover overpayments from providers from three to five years. The Medicare Access and CHIP Reauthorization Act of 2015 also introduced a quality payment program under which certain individual Medicare providers will be subject to certain incentives or penalties based on new program quality standards. In November 2019, CMS issued a final rule finalizing the changes to the Medicare Quality Payment Program.

Further, there has been heightened governmental scrutiny in the United States of pharmaceutical pricing practices in light of the rising cost of prescription drugs and biologics. Such scrutiny has resulted in several recent Congressional inquiries and proposed and enacted federal and state legislation designed to, among other things, bring more transparency to product pricing, review the relationship between pricing and manufacturer patient programs, and reform government program reimbursement methodologies for products. At the federal level, the Trump administration's budget proposal for fiscal year 2021 includes a $135 billion allowance to support legislative proposals seeking to reduce drug prices, increase competition, lower out-of-pocket drug costs for patients, and increase patient access to lower-cost generic and biosimilar drugs . For example, in May 2019, CMS issued a final rule to allow Medicare Advantage Plans the option of using step therapy for Part B drugs beginning on January 1, 2020. The final rule codified a CMS policy change that was effective January 1, 2019. While some of these and other proposed measures may require authorization through additional legislation to become effective, Congress and the Trump administration have each indicated that it will continue to seek new legislative and/or administrative measures to control drug costs. At the state level, legislatures have increasingly enacted legislation and implemented regulations designed to control pharmaceutical and biological product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain product access and marketing cost disclosure and transparency measures, and, in some cases, designed to encourage importation from other countries and bulk purchasing. In addition, regional healthcare authorities and individual hospitals are increasingly using bidding procedures to determine what pharmaceutical products and which suppliers will be included in their prescription drug and other healthcare programs.

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

The Foreign Corrupt Practices Act, or the FCPA, prohibits any U.S. individual or business from paying, offering, or authorizing payment or offering of anything of value, directly or indirectly, to any foreign official, political party or candidate for the purpose of influencing any act or decision of the foreign entity in order to assist the individual or business in obtaining or retaining business. The FCPA also obligates companies whose securities are listed in the United States to comply with accounting provisions requiring the company to maintain books and records that accurately and fairly reflect all transactions of the corporation, including international subsidiaries, and to devise and maintain an adequate system of internal accounting controls for international operations. Activities that violate the FCPA, even if they occur wholly outside the United States, can result in criminal and civil fines, imprisonment, disgorgement, oversight, and debarment from government contracts.

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

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

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

Competition

The development and commercialization for new products to treat cancer, including the indications we are pursuing, is highly competitive and considerable competition exists from major pharmaceutical, biotechnology and specialty cancer companies. 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.

Our genetically engineering T-cell programs face significant competition in the CAR and TCR technology space from multiple companies and their collaborators. Two such companies, Novartis International AG (Kymriah®) and Kite Pharma Inc./Gilead Sciences, Inc. (Yescarta®), have now commercialized autologous CAR+ T cells against CD19. Additional companies developing autologous CAR+ T targets include Bristol-Myers Squibb Company, Precigen, Inc., bluebird bio, Inc., in collaboration with Celgene Corporation, Nanjing Legend Biotech and Janssen Biotech, Inc., a subsidiary of Johnson & Johnson, Bellicum Pharmaceuticals, Inc., Autolus Therapeutics plc, Mustang Bio, Inc., Crispr Therapeutics AG, Precision Biosciences Inc., Protheragen Inc.and Marker Therapeutics, Inc. Several companies are pursuing the development of allogeneic CAR+ T therapies, including Allogene Therapeutics, Inc. (in collaboration with Pfizer Inc.), Atara Biotherapeutics, Inc. and Cellectis SA (in collaboration with Servier) which may compete with our product candidates.

Our TCR program faces competition from several companies, including from Adaptimmune Therapeutics plc in collaboration with GlaxoSmithKline plc, ArsenalBio, Lyell, bluebird bio, Kite Pharma Inc./Gilead Sciences, Inc., Achilles Therapeutics Limited, Iovance Biotherapeutics, Inc., Immatics Biotechnologies GmbH, Tmunity Therapeutics Inc, Medigene AG, Tactiva Therapeutics, LLC, Takara Bio, Inc., TC Biopharm Ltd., TCR2 Therapeutics Inc., Zelluna Immunotherapy AS, PACT Pharma, Inc. and others. Several companies, including Advaxis Inc./Amgen Inc., BioNTech AG and Gritstone Oncology, Inc., are pursuing vaccine platforms to target neoantigens for solid tumors. Other companies are developing non-viral gene therapies, including Poseida Therapeutics, Inc. and several companies developing CRISPR technology. We also face competition from companies developing therapies using cells other than T cells such as Takeda Pharmaceutical Company, Incysus Therapeutics, Inc., and TC BioPharm Limited. We also face competition from companies developing T cells with cytokines such as Torque Therapeutics and Obsidian Therapeutics, Inc.. We also face competition from non-cell-based treatments offered by other companies such as Amgen Inc., AstraZeneca plc, Bristol-Myers Squibb Company, Incyte Corporation, Merck & Co., Inc., and Roche Holding AG.

We are initially developing our Controlled IL-12 platform for the treatment of rGBM. Companies that sell marketed drugs for rGBM are Genentech Inc. and Roche Holding AG with Avastin (bevacizumab), a vascular endothelial growth factor directed antibody indicated for the treatment of adults with rGBM. Arbor Pharmaceuticals Inc. markets GLIADEL Wafer, which is indicated in patients with newly diagnosed high-grade malignant glioma as an adjunct to surgery and radiation and is also indicated in patients with recurrent glioblastoma multiforme as an adjunct to surgery. Additionally, Novocure has developed Optune (tumor treating fields) for newly diagnosed and recurrent glioblastoma. Several companies have product candidates in phase 3 development for the treatment of glioblastoma, including, but not limited to, Tocagen Inc., Vascular Biogenics Ltd., and DelMar Pharmaceuticals, Inc. Several companies and institutions have product candidates currently in

phase 2 clinical trials, including, but not limited to, Abbvie Inc., DNAtrix Therapeutics, Istari Oncology, Karyopharm and MedImmune LLC/AstraZeneca plc, and other companies are actively developing additional products to treat brain cancer including Mustang Bio Inc. and Northwest Biotherapeutics, Inc.

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

Employees

As of February 14, 2020, we had 73 full-time employees, 51 of whom were engaged in research and development activities and 22 of whom were engaged in business development, finance, information systems, facilities, human resources or administrative support. None of our employees are subject to a collective bargaining agreement.

Corporate Information

We originally incorporated in Colorado in September 1998 (under the name Net Escapes, Inc.) and later changed our name to "EasyWeb, Inc." in February 1999. We re-incorporated in Delaware on May 16, 2005 under the same name. On September 13, 2005, we completed a "reverse" acquisition of privately held Ziopharm, Inc., a Delaware corporation. To 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 Securities and Exchange Commission, or the SEC, and the historical financial statements of Ziopharm, Inc. became our historical financial statements.

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

Available Information

Our website address is www.ziopharm.com. Our website and information included in or linked to our website are not part of this Annual Report on Form 10-K. We file reports with the SEC, which we make available on our website free of charge. These reports include annual reports on Form 10-K, quarterly reports on Form 10-Q, current reports on Form 8-K and amendments to such reports, each of which is provided on our website as soon as reasonably practicable after we electronically file such materials with or furnish them to the SEC. In addition, the SEC maintains a website (www.sec.gov) that contains reports, proxy and information statements, and other information regarding issuers, like us, that file electronically with the SEC, including us.

Item 1A. Risk Factors

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

RISKS RELATED TO OUR BUSINESS

We will require substantial additional financial resources to continue ongoing development of our product candidates and pursue our business objectives; if we are unable to obtain these additional resources when needed, we may be forced to delay or discontinue our planned operations, including 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, 2019, we had a net loss of $117.8 million, and, as of December 31, 2019 we have incurred approximately $684.1 million of accumulated deficit since our inception in 2003. We expect to continue to incur significant operating expenditures and net losses. Further development of our product candidates 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; and
- hire additional personnel.

As of December 31, 2019, we have approximately $79.7 million of cash and cash equivalents and in January and February 2020 we raised an aggregate of approximately $98.0 million of net proceeds in a public offering and an at-the-market offering. Given our current development plans, we anticipate our cash resources will be sufficient to fund our operations into mid-2022 and we have no committed sources of additional capital at this time. The forecast of cash resources is forward-looking information that involves risks and uncertainties, and the actual amount of our expenses could vary materially and adversely as a result of a number of factors. We have based our estimates on assumptions that may prove to be wrong, and our expenses could prove to be significantly higher than we currently anticipate. Management does not know whether additional financing will be on terms favorable or acceptable to us when needed, if at all.

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, slower than expected progress of our research and development efforts, changes in governmental regulation, 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 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.

Until such time, if ever, as we can generate substantial revenue, we expect to finance our cash needs through a combination of equity offerings, debt financings and license and collaboration agreements. We do not have any committed external source of funds. 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.

To the extent that we raise additional capital by issuing equity securities, our existing stockholders' ownership will be diluted, and the terms of these securities may include liquidation or other preferences that adversely affect the rights of our common stockholders. Debt financing and preferred equity financing, if available, may involve agreements that include covenants limiting or restricting our ability to take specific actions, such as incurring additional debt, making capital expenditures or declaring dividends. Any debt financing that we enter into may involve covenants that restrict our operations. These restrictive covenants may include limitations on additional borrowing and specific restrictions on the use of our assets as well as prohibitions on our ability to create liens, pay dividends, redeem our stock or make investments. If we are unable to raise additional funds through equity or debt financings when needed, we may be required to delay, limit, reduce or terminate our product development or future commercialization efforts or grant rights to develop and market product candidates that we would otherwise prefer to develop and market ourselves. If we raise additional funds through collaborations, strategic alliances or marketing, distribution or licensing arrangements with third parties, we may have to relinquish valuable rights to our technologies, future revenue streams, research programs or product candidates or grant licenses on terms that may not be favorable to us.

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

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

- obtaining regulatory approval from the FDA and other regulatory authorities that have very limited experience with the commercial development of genetically modified and/or unmodified T-cell therapies for cancer;
- identifying and manufacturing appropriate TCRs from patient and from third parties that can be administered to a patient;
- developing and deploying consistent and reliable processes for engineering a patient's and/or donor's T-cells *ex vivo* and infusing the 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;
- addressing any competing technological and market developments;
- developing processes for the safe administration of these potential products, including long-term follow-up for all patients who receive the potential products;

- sourcing additional clinical and, if approved, commercial supplies for the materials used to manufacture and process the potential products;
- developing a manufacturing process and distribution network with a cost of goods that allows for an attractive return on investment;
- establishing sales and marketing capabilities after obtaining any regulatory approval to gain market acceptance;
- developing therapies for types of cancers beyond those addressed by the current potential products;
- maintaining and defending the intellectual property rights relating to any products we develop;
- and not infringing the intellectual property rights, in particular, the patent rights, of third parties, including competitors, such as those developing T-cell therapies.

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

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

The immuno-oncology effector platform in which we have acquired rights pursuant to our License Agreement with PGEN represents early-stage technology in the field of human oncology biotherapeutics, with Ad-RTS-IL-12 plus veledimex having completed trials, in melanoma, breast cancer and rGBM. Similarly, our genetically modified and/or non-modified T-cell candidates are supported by limited clinical data, all of which has been generated through trials conducted by MD Anderson and the NCI, not by us. We plan to assume control of the overall clinical and regulatory development of our T-cell product candidates, and any failure to obtain, or delays in obtaining, sponsorship of new INDs, or in filing INDs sponsored by us for these or any other product candidates we determine to advance could negatively affect the timing of our potential future clinical trials. Such an impact on timing could increase research and development costs and could delay or prevent obtaining regulatory approval for our product candidates, either of which could have a material adverse effect on our business.

Further, we did not control the design or conduct of the previous trials. It is possible that the FDA will not accept these previous trials as providing adequate support for future clinical trials, whether controlled by us or third parties, for any of one or more reasons, including the safety, purity, and potency of the product candidate, the degree of product characterization, elements of the design or execution of the previous trials or safety concerns, or other trial results. We may also be subject to liabilities arising from any treatment-related injuries or adverse effects in patients enrolled in these previous trials. As a result, we may be subject to unforeseen third-party claims and delays in our potential future clinical trials. We may also be required to repeat in whole or in part clinical trials previously conducted by MD Anderson or other entities, which will be expensive and delay the submission and licensure or other regulatory approvals with respect to any of our product candidates.

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

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

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

We face substantial competition from other biopharmaceutical companies, which may result in others discovering, developing or commercializing products before, or more successfully than, we do.

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. 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.

Our genetically engineering T-cell programs face significant competition in the CAR and TCR technology space from multiple companies and their collaborators. Two such companies, Novartis International AG (Kymriah®) and Kite Pharma Inc./Gilead Sciences, Inc. (Yescarta®), have now commercialized autologous CAR+ T cells against CD19. Additional companies developing autologous CAR+ T targets include Bristol-Myers Squibb Company, Precigen, Inc., bluebird bio, Inc., in collaboration with Celgene Corporation, Nanjing Legend Biotech and Janssen Biotech, Inc., a subsidiary of Johnson & Johnson, Bellicum Pharmaceuticals, Inc., Autolus Therapeutics plc, Mustang Bio, Inc., Crispr Therapeutics AG, Precision Biosciences Inc., Protheragen Inc.and Marker Therapeutics, Inc. Several companies are pursuing the development of allogeneic CAR+ T therapies, including Allogene Therapeutics, Inc. (in collaboration with Pfizer Inc.), Atara Biotherapeutics, Inc. and Cellectis SA (in collaboration with Servier) which may compete with our product candidates.

Our TCR program faces competition from several companies, including from Adaptimmune Therapeutics plc in collaboration with GlaxoSmithKline plc, ArsenalBio, Lyell, bluebird bio, Kite Pharma Inc./Gilead Sciences, Inc., Achilles Therapeutics Limited, Iovance Biotherapeutics, Inc., Immatics Biotechnologies GmbH, Tmunity Therapeutics Inc, Medigene AG, Tactiva Therapeutics, LLC, Takara Bio, Inc., TC Biopharm Ltd., TCR2 Therapeutics Inc., Zelluna Immunotherapy AS, PACT Pharma, Inc. and others. Several companies, including Advaxis Inc./Amgen Inc., BioNTech AG and Gritstone Oncology, Inc., are pursuing vaccine platforms to target neoantigens for solid tumors. Other companies are developing non-viral gene therapies, including Poseida Therapeutics, Inc. and several companies developing CRISPR technology. We also face competition from companies developing therapies using cells other than T cells such as Takeda Pharmaceutical Company, Incysus Therapeutics, Inc., and TC BioPharm Limited. We also face competition from companies developing T cells with cytokines such as Torque Therapeutics and Obsidian Therapeutics, Inc.. We also face competition from non-cell-based treatments offered by other companies such as Amgen Inc., AstraZeneca plc, Bristol-Myers Squibb Company, Incyte Corporation, Merck & Co., Inc., and Roche Holding AG.

We are initially developing our Controlled IL-12 platform for the treatment of rGBM. Companies that sell marketed drugs for rGBM are Genentech Inc. and Roche Holding AG with Avastin (bevacizumab), a vascular endothelial growth factor directed antibody indicated for the treatment of adults with rGBM. Arbor Pharmaceuticals Inc. markets GLIADEL Wafer, which is indicated in patients with newly diagnosed high-grade malignant glioma as an adjunct to surgery and radiation and is also indicated in patients with recurrent glioblastoma multiforme as an adjunct to surgery. Additionally, Novocure has developed Optune (tumor treating fields) for newly diagnosed and recurrent glioblastoma. Several companies have product candidates in phase 3 development for the treatment of glioblastoma, including, but not limited to, Tocagen Inc., Vascular Biogenics Ltd., and DelMar Pharmaceuticals, Inc. Several companies and institutions have product candidates currently in phase 2 clinical trials, including, but not limited to, Abbvie Inc., DNAtrix Therapeutics, Istari Oncology, Karyopharm and MedImmune LLC/AstraZeneca plc, and other companies are actively developing additional

products to treat brain cancer including Mustang Bio Inc. and Northwest Biotherapeutics, Inc. Other competitors with product candidates currently in Phase 2 clinical trials include AbbVie Inc.'s Depatus-M (ABT-414) and DNA-2401, a conditionally replicative adenovirus being evaluated in combination with pembrolizumab (KEYTRUDA®) for rGBM by DNATrix Inc. and Merck & Co., Inc. Duke University is enrolling a randomized Phase 2 study of oncolytic polio/rhinovirus recombinant (PVSRIPO) alone or in combination with lomustine in recurrent WHO Grade IV malignant glioma patients. Also, MedImmune, LLC/AstraZeneca plc's durvalumab was evaluated in a Phase 2 trial in patients with rGBM.

Even if we obtain regulatory approval of potential products, we may not be the first to market and that may affect the price or demand for our potential products. Existing or future competing products may provide greater therapeutic convenience or clinical or other benefits for a specific indication than our products or may offer comparable performance at a lower cost. Additionally, the availability and price of our competitors' products could limit the demand and the price we are able to charge for our potential products. We may not be able to implement our business plan if the acceptance of our potential products is inhibited by price competition or the reluctance of physicians to switch from existing methods of treatment to our potential products, or if physicians switch to other new drug or biologic products or choose to reserve our potential products. Additionally, a competitor could obtain orphan product exclusivity from the FDA with respect to such competitor's product. If such competitor product is determined to be the same product as one of our potential products, that may prevent us from obtaining approval from the FDA for such potential products for the same indication for seven years, except in limited circumstances. If our products fail to capture and maintain market share, we may not achieve sufficient product revenues and our business will suffer.

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

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

Our commercial opportunity could be reduced or eliminated if our competitors develop and commercialize products that are more effective, have fewer or less severe side effects, are more convenient or are less expensive than any products that we may develop. Our competitors also may obtain FDA or other regulatory approval for their products more rapidly than we may obtain approval for ours, which could result in our competitors establishing a strong market position before we are able to enter the market. In addition, our ability to compete may be affected in many cases by insurers or other third-party payors seeking to encourage the use of generic products.

Any termination of our licenses with PGEN, MD Anderson or the National Cancer Institute or our research and development agreements with MD Anderson could result in the loss of significant rights and could harm our ability to develop and commercialize our product candidates.

We are dependent on patents, know-how, and proprietary technology that are licensed from others, particularly MD Anderson, Precigen and the National Cancer Institute, or the NCI, as well as the contributions by MD Anderson under our research and development agreements. Any termination of these licenses or research and development agreements 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 PGEN, MD Anderson, the NCI and our other licensors, infringe 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 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, the License Agreement with PGEN and our patent license agreement with the NCI; and
- whether or not our partners are complying with all of their obligations to support our programs under licenses and research and development agreements; 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.

In addition, under our License Agreement, PGEN is obligated to provide certain transition services and transfer certain know-how to us. For example, PGEN was previously responsible for manufacturing the products used in our clinical programs and is now responsible for transferring the related know-how so that we can begin manufacturing products used in our clinical trials. There is no guarantee that PGEN will perform these activities to our satisfaction, if at all. If PGEN fails to perform these activities our ability to pursue our clinical programs may be adversely affected.

If disputes over intellectual property that we have licensed prevent or impair our ability to maintain our current licensing arrangements, particularly with MD Anderson, PGEN and the NCI, on acceptable terms, we may be unable to successfully develop and commercialize the affected potential products. We are generally also subject to all of the same risks with respect to protection of intellectual property that we license as we are for intellectual property that we own. If we or our licensors fail to adequately protect this intellectual property, our ability to commercialize potential products under our applicable licenses could suffer. There is a substantial amount of litigation involving patents and other intellectual property rights in the biotechnology and pharmaceutical industries, as well as administrative proceedings for challenging patents, including interference, derivation, and reexamination proceedings before the United States Patent and Trademark Office, or USPTO, or oppositions and other comparable proceedings in foreign jurisdictions. Recently, due to changes in U.S. law referred to as patent reform, new procedures including inter partes review and post-grant review have been implemented, which adds uncertainty to the possibility of challenge to our or our licensors' patents in the future.

We are partly reliant on the National Cancer Institute for research and development and early clinical testing of certain of our product candidates.

A portion of our research and development is being conducted by the NCI under the CRADA entered into in January 2017 and amended in February 2019. Under the CRADA, the NCI, with Dr. Steven A. Rosenberg as the principal investigator, is responsible for conducting a clinical trial using the *Sleeping Beauty* system to express TCRs for the treatment of solid tumors. We have limited control over the nature or timing of the NCI's clinical trial and limited visibility into their day-to-day activities, including with respect to how they are providing and administering T cell therapy. For example, the research we are funding constitutes only a small portion of the NCI's overall research. Additionally, other research being conducted by Dr. Rosenberg may at times receive higher priority than research on our program.

The CRADA terminates on January 9, 2022 unless it is extended in writing by the parties, and either party may terminate the CRADA by providing at least 60 days' prior written notice to the other party. If the NCI unilaterally

terminates the CRADA or the CRADA lapses without any extension, part or all of the research and development of the *Sleeping Beauty* system conducted at the NCI would be suspended, and the research and development of our TCR program would be impacted.

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

Human clinical trials are very expensive and difficult to design, initiate and implement, in part because they are subject to rigorous regulatory requirements. The clinical trial start-up and process itself is also time-consuming and results are inherently uncertain. We estimate that clinical trials of our product candidates will take at least several years to complete. Furthermore, failure can occur at any stage of the trials, and we could encounter problems that cause us to delay the start of, abandon or repeat clinical trials. The commencement and completion of clinical trials may be delayed by several factors, including:

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

Success in preclinical testing and early clinical trials does not ensure that later clinical trials will be successful. In addition, we or the FDA may suspend our clinical trials at any time if it appears that we are exposing participants to unacceptable health risks or if the FDA finds deficiencies in our IND submission or in the conduct of these trials. In June 2018, we announced that the FDA placed our Phase 1 trial on clinical hold to evaluate CD19-specific CAR-T therapies manufactured using our rapid personalized manufacturing technology with patient-derived (autologous) T cells in order to treat patients with relapsed or refractory CD19+ leukemias and lymphomas. The FDA requested additional information in support of the IND submission for the trial. Our business may be materially harmed if we or our partners are unable to adequately address the FDA's requests for this trial.

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

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

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

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

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

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

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

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

Under the MD Anderson License, we, together with PGEN, received an exclusive, worldwide license to certain technologies owned and licensed by MD Anderson including technologies relating to novel CAR$^+$ T cell and TCR cell therapies arising from the laboratory of Laurence Cooper, M.D., Ph.D., who was then at MD Anderson, as well as either co-exclusive or non-exclusive licenses under certain related technologies. When combined with PGEN's technology suite and Ziopharm's clinically tested RTS® interleukin 12 modules, the resulting proprietary methods and technologies may help realize the promise of genetically modified CAR$^+$ T cells and TCR therapies by controlling cell expansion and activation in the body, minimizing off-target and unwanted on-target effects and toxicity while maximizing therapeutic efficacy. The term of the MD Anderson License expires on the last to occur of (a) the expiration of all patents licensed thereunder, or (b) the twentieth anniversary of the date of the MD Anderson License; provided, however, that following the expiration of the term, we and PGEN 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 PGEN 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 PGEN are not meeting the diligence requirements in such funding agreement or contract, as applicable. MD Anderson may also terminate the agreement with written notice upon material breach by us or PGEN, 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 PGEN and may be terminated by the mutual written agreement of us, PGEN and MD Anderson.

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

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

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

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

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

We may not be successful in establishing development and commercialization collaborations, which failure could adversely affect, and potentially prohibit, our ability to develop our product candidates.

Developing biopharmaceutical products and complementary technologies, conducting clinical trials, obtaining marketing approval, establishing manufacturing capabilities and marketing approved products is expensive and, therefore, we anticipate exploring collaborations with third parties that have alternative technologies, more resources and more experience than we do. In situations where we enter into a development and commercial collaboration arrangement for a product candidate or complementary technology, we may also seek to establish additional collaborations for development and commercialization in territories outside of those addressed by the first collaboration arrangement for such product candidate or technology. There are a limited number of potential partners, and we expect to face competition in seeking appropriate partners. If we are unable to enter into any development and commercial collaborations and/or sales and marketing arrangements on reasonable and acceptable terms, if at all, we may be unable to successfully develop and seek regulatory approval for our product candidates and/or effectively market and sell future approved products, if any, in some or all of the territories outside of the United States where it may otherwise be valuable to do so.

Because we currently do not have 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 or complementary technology 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 product candidates are subject to the risks of failure inherent in biopharmaceutical 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 complementary technologies to acquire or license. Such complementary technologies 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 research and development 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. Further, to advance our TCR program, we anticipate significantly expanding our internal research capabilities, including hiring additional employees focusing on pre-clinical research. This 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 may not be able to attract or retain qualified management and commercial, scientific and clinical personnel due to the intense competition for qualified personnel among biotechnology, pharmaceutical and other businesses. If we are not able to attract and retain necessary personnel to accomplish our business objectives, we may experience constraints that will significantly impede the achievement of our development objectives, our ability to raise additional capital and our ability to implement our business strategy.

We are highly dependent on Dr. Laurence J.N. Cooper, our Chief Executive Officer; Dr. David Mauney, our President; and our principal scientific, regulatory, and medical advisors. Each of Dr. Cooper or Dr. Mauney may terminate their employment with us at any time, subject, however, to certain non-compete and non-solicitation covenants. The loss of the technical knowledge and management and industry expertise of each of Dr. Cooper or Dr. Mauney, or any of our other key personnel, could result in delays in product development, loss of key personnel or partnerships, 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. In particular, we expect to significantly expand our internal cell therapy capabilities in our Houston, Texas facilities by hiring additional research and development personnel. We compete for qualified individuals with numerous biopharmaceutical companies, universities, and other research institutions. Competition for such individuals is

intense and we cannot be certain that our search for such personnel will be successful. Attracting and retaining qualified personnel will be critical to our success. If we are unable to hire additional qualified personnel, our ability to grow our business may be harmed.

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

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

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

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

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

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

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

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

We may not be able to obtain the approvals necessary to commercialize our product candidates, or any product candidate that we may acquire or develop in the future for commercial sale. We will need FDA approval to

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

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

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

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

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

Our product candidates are in various stages of development and require extensive clinical testing. Notwithstanding our current clinical trial plans for each of our existing product candidates, we may not be able to commence additional trials or see results from these trials within our anticipated timelines. As they enter later stages of development, our product candidates generally will become subject to more stringent regulatory requirements, including the FDA's requirements for chemistry, manufacturing and controls for product candidates entering phase 3 clinical trials. There is no guarantee the FDA will allow us to commence phase 3 clinical trials for product candidates studied in early clinical trials. For example, we are currently evaluating Ad-RTS-hIL-12 plus veledimex in combination with PD-1 antibody Libtayo® (cemiplimab-rwlc) in a Phase 2 clinical trial for the treatment of recurrent or progressive glioblastoma multiforme in adults. If we elect to advance Ad-RTS-hIL-12 plus veledimex into a Phase 3 clinical trial, we will need to meet all of the FDA's requirements for this clinical trial. We previously announced that we were pausing a pivotal randomized control trial for Ad-RTS-hIL-12 plus veledimex for the treatment of rGBM and that were resolving previously disclosed technical requirements related to chemistry, manufacturing and controls prior to commencing a phase 3 clinical trial. These efforts remain ongoing and there is no guarantee we will be able to meet the FDA's requirements for a Phase 3 clinical trial or that the development of Ad-RTS-hIL-12 plus veledimex will not be delayed in order to address these requirements.

If the FDA does not allow our product candidates to enter later stage clinical trials, or requires changes to the formulation or manufacture of our product candidates before commencing phase 3 clinical trials, our ability to further develop, or seek approval for, such product candidates may be materially impacted. As such, we cannot

predict with any certainty if or when we might submit a BLA for regulatory approval of our product candidates or whether such a BLA will be accepted. Because we do not anticipate generating revenues unless and until we submit one or more BLAs and thereafter obtain requisite FDA approvals, the timing of our BLA submissions and FDA determinations regarding approval thereof, will directly affect if and when we are able to generate revenues.

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

As with many pharmaceutical and biological products, treatment with our product candidates may produce undesirable side effects or adverse reactions or events, including potential adverse side effects related to cytokine release. If our product candidates or similar products or product candidates under development by third parties demonstrate unacceptable AEs, we may be required to halt or delay further clinical development of our product candidates. The FDA or other foreign regulatory authorities could order us to cease further development of or deny approval of our product candidates for any or all targeted indications. For instance, Ad-RTS-hIL-12 plus veledimex may result in local reactions during the time of injection, including severe swelling and bleeding. If a serious adverse event was to occur in any of our clinical trials, including in our trial of Ad-RTS-hIL-12 plus veledimex for the treatment of DIPG, the FDA may place a hold on the clinical trial for this indication and, potentially, our clinical trials of Ad-RTS-hIL-12 plus veledimex in other indications.

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

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

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

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

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

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

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

In addition, some of the reagents and products used by us, including in our clinical trials, may be stored at a single vendor. The loss of materials located at a single vendor, or the failure of such a vendor to manufacture clinical product in accordance with our specifications, would impact our ability to conduct ongoing or planned clinical trials and continue the development of our products. Further, manufacturing replacement material may be expensive and require a significant amount of time, which may further impact our clinical programs.

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

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

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

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

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

In addition, the clinical study requirements of the FDA, the EMA and other regulatory agencies and the criteria these regulators use to determine the safety and efficacy of a product candidate vary substantially according to the type, complexity, novelty and intended use and market of the potential products. The regulatory approval process for novel product candidates such as ours can be more expensive and take longer than for other, better known or extensively studied pharmaceutical or other product candidates. These factors make it difficult to determine how long it will take or how much it will cost to obtain regulatory approvals for our product candidates in either the United States or Europe. Approvals by the EMA may not be indicative of what the FDA may require for approval.

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 Tissue and Advanced 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. Also, before a clinical trial can begin at an institution, that institution's institutional review board, or IRB, and its Institutional Biosafety Committee will have to review the proposed clinical trial to assess the safety of the trial. In addition, adverse developments in clinical trials of gene therapy products conducted by others may cause the FDA or other regulatory bodies to change the requirements for approval of any of our product candidates.

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

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

We materially rely upon independent investigators and collaborators, such as universities and medical institutions, to conduct our preclinical and clinical trials under agreements with us. These collaborators are not our employees and we cannot control the amount or timing of resources that they devote to our programs. These investigators may not assign as great a priority to our programs or pursue them as diligently as we would if we were undertaking such programs ourselves. If outside collaborators fail to devote sufficient time and resources to our product 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 have limited experience in biopharmaceutical manufacturing. We currently lack the internal resources and expertise to formulate or manufacture our own product candidates and, therefore, contract the manufacture of our product candidates with third parties. We intend to contract with one or more manufacturers to manufacture, supply, store, and distribute supplies for our clinical trials. If a product candidate we develop or acquire in the future receives FDA approval, we may rely on one or more third-party contractors 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.
- Biopharmaceutical manufacturers are subject to ongoing periodic unannounced inspection by the FDA, the Drug Enforcement Administration and corresponding state and foreign agencies to ensure strict compliance with current good manufacturing practices, or cGMP, and other government regulations and corresponding foreign standards. We do not have control over third-party manufacturers' compliance with these regulations and standards.
- If any third-party manufacturer makes improvements in the manufacturing process for our products, we may not own, or may have to share, the intellectual property rights to the innovation.
- Our third-party manufacturers may not be able to comply with cGMP regulations or similar regulatory requirements outside the United States. Our failure, or the failure of our third-party manufacturers, to comply with applicable regulations could result in sanctions being imposed on us, including clinical holds, fines, injunctions, civil penalties, delays, suspension or withdrawal of approvals, license revocation, seizures or recalls of products, operating restrictions and criminal prosecutions, any of which could significantly and adversely affect supplies of our products.

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

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

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

for a restricted distribution system. If any of our product candidates receives marketing approval, the accompanying label may limit the approved uses, which could limit sales of the product.

The FDA may also impose requirements for costly post-marketing studies or clinical trials and surveillance to monitor the safety or efficacy of our approved products. The FDA closely regulates the post-approval marketing and promotion of products to ensure that they are marketed only for the approved indications and in accordance with the provisions of the approved labeling. However, companies may share truthful and not misleading information that is otherwise consistent with the labeling. The FDA imposes stringent restrictions on manufacturers' communications regarding off-label use and if we market our products outside of their approved indications, we may be subject to enforcement action for off-label marketing. Violations of the Federal Food, Drug and Cosmetic Act relating to the promotion of prescription drugs may lead to investigations alleging violations of federal and state health care fraud and abuse laws, as well as state consumer protection laws.

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

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

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

RISKS RELATED TO OUR ABILITY TO COMMERCIALIZE OUR PRODUCT CANDIDATES

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

We currently have no marketing, sales, or distribution capabilities. If and when we become reasonably certain that we will be able to commercialize our current or future product candidates, we anticipate allocating resources to the marketing, sales and distribution of our proposed products in North America and in certain other countries;

however, we cannot assure that we will be able to market, sell, and distribute our products successfully. Our future success also may depend, in part, on our ability to enter into and maintain collaborative relationships for such capabilities and to encourage the collaborator's strategic interest in the products under development, and such collaborator's ability to successfully market and sell any such products. Although we intend to pursue certain collaborative arrangements regarding the sale and marketing of certain of our product candidates, there are no assurances that we will be able to establish or maintain collaborative arrangements or, if we are able to do so, whether we would be able to conduct our own sales efforts. There can also be no assurance that we will be able to establish or maintain relationships with third-party collaborators or develop in-house sales and distribution capabilities. To the extent that we depend on third parties for marketing and distribution, any revenues we receive will depend upon the efforts of such third parties, and there can be no assurance that such efforts will be successful. In addition, there can also be no assurance that we will be able to market and sell our product candidates in the United States or overseas.

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

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

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

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

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

Our commercial opportunity could be reduced or eliminated if our competitors develop and commercialize products that are more effective, have fewer or less severe side effects, are more convenient or are less expensive than any products that we may develop. Our competitors also may obtain FDA or other regulatory approval for their products more rapidly than we may obtain approval for ours, which could result in our competitors establishing a strong market position before we are able to enter the market. In addition, our ability to compete may be affected in many cases by insurers or other third-party payors seeking to encourage the use of generic products.

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

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

- Perceptions by members of the healthcare community, including physicians, about the safety and effectiveness of our products;
- 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 third-party 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 product to find market acceptance would harm our business and could require us to seek additional financing in order to fund the development of future product candidates.

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

Our ability to commercialize our product candidates, if approved, alone or with collaborators, will depend in part on the extent to which coverage and reimbursement will be available from third-party payors, including government and health administration authorities, private health maintenance organizations and health insurers and other 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. Sufficient coverage and adequate reimbursement from third-party payors are 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. It is difficult to predict the coverage and reimbursement decisions that will be made by third-party payors for novel gene and cell therapy products such as ours. Even if we obtain coverage for our product candidates, the resulting reimbursement payment rates might not be adequate or may require co-payments that patients find unacceptably high. Patients are unlikely to use our product candidates unless coverage is provided and reimbursement is adequate to cover a significant portion of the cost of our product candidates.

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

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

patients may decline to purchase them. This in turn could affect our ability to successfully commercialize our products and impact our profitability, results of operations, financial condition, and future success.

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

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

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

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

Our projections of both the number of people who have the cancers we are targeting, as well as the subset of people with these cancers in a position to receive therapy and who have the potential to benefit from treatment with our product candidates, are based on our beliefs and estimates. These estimates have been derived from a variety of sources, including scientific literature, surveys of clinics, patient foundations, or market research and may prove to be incorrect. Further, new studies may change the estimated incidence or prevalence of these cancers. The number of patients may turn out to be lower than expected. Additionally, the potentially addressable patient population for our product candidates may be limited or may not be amenable to treatment with our product candidates.

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

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

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

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

- Created 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;
- Increased the statutory minimum rebates a manufacturer must pay under the Medicaid Drug Rebate Program to 23.1% and 13% of the average manufacturer price for most branded and generic drugs, respectively;
- Created a new Medicare Part D coverage gap discount program, in which manufacturers must now agree to offer 70% 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;
- Extended manufacturers' Medicaid rebate liability to covered drugs dispensed to individuals who are enrolled in Medicaid managed care organizations;
- Created new methodologies by which rebates owed by manufacturers under the Medicaid Drug Rebate Program are calculated for drugs that are inhaled, infused, instilled, implanted or injected, and for drugs that are line extensions;
- Expanded eligibility criteria for Medicaid programs by, among other things, allowing states to offer Medicaid coverage to additional individuals with income at or below 133% of the Federal Poverty Level, thereby potentially increasing both the volume of sales and manufacturers' Medicaid rebate liability;
- Expanded the entities eligible for discounts under the Public Health Service pharmaceutical pricing program;
- Created a new requirement to annually report drug samples that certain manufacturers and authorized distributors provide to physicians;
- Expanded healthcare fraud and abuse laws, including the False Claims Act and the federal Anti-Kickback Statute, new government investigative powers, and enhanced penalties for noncompliance;
- Created a licensure framework for follow-on biologic products;
- Created new requirements under the federal Physician Payments Sunshine Act for certain drug manufacturers to annually report information related to payments and other transfers of value made to physicians, as defined by such law, and teaching hospitals as well as ownership or investment interests held by physicians and their immediate family members;
- Created a Patient-Centered Outcomes Research Institute to oversee, identify priorities in, and conduct comparative clinical effectiveness research, along with funding for such research; and
- Established a Center for Medicare & Medicaid Innovation at the Centers for Medicare & Medicaid Services, or CMS, to test innovative payment and service delivery models to lower Medicare and Medicaid spending, potentially including prescription drug spending.

There remain legal and political challenges to certain aspects of the ACA. Since January 2017, President Trump has signed several executive orders and other directives designed to delay, circumvent, or loosen certain requirements mandated by the ACA. Concurrently, Congress has considered legislation that would repeal or repeal and replace all or part of the ACA. While Congress has not passed comprehensive repeal legislation, several bills affecting the implementation of certain taxes under the ACA have been signed into law. In

December 2017, Congress repealed the tax penalty, effective January 1, 2019, for an individual's failure to maintain ACA-mandated health insurance as part of the Tax Cuts and Jobs Act of 2017, or Tax Act. Further, the 2020 federal spending package permanently eliminated effective January 1, 2020, the PPALA-mandated "Cadillac" tax on high-cost employer-sponsored health coverage and medical device tax and effective January 1, 2021 also eliminates the health insurance tax. The Bipartisan Budget Act of 2018, or the BBA, among other things, amended the ACA, effective January 1, 2019, to increase from 50 percent to 70 percent the point-of-sale discount that is owed by pharmaceutical manufacturers who participate in Medicare Part D and close the coverage gap in most Medicare drug plans, commonly referred to as the "donut hole". In December 2018, CMS published a new final rule permitting further collections and payments to and from certain ACA qualified health plans and health insurance issuers under the ACA risk adjustment program. On December 14, 2018, a Texas U.S. District Court Judge ruled that ACA is unconstitutional in its entirety because the "individual mandate" was repealed by Congress as part of the Tax Act. Additionally, on December 18, 2019, the U.S. Court of Appeals for the 5th Circuit upheld the District Court ruling that the individual mandate was unconstitutional and remanded the case back to the District Court to determine whether the remaining provisions of the ACA are invalid as well. It is unclear how this decision, future decisions, subsequent appeals, and other efforts to repeal and replace ACA will impact ACA and our business. The ultimate content, timing or effect of any healthcare reform measures on the U.S. healthcare industry is unclear.

In addition, other legislative changes have been proposed and adopted since the ACA was enacted. For example, in August 2011, President Obama signed into law the Budget Control Act of 2011, which, among other things, created the Joint Select Committee on Deficit Reduction to recommend proposals in spending reductions to Congress. The Joint Select Committee on Deficit Reduction did not achieve its targeted deficit reduction of at least $1.2 trillion for the years 2013 through 2021, triggering the legislation's automatic reductions to several government programs. These reductions include aggregate reductions to Medicare payments to providers of 2% per fiscal year, which went into effect on April 1, 2013, and, due to subsequent legislative amendments, including the BBA, will stay in effect through 2029 unless additional Congressional action is taken. In January 2013, President Obama signed into law the American Taxpayer Relief Act of 2012, which, among other things, further reduced Medicare payments to several providers and increased the statute of limitations period for the government to recover overpayments to providers from three to five years.

Further, there has been increasing legislative and enforcement interest in the United States with respect to specialty drug pricing practices. As a result, there have been several U.S. Congressional inquiries and proposed and enacted federal and state legislation designed to, among other things, bring more transparency to drug pricing, review the relationship between pricing and manufacturer patient programs, and reform government program reimbursement methodologies for drugs. At the federal level, the Trump administration's budget proposal for fiscal year 2021 includes a $135 billion allowance to support legislative proposals seeking to reduce drug prices, increase competition, lower out-of-pocket drug costs for patients, and increase patient access to lower cost generic and biosimilar drugs. Further, the Trump administration previously released a "Blueprint", or plan, to lower drug prices and reduce out of pocket costs of drugs that contains additional proposals to increase drug manufacturer competition, increase the negotiating power of certain federal healthcare programs, incentivize manufacturers to lower the list price of their products, and reduce the out of pocket costs of drug products paid by consumers. The Department of Health and Human Services, or HHS, has solicited feedback on some of these measures and, has implemented others under its existing authority. For example in May 2019, CMS issued a final rule to allow Medicare Advantage Plans the option of using step therapy for Part B drugs beginning January 1, 2020. This final rule codified a CMS policy change that was effective January 1, 2019.] While some measures may require additional authorization to become effective, Congress and the Trump administration have each indicated that it will continue to seek new legislative, administrative and/or executive measures to control drug costs. Individual states in the United States have also increasingly passed legislation and implemented regulations designed to control pharmaceutical product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain product access and marketing cost disclosure and transparency measures, and, in some cases, designed to encourage importation from other countries and bulk purchasing.

Additionally, on May 30, 2018, the Trickett Wendler, Frank Mongiello, Jordan McLinn, and Matthew Bellina Right to Try Act of 2017, or the Right to Try Act, was signed into law. The law, among other things, provides a federal framework for certain patients to access certain investigational new drug products that have completed a phase 1 clinical trial and that are undergoing investigation for FDA approval. Under certain circumstances, eligible patients can seek treatment without enrolling in clinical trials and without obtaining FDA permission under the FDA expanded access program. There is no obligation for a manufacturer to make its products available to eligible patients as a result of the Right to Try Act.

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

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

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

- The federal Anti-Kickback Statute, which regulates our business activities, including our marketing practices, educational programs, pricing policies, and relationships with healthcare providers or other entities, by prohibiting, among other things, soliciting, receiving, offering or paying remuneration, directly or indirectly, to induce, or in return for, either the referral of an individual or the purchase or recommendation of an item or service reimbursable under a federal healthcare program, such as the Medicare and Medicaid programs;
- Federal civil and criminal false claims laws, including the False Claims Act which permits a private individual acting as a "whistleblower" to bring actions on behalf of the federal government alleging violations of the False Claims Act, 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 civil and criminal statutes that prohibit, among other things, executing a scheme to defraud any healthcare benefit program or making false statements relating to healthcare matters;
- HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act of 2009, or HITECH, and their implementing regulations, which imposes certain requirements relating to the privacy, security and transmission of individually identifiable health information on entities and individuals subject to the law including certain healthcare providers, health plans, and healthcare clearinghouses, known as covered entities, as well as individuals and entities that perform services for them which involve the use, or disclosure of, individually identifiable health information, known as business associates;
- Requirements under the Physician Payments Sunshine Act to report annually to CMS certain financial arrangements with physicians, as defined by such law, and teaching hospitals, as defined in the ACA and its implementing regulations, including reporting any "transfer of value" made or distributed to

teaching hospitals, prescribers, and other healthcare providers and reporting any ownership and investment interests held by physicians and their immediate family members and applicable group purchasing organizations during the preceding calendar year; and

- State and foreign law equivalents of each of the above federal laws, such as anti-kickback and false claims laws which may apply to items or services reimbursed by any third-party payor, including commercial insurers; state laws that require pharmaceutical companies to comply with the industry's voluntary compliance guidelines and the applicable compliance guidance promulgated by the federal government that otherwise restricts certain payments that may be made to healthcare providers and entities; state laws that require drug manufacturers to report information related to payments and other transfer of value to physicians and other healthcare providers and entities; state laws that require the reporting of information related to drug pricing; state and local laws that require the registration of pharmaceutical sales representatives; and state and foreign laws governing the privacy and security of health information in certain circumstances, many of which differ from each other in significant ways and often are not preempted by HIPAA, thus complicating compliance efforts.

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

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

Efforts to ensure that our business arrangements comply with applicable healthcare laws involve substantial costs. It is possible that governmental and enforcement authorities will conclude that our business practices do not comply with current or future statutes, regulations or case law interpreting applicable fraud and abuse or other healthcare laws and regulations. If any such actions are instituted against us, and we are not successful in defending ourselves or asserting our rights, we may be subject to significant penalties, including administrative, civil and criminal penalties, damages, fines, exclusion from participation in United States federal or state health care programs, such as Medicare and Medicaid, disgorgement, imprisonment, integrity oversight and reporting obligations, and the curtailment or restructuring of our operations any of which could materially adversely affect our ability to operate our business and our financial results. Although compliance programs can mitigate the risk of investigation and prosecution for violations of these laws, the risks cannot be entirely eliminated. Any action against us for violation of these laws, even if we successfully defend against it, could cause us to incur significant legal expenses and divert our management's attention from the operation of our business. Moreover, achieving and sustaining compliance with applicable federal and state privacy, security and fraud laws may prove costly.

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

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

RISKS RELATED TO OUR INTELLECTUAL PROPERTY

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

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

To date, we have exclusive rights in the field of cancer treatment to certain U.S. and foreign intellectual property with respect to the PGEN technology, including Ad-RTS-IL-12 plus veledimex, and with respect to CAR+ T, NK and TCR cell therapies arising from the laboratory of Laurence Cooper, M.D., Ph.D., who was then at MD Anderson. Under our License Agreement with PGEN, PGEN has the right, but not the obligation, to prepare, file, prosecute, and maintain the patents and patent applications licensed to us and shall bear any related costs incurred by it in regard to those actions. PGEN is required to consult with us and keep us reasonably informed of the status of the patents and patent applications licensed to us, and to confer with us and incorporate our comments prior to submitting any related filings and correspondence. Although under the agreement PGEN has agreed to consider in good faith and consult with us regarding any comments we may have regarding these patents and patent applications, we cannot guarantee that our comments will be solicited or followed. Under the MD Anderson License, future filings and applications require the agreement of each of MD Anderson, PGEN 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 PGEN may prosecute the application directly. Although under the agreement MD Anderson has agreed to review and incorporate any reasonable comments that we or PGEN may have regarding these patents and patent applications, we cannot guarantee that our comments will be solicited or followed. Under the patent license agreement with the NCI, the NCI is responsible for the preparation, filing, prosecution, and maintenance of patent applications or patents licensed to us. Although under the agreement, the NCI is required to consult with us in the preparation, filing, prosecution, and maintenance of all patent applications or patents licensed to us, we cannot guarantee that our comments will be solicited or followed. Without direct control of the in-licensed patents and patent applications, we are dependent on PGEN, MD Anderson or the NCI, as applicable, to keep us advised of prosecution, particularly in foreign jurisdictions where prosecution information may not be publicly available. We anticipate that we, PGEN, MD Anderson and the NCI will file additional patent applications both in the United States and in other countries. However, we cannot predict or guarantee:

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

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

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

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

Certain technologies utilized in our research and development programs are already in the public domain. Moreover, a number of our competitors have developed technologies, filed patent applications or obtained patents on technologies, compositions and methods of use that are related to our business and may cover or conflict with our owned or licensed patent applications, technologies or product candidates. Such conflicts could limit the scope of the patents that we may be able to obtain or may result in the rejection of claims in our patent applications. Because patent applications in the United States and many foreign jurisdictions are typically not published until 18 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 PGEN MD Anderson, or NCI may limit the scope of later patents we obtain or may result in the rejection of claims in our later filed patent applications. If third parties filed patent applications or obtained patents on technologies, compositions and methods of use that are related to our business and that cover or conflict with our owned or licensed patent applications, technologies or product candidates, we may be required to challenge such protection, terminate or modify our programs impacted by such protection or obtain licenses from such third parties, which might not be available on acceptable terms, or at all.

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

The issuance of a patent is not conclusive as to its inventorship, scope, validity or enforceability, and our owned and licensed patents may be challenged in the courts or patent offices in the United States and abroad. Such

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

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

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

date. Therefore, patent applications covering our products or technology could have been filed by others without our knowledge. Additionally, pending patent applications which have been published can, subject to certain limitations, be later amended in a manner that could cover our products or the use of our products.

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

The patent landscape in the field of immuno-oncology 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 immuno-oncology products. In addition, there may be patents and patent applications in the field of which we are not aware. The technology we license from PGEN, MD Anderson and NCI is early-stage technology and we are in the process of designing and developing products using this technology. Although we will seek to avoid pursuing the development of products that may infringe any patent claims that we believe to be valid and enforceable, we may fail to do so. Moreover, given the breadth and number of claims in patents and pending patent applications in the field of immuno-oncology and the complexities and uncertainties associated with them, third parties may allege that we are infringing 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 substitutes, including biosimilar or generic substitutes, for our products.

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

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

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

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

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

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

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

Many of our employees were previously employed at universities or other biotechnology or pharmaceutical companies, including our competitors or potential competitors. Although we try to ensure that our employees do not use the proprietary information or know-how of others in their work for us, we may be subject to claims that these employees or we have used or disclosed intellectual property, including trade secrets or other proprietary information, of any such employee's former employer. Litigation may be necessary to defend against these claims.

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

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

OTHER RISKS RELATED TO OUR COMPANY

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

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

- Price and volume fluctuations in the overall stock market;
- Market conditions or trends in our industry or the economy as a whole;
- Preclinical or clinical trial results;
- Public concern as to the safety of drugs developed by us or others;

- Changes in operating results and performance and stock market valuations of other biopharmaceutical companies generally, or those that develop and commercialize cancer drugs in particular;
- The financial or operational projections we may provide to the public, any changes in these projections or our failure to meet these projections;
- Comments by securities analysts or changes in financial estimates or ratings by any securities analysts who follow our common stock, our failure to meet these estimates or failure of those analysts to initiate or maintain coverage of our common stock;
- The public's response to press releases or other public announcements by us or third parties, including our filings with the SEC, as well as announcements of the status of development of our products, announcements of technological innovations or new therapeutic products by us or our competitors, announcements regarding collaborative agreements and other announcements relating to product development, litigation and intellectual property impacting us or our business;
- Government regulation;
- FDA determinations on the approval of a product candidate BLA submission;
- The sustainability of an active trading market for our common stock;
- Future sales of our common stock by us, our executive officers, directors and significant stockholders;
- Announcements of mergers or acquisition transactions;
- Our inclusion or deletion from certain stock indices;
- Developments in patent or other proprietary rights;
- Changes in reimbursement policies;
- Announcements of medical innovations or new products by our competitors;
- Announcements of changes in our senior management;
- Other events or factors, including those resulting from war, incidents of terrorism, natural disasters or responses to these events; and
- Changes in accounting principles.

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

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

Provisions of our amended and restated certificate of incorporation and bylaws, as well as provisions of Delaware law, could make it more difficult for a third party to acquire us, even if doing so would benefit our stockholders. These provisions authorize the issuance of "blank check" preferred stock that could be issued by our board of directors to increase the number of outstanding shares and hinder a takeover attempt, and limit who may call a special meeting of stockholders. In addition, Section 203 of the Delaware General Corporation Law generally prohibits a publicly-held Delaware corporation from engaging in a business combination with a party that owns

at least 15% of its common stock unless the business combination is approved by the company's board of directors before the person acquires the 15% ownership stake or later by its board of directors and two-thirds of its stockholders. Section 203 could have the effect of delaying, deferring or preventing a change in control that our stockholders might consider to be in their best interests.

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

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

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

We have generated significant net operating loss carryforwards, or NOLs, and research and development tax credits, or R&D credits, as a result of our incurrence of losses and our conduct of research activities since inception. We generally are able to carry NOLs and R&D credits forward to reduce our tax liability in future years. However, our ability to utilize the NOLs and R&D credits is subject to the rules of Sections 382 and 383 of the Internal Revenue Code of 1986, as amended, or the Code, respectively. Those sections generally restrict the use of NOLs and R&D credits after an "ownership change." An ownership change occurs if, among other things, the stockholders (or specified groups of stockholders) who own or have owned, directly or indirectly, 5% or more of a corporation's common stock or are otherwise treated as 5% stockholders under Section 382 of the code and the United States Treasury Department regulations promulgated thereunder increase their aggregate percentage ownership of that corporation's stock by more than 50 percentage points over the lowest percentage of the stock owned by these stockholders over the applicable testing period. In the event of an ownership change, Section 382 imposes an annual limitation on the amount of taxable income a corporation may offset with NOL carry forwards and Section 383 imposes an annual limitation on the amount of tax a corporation may offset with business credit (including the R&D credit) carry forwards.

We may have experienced an "ownership change" within the meaning of Section 382 in the past and there can be no assurance that we will not experience additional ownership changes in the future. As a result, our NOLs and business credits (including the R&D credit) may be subject to limitations and we may be required to pay taxes earlier and in larger amounts than would be the case if our NOLs or R&D credits were freely usable.

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

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

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

As of December 31, 2019, our executive officers, directors and holders of five percent or more of our outstanding common stock, beneficially owned, in the aggregate, 37.9% 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.

We have identified a material weakness in our internal control over financial reporting for the year ended December 31, 2019 and may identify additional material weaknesses in the future or otherwise fail to maintain an effective system of internal controls, which may result in material misstatements of our financial statements or could have a material adverse effect on our business and trading price of our securities.

We are subject to the reporting requirements of the Securities Exchange Act of 1934, as amended, the Sarbanes-Oxley Act of 2002 and the rules and regulations of The Nasdaq Global Market. Pursuant to Section 404 of the Sarbanes-Oxley Act of 2002, we are required to perform system and process evaluation and testing of our internal control over financial reporting to allow our management to report on the effectiveness of our internal control over financial reporting. We are also required to have our independent registered public accounting firm issue an opinion on the effectiveness of our internal control over financial reporting on an annual basis.

In connection with the audit of our consolidated financial statements as of and for the year ended December 31, 2019, we identified a material weakness in our internal control over financial reporting. A material weakness is a deficiency, or combination of deficiencies, in internal control over financial reporting such that there is a reasonable possibility that a material misstatement of our consolidated financial statements will not be prevented or detected on a timely basis. The material weakness is related to the design and maintenance of effective controls relating to the monitoring and oversight of expensing third party clinical trial costs. Specifically, our internal controls were not designed effectively to provide reasonable assurance regarding the accurate and timely evaluation of the amount of third party costs to record.

We are in the process of designing and implementing measures to remediate the underlying causes of the control deficiencies that gave rise to the material weakness. In addition, we are providing in-house accounting personnel training to ensure that they have the relevant expertise related to the monitoring and oversight of expensing third party clinical trial costs. We will continue to monitor the effectiveness of these controls and will make any further changes management determines appropriate.

We cannot assure you that the measures we have taken to date, together with any measures we may take in the future, will be sufficient to remediate the control deficiencies that led to the material weakness in our internal control over financial reporting or to avoid potential future material weaknesses. If we are unable to successfully remediate our existing or any future material weakness in our internal control over financial reporting, or if we identify any additional material weaknesses, the accuracy and timing of our financial reporting may be adversely affected. If we are unable to maintain effective internal controls, we may not have adequate, accurate or timely financial information, and we may be unable to meet our reporting obligations as a public company, including the requirements of the Sarbanes-Oxley Act, we may be unable to accurately report our financial results in future periods, or report them within the timeframes required by the requirements of the SEC, Nasdaq or the Sarbanes-Oxley Act. Failure to comply with the Sarbanes-Oxley Act, when and as applicable, could also potentially subject us to sanctions or investigations by the SEC or other regulatory authorities. Any failure to maintain or implement required new or improved controls, or any difficulties we encounter in their implementation, could result in identification of additional material weaknesses or significant deficiencies, cause us to fail to meet our reporting obligations or result in material misstatements in our financial statements. Furthermore, if we cannot provide reliable financial reports or prevent fraud, our business and results of operations could be harmed and investors could lose confidence in our reported financial information.

The Tax Cuts and Jobs Act, signed into law in 2017 could adversely affect our business and financial condition.

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

Item 1B. Unresolved Staff Comments

None.

Item 2. Properties

Our corporate office is located at One First Avenue, Parris Building #34, Navy Yard Plaza, Boston, Massachusetts 02129. The Boston office is leased pursuant to a lease agreement that expires in August 2021. On December 21, 2015, we renewed a portion of the lease for Boston office through August 31, 2021 at an average monthly rate of approximately $60 thousand.

In October 2019, we entered into an agreement with MD Anderson to lease office and lab space. The monthly rent expense of this lease with MD Anderson is deducted from our prepayment at MD Anderson. See Note 8 to the accompanying financial statements for further details.

We believe that our existing facilities are adequate to meet our current needs.

Item 3. Legal Proceedings

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

There are no matters, as of December 31, 2019, 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."

Record Holders

As of February 14, 2020, we had approximately 270 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.

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

During the quarter ended December 31, 2019, we granted a new employee an inducement award in the form of an option to purchase an aggregate of 65,000 shares of our common stock at an exercise price of $4.59 per share, the closing price of our common stock on November 21, 2019. The options were granted as an inducement material to such employee's entry into employment with us in accordance with Nasdaq Listing Rule 5635(c)(4) and Section 4(a)(2) of the Securities Act of 1933, as amended. The option has a ten-year term and vests over four years, subject to the new employee's continued service with us on each applicable vesting date. The option was granted the inducement award outside of, but subject to terms generally consistent with, our Amended and Restated 2012 Equity Incentive Plan.

We intend to file a registration statement on a Form S-8 to register the shares of common stock underlying the options granted to this employee prior to the time at which the shares underlying such options become exercisable.

Issuer Purchases of Equity Securities

During the three months ended December 31, 2019, we purchased an aggregate of 60,161 shares of restricted stock from certain members of our board of directors to cover the applicable withholding taxes due from them for the shares of restricted stock at the time that the applicable forfeiture restrictions lapsed. The following table provides information about these purchases of restricted shares for the three months ended December 31, 2019:

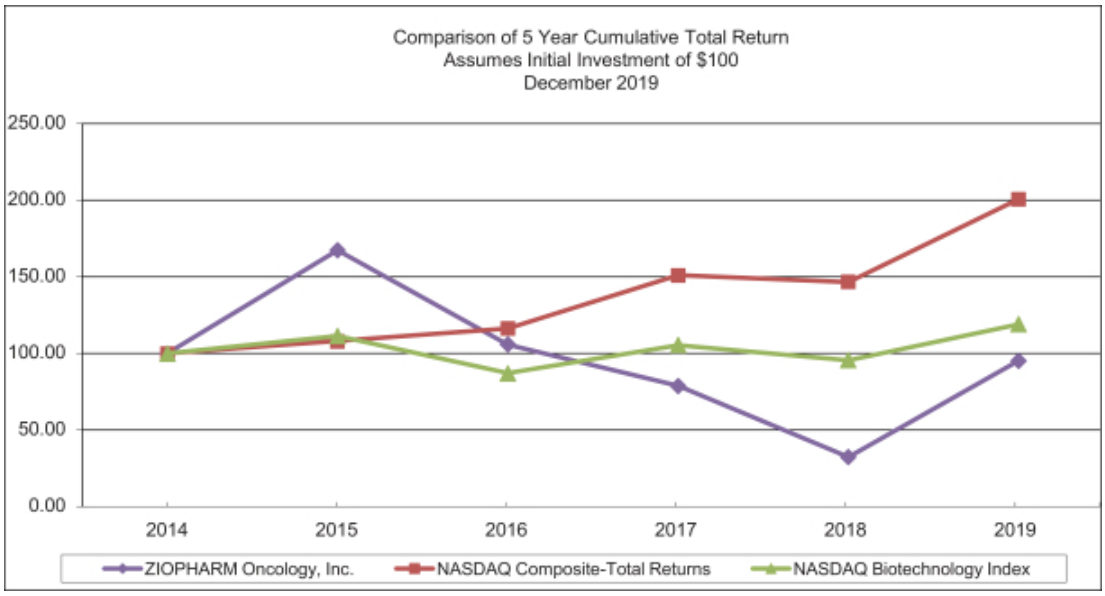
Period	Total Number of Shares Purchased	Average Price Paid Per Share	Total Number of Shares Purchased as Part of Publicly Announced Plans or Programs	Maximum Number of Shares that May Yet Be Purchased Under Plans or Programs
October 1 to 31, 2019	—	$ —	—	—
November 1 to 30, 2019	—	—	—	—
December 1 to 31, 2019	60,161	4.72	—	—
Total	60,161	$ 4.72		

Stockholder Return Comparison

The following shall not be deemed incorporated by reference into any of our other filings under the Securities Exchange Act of 1934, as amended, or the Securities Act of 1933, as amended, except to the extent we specifically incorporate it by reference into such filings.

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, 2014 and tracks it through December 31, 2019.

The comparisons in the graph below are based upon historical data and are not indicative of, nor intended to forecast, future performance of our common stock.



Item 6. Selected Financial Data

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

	Year Ended December 31, (in thousands, except share data and per share amounts)				
	2019	2018	2017	2016	2015
Statements of Operations Data:					
Collaboration revenue	$ —	$ 146	$ 6,389	$ 6,861	$ 4,332
Total operating expenses	57,858	54,052	59,882	172,168	124,432
Loss from operations	(57,858)	(53,906)	(53,493)	(165,307)	(120,100)
Other income (expense), net	813	631	465	134	12
Non-cash inducement warrant expense	(60,751)	—	—	—	—
Change in fair value of derivative liabilities	—	158	(1,295)	(124)	—
Net loss	(117,796)	(53,117)	(54,323)	(165,297)	(120,088)
Preferred stock dividends	—	(16,998)	(18,938)	(7,123)	—
Settlement of a related party relationship	—	207,361	—	—	—
Net income (loss) applicable to common stockholders	(117,796)	137,246	(73,261)	(172,420)	(120,088)
Net income (loss) per share - basic	$ (0.70)	$ 0.96	$ (0.53)	$ (1.32)	$ (0.96)
Net income (loss) per share - diluted	$ (0.70)	$ 0.96	$ (0.53)	$ (1.32)	$ (0.96)
Weighted average number of common shares outstanding: basic	167,952,114	143,508,674	136,938,264	130,391,463	125,416,084
Weighted average number of common shares outstanding: diluted	167,952,114	143,710,160	136,938,264	130,391,463	125,416,084

	Year Ended December 31, (in thousands)				
	2019	2018	2017	2016	2015
Balance Sheet Data:					
Cash and cash equivalents	$ 79,741	$ 61,729	$ 70,946	$ 81,053	$ 140,717
Total assets	109,114	95,051	105,606	106,348	153,724
Derivative liabilities	—	—	2,424	862	—
Total liabilities	14,104	9,487	58,420	58,325	66,353
Series 1 Preferred Stock	—	—	143,992	125,321	—
Stockholders' equity (deficit)	95,010	85,564	(96,806)	(77,298)	87,371

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

The following discussion and analysis of our financial condition and results of operations should be read in conjunction with our consolidated financial statements and related notes appearing elsewhere in this Annual Report on Form 10-K. In addition to historical financial information, the following discussion contains forward-looking statements that reflect our plans, estimates and beliefs. Our actual results could differ materially from

those contained in or implied by any forward-looking statements. Factors that could cause or contribute to these differences include those under "Risk Factors" included in Part I, Item 1A and under "Special Note Regarding Forward-Looking Statements" or in other parts of this Annual Report on Form 10-K.

Business Overview

We are a clinical-stage biopharmaceutical company focused on discovering, acquiring, developing and commercializing next generation immuno-oncology platforms that leverage cell- and gene-based therapies to treat patients with cancer. We are developing two immuno-oncology platform technologies that utilize the immune system by employing novel, controlled gene expression and innovative cell engineering technologies designed to deliver safe, effective, and scalable non-viral cell- and viral-based gene therapies for the treatment of multiple cancer types. Our first platform is referred to as *Sleeping Beauty* and is based on the genetic engineering of immune cells using a non-viral transposon/transposase system that is intended to stably reprogram T cells outside of the body for subsequent infusion. Our second platform is referred to as Controlled IL-12 and is designed to stimulate expression of interleukin 12, or IL-12, a master regulator of the immune system, in a controlled and safe manner to focus the patient's immune system to attack cancer cells. We intend to use both of our platforms to become a leading immuno-oncology company focused on developing individualized, cost-effective therapies primarily aimed at the large unmet needs in solid tumors.

Using our *Sleeping Beauty* platform, we are developing T cell receptor, or TCR, T cell therapies to target solid tumors. Our program designs and manufactures T cells that are intended to target tumor-specific antigens, thereby delivering personalized therapy that can attack patients' malignancies. These genetic changes are referred to as neoantigens as they are only expressed by the tumor, reducing the potential for toxicity upon targeting normal cells. Under our Cooperative Research and Development Agreement, the NCI is conducting a Phase 2 clinical trial to evaluate autologous peripheral blood lymphocytes genetically modified with the Sleeping Beauty system to express autologous (personalized) TCRs. The U.S. Food and Drug Administration, or FDA, has cleared the investigational new drug, or IND, application submitted by the NCI for this clinical trial. The trial was initiated in October 2019 and preparations to enable patient enrollment by the NCI are underway. We expect the trial will enroll patients with a broad range of solid tumors over the next several years. In addition, we are currently planning a clinical program to study our TCR approaches with The University of Texas MD Anderson Cancer Center, or MD Anderson. Under this program, we expect to clinically evaluate both our personalized autoTCR approach and our library alloTCR approach.

Our Controlled IL-12 platform uses virotherapy based on an engineered replication-incompetent adenovirus, referred to as Ad-RTS-hIL-12, plus veledimex as a gene delivery system to conditionally produce IL-12, a potent, naturally occurring anti-cancer protein, to treat patients with solid tumors where a specific target is unknown. Our Controlled IL-12 platform allows us to deliver IL-12 in a tunable dose as the cytokine is under transcriptional control of the RheoSwitch Therapeutic System® (RTS®). We are currently studying our Controlled IL-12 Platform as a monotherapy in a Phase 1 clinical trial of patients with recurrent glioblastoma multiforme, or rGBM. Our substudy of this clinical trial is fully enrolled with 36 patients and is designed to encourage use of low-dose steroids and 20 mg veledimex to further understand the potential of Controlled IL-12 as a monotherapy. We are also developing our Controlled IL-12 platform in combination with immune checkpoint inhibitors. We have completed dosing in a Phase 1 dose-escalation clinical trial of Ad-RTS-hIL-12 plus veledimex in combination with OPDIVO® (nivolumab) in patients with rGBM. Dosing is ongoing in a Phase 2 clinical trial evaluating Ad-RTS-hIL-12 plus veledimex in combination with PD-1 antibody Libtayo® (cemiplimab-rwlc) for the treatment of recurrent or progressive glioblastoma multiforme in adults.

We are developing chimeric antigen receptor, or CAR, T cell, or CAR$^+$ T, therapies targeting CD19 on malignant B cells using our *Sleeping Beauty* platform in collaboration with MD Anderson. In a Phase 1 trial, we plan to infuse donor-derived T cells after allogeneic bone marrow transplantation, or BMT, for recipients who have relapsed with CD19$^+$ leukemias and lymphomas with our CD19-specific CAR$^+$ T therapies manufactured using

our rapid personalized manufacture, or RPM, technology. RPM enables T cells to be infused as soon as the day after gene transfer which is made possible by the genetic modification of resting T cells to express CAR and membrane bound IL-15, or mbIL15. We are also advancing our RPM technology in Greater China with Eden BioCell, Ltd., or Eden BioCell, our joint venture with TriArm Therapeutics, Ltd. Eden BioCell will lead the clinical development and commercialization of *Sleeping Beauty*-generated CD19-specific RPM CAR$^+$ T therapies using patient-derived (autologous) T cells in order to treat patients with relapsed or refractory CD19$^+$ leukemias and lymphomas.

As of December 31, 2019, we have approximately $79.7 million of cash and cash equivalents in addition to an aggregate of approximately $98.0 million of net proceeds that we raised in January and February 2020 from an underwritten public offering and our at-the-market facility. Given our current development plans, we anticipate our cash resources, along with the proceeds raised from these recent financing activities, will be sufficient to fund our operations into mid-2022 and we have no committed sources of additional capital at this time. The forecast of cash resources is forward-looking information that involves risks and uncertainties, and the actual amount of our expenses could vary materially and adversely as a result of a number of factors. We have based our estimates on assumptions that may prove to be wrong, and our expenses could prove to be significantly higher than we currently anticipate. Management does not know whether additional financing will be on terms favorable or acceptable to us when needed, if at all. If adequate additional funds are not available when required, or if we are unsuccessful in entering into partnership agreements for further development of our product candidates, management may need to curtail its development efforts and planned operations.

We have not generated significant revenue and have incurred significant net losses in each year since our inception. For the year ended December 31, 2019, we had a net loss of $117.8 million, and through December 31, 2019, we have incurred approximately $684.1 million of accumulated deficit since our inception in 2003. We expect to continue to incur significant operating expenditures and net losses. Further development of our product candidates will likely require substantial increases in our expenses as we:

- continue to undertake clinical trials for 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; and
- scale-up the formulation and manufacturing of our product candidates.

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 delayed, and we may be unable to continue our operations at planned levels and be forced to reduce our operations. Because of the numerous risks and uncertainties associated with product development, we are unable to predict the timing or amount of increased expenses or when or if we will be able to achieve or maintain profitability.

Financial Overview

Collaboration Revenue

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

Research and Development Expenses

Our research and development expense consists primarily of salaries and related expenses for personnel, costs of contract manufacturing services, costs of facilities and equipment, fees paid to professional service providers in

conjunction with our clinical trials, fees paid to contract research organizations in conjunction with preclinical animal studies, costs of materials used in research and development, consulting, license and milestone payments and sponsored research fees paid to third parties.

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

For the year ended December 31, 2019, our clinical stage projects included a Phase 1 clinical trial with Ad-RTS-IL-12 plus veledimex in progressive glioblastoma; a Phase 1 Ad-RTS-hIL-12 plus veledimex in combination with Bristol-Myers Squibb Company's OPDIVO® (nivolumab); an investigator-led Phase 1 clinical trial infusing our 2nd generation CD19-specific CAR+ T cells in patients with advanced lymphoid malignancies; an investigator-led Phase 1 clinical trial infusing our CD33-specific CAR+ T therapy for relapsed or refractory acute myeloid leukemia; and a Phase 1 clinical trial of Ad-RTS-hIL-12 with veledimex for the treatment of pediatric brain tumors. The expenses incurred by us to third parties for our Phase 1 clinical trial with Ad-RTS-IL-12 plus veledimex in progressive glioblastoma were $4.5 million for the year ended December 31, 2019, and $11.3 million from the project's inception in June 2015 through December 31, 2019. The expenses incurred by us to third parties for our Ad-RTS-hIL-12 plus veledimex in combination with Bristol-Myers Squibb Company's OPDIVO® (nivolumab) were $1.7 million for the year ended December 31, 2019 and from the project's inception in November 2018 through December 31, 2019. The expenses incurred by us to third parties for our investigator-led Phase 1 clinical trial infusing our 2nd generation CD19-specific CAR+ T cells in patients with advanced lymphoid malignancies were $1.4 million for the year ended December 31, 2019 and $6.1 million from the project's inception in December 2015 through December 31, 2019. The expenses incurred by us to third parties for our investigator-led Phase 1 clinical trial infusing our CD33-specific CAR+ T therapy for relapsed or refractory acute myeloid leukemia were $0.1 million for the year ended December 31, 2019 and $3.8 million from the project's inception in September 2017 through December 31, 2019. The expenses incurred by us to third parties for our investigator-led Phase 1 clinical trial of Ad-RTS-hIL-12 with veledimex for the treatment of pediatric brain tumors were $0.5 million for the year ended December 31, 2019 and the $2.0 million from the project's inception in October 2017 through December 31, 2019.

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 patients;
- 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 interest income and changes in the fair value of our Series 1 preferred stock. All of the Series 1 preferred stock was forfeited on October 5, 2018 in conjunction with entering the License Agreement with PGEN Therapeutics, or PGEN, a wholly owned subsidiary of Precigen Inc., or Precigen, which was formerly known as Intrexon Corporation.

Results of Operations for the Fiscal Year ended December 31, 2019 and 2018

Collaboration Revenues

Revenues for the years ended December 31, 2019 and 2018 were as follows:

	Year ended December 31,			
	2019	2018	Change	
($ in thousands)				
Collaboration revenue	$ —	$ 146	$(146)	-100%

Revenue for the year ended December 31, 2019 decreased by $146 thousand in comparison to revenue for the year ended December 31, 2018. During the year ended December 31, 2019, there was no recognized revenue. During the year ended December 31, 2018, we recognized $146 thousand of revenue related to the Ares Trading Agreement under ASC 606 (Note 3).

Research and Development Expenses

Research and development expenses during the years ended December 31, 2019 and 2018 were as follows:

	Year ended December 31,			
	2019	2018	Change	
($ in thousands)				
Research and development	$ 38,331	$ 34,134	$4,197	12%

Research and development expenses for the year ended December 31, 2019 increased by $4.2 million when compared to the year ended December 31, 2018. The increase in expense during the year ended December 31, 2019 was due to an increase of $1.5 million in T cell therapy expenses, driven primarily by manufacturing costs and costs associated with our Patent License with the NCI, an increase of $1.2 million in employee related expenses, driven primarily by increased headcount in 2019 compared to 2018, $1.1 million of Gorilla IL-12 expenses driven by increased manufacturing and trial cost to support our ongoing clinical initiatives and $0.4 million of contracted outside services due to the buildout of the Houston facility (Note 8).

General and Administrative Expenses

General and administrative expenses during the years ended December 31, 2019 and 2018 were as follows:

	Year ended December 31,		Change	
($ in thousands)	**2019**	**2018**		
General and administrative	$ 19,527	$ 19,918	$(391)	-2%

General and administrative expenses for the year ended December 31, 2019 decreased by $0.4 million as compared to the prior year. The change was primarily due to decreased stock compensation of $0.9 million and decreased contracted outside services and advisory fees related to our License Agreement with PGEN in 2018 (Note 7) of $0.9 million. The decreased costs in 2019 were offset by an increase of employee related costs of $0.8 million, an increase of facilities related costs of $0.4 million, and an increase of travel related costs due to international travel by executives of $0.2 million.

Other Income (Expense)

Other income (expense) during the years ended December 31, 2019 and 2018 were as follows:

	Year ended December 31,		Change	
($ in thousands)	**2019**	**2018**		
Other income (expense), net	$ 813	$ 631	$ 182	29%
Non-cash inducement warrant expense	(60,751)	—	(60,751)	-100%
Change in fair value of derivative liabilities	—	158	(158)	-100%
Total	$ (59,938)	$ 789	$(60,727)	

During the year ended December 31, 2019, we recorded a non-cash inducement warrant expense of $60.8 million (Note 10) relating to the issuance of new warrants as an inducement for warrant holders to exercise their 2018 warrants early. During the year ended December 31, 2018 we recorded a gain on the change in fair value of the derivative liabilities of $158 thousand, which was derived from the number of previously outstanding shares of Series 1 preferred stock and their respective valuations. Additionally, we recorded $813 thousand in other income for the year ended December 31, 2019, compared to $631 thousand earned in the prior year, due to increases in our cash equivalent accounts (Note 3).

Results of Operations for the Fiscal Year ended December 31, 2018 versus December 31, 2017

Collaboration Revenues

Revenues for the years ended December 31, 2018 and 2017 were as follows:

	Year ended December 31,		Change	
($ in thousands)	**2018**	**2017**		
Collaboration revenue	$ 146	$ 6,389	$(6,243)	-98%

Revenue for the year ended December 31, 2018 decreased by $6.2 million in comparison to revenue for the year ended December 31, 2017 due to the adoption of ASC 606 (Note 3). During the year ended December 31, 2018,

we recognized $146 thousand of revenue related to the Ares Trading Agreement under ASC 606. During the year ended December 31, 2017, we recognized $6.4 million of revenue through our Ares Trading Agreement under ASC 605. (Note 3).

Research and Development Expenses

Research and development expenses during the years ended December 31, 2018 and 2017 were as follows:

	Year ended December 31,		Change	
	2018	2017		
($ in thousands)				
Research and development	$ 34,134	$ 45,084	$(10,950)	-24%

Research and development expenses for the year ended December 31, 2018 decreased by $11.0 million when compared to the year ended December 31, 2017. The decrease in expense during the year ended December 31, 2018 was due to a decrease of $10.4 million in preclinical activities, a decrease of $1.7 million related to graft versus host disease, or GvHD, expenses, and a reduction of $0.6 million in other clinical expenses. The decrease in preclinical, GvHD, and other clinical expenses was offset by increases in Gorilla IL-12 expenses due to PGEN under the License Agreement of $1.0 million (Note 7) and of $0.7 million related to salary and employee related expense during the year ended December 31, 2018. We previously determined that the pursuit of GvHD as an indication was not a material part of its corporate strategy and decided to stop pursuing the development of engineered cell therapy strategies, used either separately or in combination, for targeted treatment of GvHD.

General and Administrative Expenses

General and administrative expenses during the years ended December 31, 2018 and 2017 were as follows:

	Year ended December 31,		Change	
	2018	2017		
($ in thousands)				
General and administrative	$ 19,918	$ 14,798	$5,120	35%

General and administrative expenses for the year ended December 31, 2018 increased by $5.1 million as compared to the prior year. The change was primarily due to increased contracted outside services and advisory fees related to our license agreement with PGEN (Note 7) of $4.1 million and an increase of $1.3 million related to salary and employee related expense during the year ended December 31, 2018. The increased costs in 2018 were offset by a reduction of milestone payments of $0.3 million due to Baxter Healthcare S.A., or Baxter, as our license agreement with Baxter expired in November 2017.

Other Income (Expense)

Other income (expense) during the years ended December 31, 2018 and 2017 were as follows:

	Year ended December 31,		Change	
	2018	2017		
($ in thousands)				
Other income (expense), net	$ 631	$ 465	$ 166	36%
Change in fair value of derivative liabilities	158	(1,295)	1,453	-112%
Total	$ 789	$ (830)	$1,619	

During the year ended December 31, 2018, we recorded a gain on the change in fair value of the derivative liabilities of $158 thousand, compared to a loss of $1.3 million during the year ended December 31, 2017

(Note 13). These changes are derived from the number of previously outstanding shares of Series 1 preferred stock and their respective valuations. Additionally, we recorded $631 thousand in other income for the year ended December 31, 2018, compared to $465 thousand earned in the prior year, due to increases in our cash equivalent accounts (Note 3).

Liquidity and Capital Resources

As of December 31, 2019, we have approximately $79.7 million of cash and cash equivalents and in January and February 2020 we raised an aggregate of approximately $98.0 million of net proceeds in a public offering and an at-the-market offering. Given our current development plans, in addition to our recent financing, we anticipate cash resources will be sufficient to fund our operations into mid-2022 and we have no committed sources of additional capital at this time. The forecast of cash resources is forward-looking information that involves risks and uncertainties, and the actual amount of our expenses could vary materially and adversely as a result of a number of factors. We have based our estimates on assumptions that may prove to be wrong, and our expenses could prove to be significantly higher than we currently anticipate. Management does not know whether additional financing will be on terms favorable or acceptable to us when needed, if at all. If adequate additional funds are not available when required, or if we are unsuccessful in entering into partnership agreements for further development of our products, management may need to curtail development efforts.

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

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

Recent Financing Transactions

February 2020 Public Offering

On February 5, 2020, we entered into an underwriting agreement with Jefferies, as representative of the several underwriters named therein, relating to the issuance and sale of 27,826,086 shares of our common stock. The price to the public in the offering was $3.25 per share, and the underwriters agreed to purchase the shares from us pursuant to the underwriting agreement at a purchase price of $3.055 per share. Under the terms of the underwriting agreement, we also granted the underwriters an option, exercisable for 30 days, to purchase up to an additional 4,173,912 shares of common stock at a purchase price of $3.055 per share. The offering, which closed on February 7, 2020, was made pursuant to our effective registration statement on Form S-3ASR (File No. 333-232283) previously filed with the SEC, and a prospectus supplement thereunder. The net proceeds from the offering were approximately $85.0 million after deducting underwriting discounts and our offering expenses.

At-the-Market Offering

Subsequent to December 31, 2019, we sold an aggregate of 2,814,673 shares of our common stock. The offering was made pursuant to our effective registration statement on Form S-3ASR (File No. 333-232283) previously filed with the SEC, and a prospectus supplement thereunder. The net proceeds from the offering were approximately $13.0 million after deducting underwriting discounts and our offering expenses.

During the year ended December 31, 2019, we sold an aggregate of 1,271,274 shares of our common stock. The offering was made pursuant to our effective registration statement on Form S-3ASR (File No. 333-232283) previously filed with the SEC, and a prospectus supplement thereunder. The net proceeds from the offering were approximately $6.1 million after deducting underwriting discounts and our offering expenses.

July 2019 and September 2019 Warrant Exercise

On July 26, 2019 and September 12, 2019, we entered into agreements for the exercise of the warrants issued in November 2018 to purchase common stock in a private placement. Pursuant to the terms of the agreements, investors exercised warrants for an aggregate of 17,803,031 shares of common stock, at an exercise price of $3.01 per share. We issued new warrants to purchase up to 17,803,031 additional shares of common stock as an inducement for warrant holders to exercise their 2018 warrants early. The new warrants will become exercisable six months following the date of issuance, will expire on the fifth anniversary of the initial exercise date, and have an exercise price of $7.00 (Note 10). Proceeds from the exercise of the warrants, before deducting placement agent fees and other related expenses of $1.1 million were approximately $52.5 million. For the year ended December 31, 2019, we also recorded $60.8 million in non-cash inducement warrant expense, which is included in our statement of operations.

November 2018 Private Placement

On November 11, 2018, we entered into a securities purchase agreement with certain institutional and accredited investors pursuant to which we agreed to issue and sell to the investors an aggregate of 18,939,394 immediately separable units at a price per unit of $2.64, for net proceeds of approximately $47.1 million. Each unit was comprised of (i) one share of our common stock, par value $0.001 per share and (ii) a warrant to purchase one share of common stock. The securities issued by us pursuant to the securities purchase agreement and to be issued upon exercise of the warrants were not registered under the Securities Act and may not be offered or sold in the United States absent registration or an applicable exemption from registration requirements. When issuing the units, we relied on the private placement exemption from registration provided by Section 4(a)(2) of the Securities Act and by Rule 506 of Registration D, promulgated thereunder and on similar exemptions under applicable state laws and filed a Form D with the SEC on November 19, 2018. On February 7, 2019, we filed a registration statement on Form S-3 registering the resale of shares issued pursuant to the securities purchase agreement and the resale of shares that may be issued upon exercise of the warrants.

May 2017 Offering

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

The following table summarizes our net increase (decrease) in cash and cash equivalents for the years ended December 31, 2019, 2018 and 2017:

	Year ended December 31,		
($ in thousands)	**2019**	**2018**	**2017**
Net cash provided by (used in):			
Operating activities	$(40,854)	$(49,457)	$(54,669)
Investing activities	(284)	(459)	(737)
Financing activities	59,150	40,311	45,299
Net increase (decrease) in cash and cash equivalents	$ 18,012	$ (9,605)	$(10,107)

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

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

Net cash used in operating activities for the year ended December 31, 2019 was $40.9 million, as compared to net cash used in operating activities of $49.5 million and $54.7 million for the years ended December 31, 2018 and 2017, respectively. The net cash used in operating activities for the year ended December 31, 2019 was primarily a result of our net loss of $117.8 million, an increase in receivables of $1.5 million, an increase in prepaid expenses and other current assets of $1.7 million, offset by a decrease in other noncurrent assets of $9.4 million, and an increase in accounts payable and accrued expenses of $1.9 million. The net cash used in operating activities for the year ended December 31, 2018 was primarily a result of our net loss of $53.1 million, an increase in receivables of $1.9 million, an increase of prepaid expenses and other current assets of $1.3 million, and a decrease in accounts payable and accrued expenses of $4.8 million, offset by a decrease of other noncurrent assets of $4.0 million. The net cash used in operating activities for the year ended December 31, 2017 was primarily a result of our net loss of $54.3 million, a decrease in prepaid expenses of $4.0 million, an increase in other noncurrent assets of $13.0 million and an increase in accounts payable and accrued expenses of $5.1 million.

Net cash used in investing activities was $284 thousand for the year ended December 31, 2019 compared to $459 thousand and $737 thousand for the years ended December 31, 2018 and December 31, 2017, respectively. The change was due primarily to increases in equipment purchases under our agreement with MD Anderson to support our ongoing clinical trials in Houston, Texas during the years ended December 31, 2019, 2018 and 2017.

Net cash provided by financing activities was $59.2 million for the year ended December 31, 2019 compared to net cash provided by financing activities of $40.3 million and $45.3 million used in financing activities for the years ended December 31, 2018 and 2017, respectively. The $59.2 million provided by financing activities during the year ended December 31, 2019 is a result of net proceeds from the issuance of common stock upon exercise of warrants (Note 2) of $52.5 million, net proceeds from the issuance in connection with an at the market offering of $6.1 million, proceeds from the exercise of stock options of $1.2 million, offset by $0.7 million used to repurchase common stock. The $40.3 million provided by financing activities during the year ended December 31, 2018 is a result of net proceeds of $47.1 million from our November 2018 financing (Note 2) which were offset by cash paid of $5.4 million from our License Agreement and $1.6 million paid for the repurchase of common stock. The $45.3 million provided by financing activities during the year ended December 31, 2017 is a result of net proceeds of $47.3 million from our May 2017 offering (Note 2) which was offset by $2.1 million in cash used in the issuance of restricted common stock.

Operating Capital and Capital Expenditure Requirements

We anticipate that losses will continue for the foreseeable future. At December 31, 2019, our accumulated deficit was approximately $684.1 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 I – Item 1A. “Risk Factors.”

Working capital as of December 31, 2019 was $93.0 million, consisting of $105.5 million in current assets and $12.5 million in current liabilities. Working capital as of December 31, 2018 was $74.8 million, consisting of $84.3 million in current assets and $9.5 million in current liabilities.

Contractual Obligations

The following table summarizes our outstanding obligations as of December 31, 2019 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	$ 2,799	$ 925	$ 914	$ 446	$ 514
CRADA	$ 5,000	2,500	2,500	—	—
Royalty and license fees	$ 4,150	850	700	700	1,900
Total	$11,949	$ 4,275	$ 4,114	$ 1,146	$ 2,414

Our commitments for operating leases relate to the lease for our corporate headquarters in Boston, Massachusetts, and office space in Houston, Texas. On December 21, 2015 and April 15, 2016, we renewed the sublease for our corporate headquarters in Boston, MA through August 31, 2021. On January 30, 2018, we entered into a lease agreement for office space in Houston, TX at MD Anderson through April 2021. On March 12, 2019, we entered into a lease agreement for additional office Space in Houston through April 2021. On October 15, 2019, we entered into another lease agreement for additional office space in Houston through February 2027.

On January 10, 2017, we announced the signing of a CRADA with the NCI for the development of ACT-based immunotherapies genetically modified using the *Sleeping Beauty* transposon/transposase system for the treatment of solid tumors. In February 2019, we extended the CRADA with the NCI until January 9, 2022.

On May 28, 2019, we entered into a patent license agreement, or the Patent License, with the NCI. The terms of the Patent License require us to pay the NCI minimum annual royalties in the amount of $0.3 million, which amount will be reduced to $0.1 million once the aggregate minimum annual royalties paid by us equals $1.5 million. The first minimum annual royalty payment is payable on the date that is eighteen months following the date of the Patent License.

On October 5, 2018, we entered into the License Agreement with Precigen. Under the License Agreement, we are obligated to pay PGEN an annual licensing fee of $100 thousand expected to be paid through the term of the agreement.

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;
- Revenue Recognition from collaboration agreements;
- Fair value measurements of stock-based compensation; and Series 1 Preferred Stock (including related dividends)
- Income taxes.

Clinical Trial Expenses

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

Revenue Recognition from Collaboration Agreements

We primarily generate revenue through collaboration arrangements with strategic partners for the development and commercialization of product candidates. Commencing January 1, 2018, we recognized revenue in accordance with ASC 606 which replaced ASC 605, *Multiple Element Arrangements*, as used in historical years. The core principle of ASC 606 is that an entity should recognize revenue to depict the transfer of promised goods and/or services to customers in an amount that reflects the consideration to which the entity expects to be entitled in exchange for those goods and/or services. To determine the appropriate amount of revenue to be recognized for arrangements that we determine are within the scope of ASC 606, we perform the following steps: (i) identify the contract(s) with the customer, (ii) identify the performance obligations in the contract, (iii) determine the transaction price, (iv) allocate the transaction price to the performance obligations in the contract and (v) recognize revenue when (or as) each performance obligation is satisfied.

We recognize collaboration revenue under certain of our license or collaboration agreements that are within the scope of ASC 606. Our contracts with customers typically include promises related to licenses to intellectual property, research and development services and options to purchase additional goods and/or services. If the license to our intellectual property is determined to be distinct from the other performance obligations identified in the arrangement, we recognize revenue from non-refundable, up-front fees allocated to the license when the license is transferred to the licensee and the licensee is able to use and benefit from the license. For licenses that are bundled with other promises, we utilize judgment to assess the nature of the combined performance obligation to determine whether the combined performance obligation is satisfied over time or at a point in time and, if over time, the appropriate method of measuring progress for purposes of recognizing revenue from non-refundable, up-front fees. Contracts that include an option to acquire additional goods and/or services are evaluated to determine if such option provides a material right to the customer that it would not have received

without entering into the contract. If so, the option is accounted for as a separate performance obligation. If not, the option is considered a marketing offer which would be accounted for as a separate contract upon the customer's election.

The terms of our arrangements with customers typically include the payment of one or more of the following: (i) non-refundable, up-front payment, (ii) development, regulatory and commercial milestone payments, (iii) future options and (iv) royalties on net sales of licensed products. Accordingly, the transaction price is generally comprised of a fixed fee due at contract inception and variable consideration in the form of milestone payments due upon the achievement of specified events and tiered royalties earned when customers recognize net sales of licensed products. We measure the transaction price based on the amount of consideration to which it expects to be entitled in exchange for transferring the promised goods and/or services to the customer. We utilize the most likely amount method to estimate the amount of variable consideration, to predict the amount of consideration to which we will be entitled for our one open contract. Amounts of variable consideration are included in the transaction price to the extent that it is probable that a significant reversal in the amount of cumulative revenue recognized will not occur when the uncertainty associated with the variable consideration is subsequently resolved. At the inception of each arrangement that includes development and regulatory milestone payments, we evaluate whether the associated event is considered probable of achievement and estimates the amount to be included in the transaction price using the most likely amount method. Milestone payments that are not within the control of us or the licensee, such as those dependent upon receipt of regulatory approval, are not considered to be probable of achievement until the triggering event occurs. At the end of each reporting period, we reevaluate the probability of achievement of each milestone and any related constraint, and if necessary, adjusts its estimate of the overall transaction price. Any such adjustments are recorded on a cumulative catch-up basis, which would affect revenue and net loss in the period of adjustment. For arrangements that include sales-based royalties, including milestone payments based upon the achievement of a certain level of product sales, we recognize revenue upon the later of: (i) when the related sales occur or (ii) when the performance obligation to which some or all of the payment has been allocated has been satisfied (or partially satisfied). To date, we have not recognized any development, regulatory or commercial milestones or royalty revenue resulting from any of our collaboration arrangements. Consideration that would be received for optional goods and/or services is excluded from the transaction price at contract inception.

We allocate the transaction price to each performance obligation identified in the contract on a relative standalone selling price basis. However, certain components of variable consideration are allocated specifically to one or more particular performance obligations in a contact to the extent both of the following criteria are met: (i) the terms of the payment relate specifically to the efforts to satisfy the performance obligation or transfer the distinct good or service and (ii) allocating the variable amount of consideration entirely to the performance obligation or the distinct good or service is consistent with the allocation objective of the standard whereby the amount allocated depicts the amount of consideration to which the entity expects to be entitled in exchange for transferring the promised goods or services. We develop assumptions that require judgment to determine the standalone selling price for each performance obligation identified in each contract. The key assumptions utilized in determining the standalone selling price for each performance obligation may include forecasted revenues, development timelines, estimated research and development costs, discount rates, likelihood of exercise and probabilities of technical and regulatory success.

Revenue is recognized based on the amount of the transaction price that is allocated to each respective performance obligation when or as the performance obligation is satisfied by transferring a promised good and/or service to the customer. For performance obligations that are satisfied over time, we recognize revenue by measuring the progress toward complete satisfaction of the performance obligation using a single method of measuring progress which depicts the performance in transferring control of the associated goods and/or services to the customer. We use input methods to measure the progress toward the complete satisfaction of performance obligations satisfied over time. We evaluate the measure of progress each reporting period and, if necessary, adjusts the measure of performance and related revenue recognition. Any such adjustments are recorded on a cumulative catch-up basis, which would affect revenue and net loss in the period of adjustment.

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

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

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

We make certain assumptions to value and expense our share-based compensation awards, as well as our Series 1 preferred stock (including related dividends), which as of October 2018 is no longer outstanding. In connection with valuing stock options we use the Black-Scholes valuation model, which requires us to estimate certain subjective assumptions. The key assumptions we make are: the expected volatility of our stock and the expected term of the award.

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. Such changes may lead to a significant change in the expense we recognize in connection with share-based payments.

Income Taxes

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

We account for uncertain tax positions using a “more-likely-than-not” threshold for recognizing and resolving uncertain tax positions. The evaluation of uncertain tax positions is based on factors that include, but are not limited to, changes in tax law, the measurement of tax positions taken or expected to be taken in tax returns, the effective settlement of matters subject to audit, new audit activity and changes in facts or circumstances related to a tax position. We evaluate uncertain tax positions on an annual basis and adjust the level of the liability to

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

Recent Accounting Pronouncements

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

Off-Balance Sheet Arrangements

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

Item 7A. Quantitative and Qualitative Disclosures About Market Risk

Our exposure to market risk is limited to our cash. The goals of our investment policy is the preservation of capital, fulfillment of liquidity needs, fiduciary control of cash and investments. We also seek to maximize income from our investments without assuming significant risk and consistent with regulatory limitations. 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, which is subject to minimal interest rate risk.

Effect of Currency Exchange Rates and Exchange Rate Risk Management

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

Item 8. Financial Statements and Supplementary Data

The information required by this Item 8 is contained on pages F-1 through F-40 of this Annual Report 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 Financial 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, 2019. Based on that evaluation, our Chief Executive Officer and Chief Financial Officer have concluded that as of December 31, 2019, our disclosure controls and procedures were not effective due to a material weakness identified in our internal control over financial reporting as described below under "Management's Report on Internal Control over Financial Reporting".

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. 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, 2019, 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. A material weakness is a deficiency, or a combination of deficiencies, in internal control over financial reporting, such that there is a reasonable possibility that a material misstatement of our annual or interim financial statements will not be prevented or detected on a timely basis. Based on this evaluation, management concluded that our internal control over financial reporting was not effective at December 31, 2019 because of the material weakness described below.

As of December 31, 2019, management identified a material weakness in the design and effectiveness of our internal control over financial reporting. We did not design and maintain effective controls relating to the monitoring and oversight of expensing third party clinical trial costs. Specifically, our internal controls were not designed effectively to provide reasonable assurance regarding the accurate and timely evaluation of the amount of third-party costs to record. There were no changes to any of our previously released financial statements. Based on this material weakness, our management concluded that at December 31, 2019, our internal control over financial reporting was not effective.

Remediation

We are committed and are taking steps necessary to remediate the control deficiencies that constituted the above material weakness by implementing changes to our internal control over financial reporting. We are in the process of designing and implementing measures to remediate the underlying causes of the control deficiencies that gave rise to the material weakness. In addition, we are providing in-house accounting personnel training to ensure that they have the relevant expertise related to the monitoring and oversight of expensing third party clinical trial costs. We will continue to monitor the effectiveness of these controls and will make any further changes management determines appropriate.

Changes in Internal Controls over Financial Reporting

Except for the material weakness discussed above, that has been assessed as a material weakness as of December 31, 2019, there were no other changes in our internal control over financial reporting (as defined in Rule 13a-15(f) of the Exchange Act) that occurred during the fiscal quarter ended December 31, 2019 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 under the sections titled *Proposal No. 1—Election of Directors, Current Directors, Director Nominees and Executive Officers, Information Regarding the Board of Directors and Corporate Governance* and *Beneficial 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 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, 2019 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	185,000	$ 4.80	—
2012 Stock Option Plan	5,657,879	3.90	2,503,508
Total:	5,842,879	$ 3.93	2,503,508
Equity compensation plans not approved by stockholders:			
Inducement Awards	1,030,000	5.80	—
Total:	1,030,000	$ 5.80	—

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 under the section titled *Beneficial 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 under the section titled *Certain Relationships and Related Transactions and Information Regarding the Board of Directors and Corporate Governance*.

Item 14. Principal Accountant Fees and Services

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

PART IV

Item 15. Exhibits, Financial Statement Schedules

(1) Financial Statements:

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

	Page
Reports of Independent Registered Public Accounting Firm	F-1
Balance Sheets as of December 31, 2019 and 2018	F-5
Statements of Operations for the Years Ended December 31, 2019, 2018, and 2017	F-6
Statements of Changes Stockholders' Equity (Deficit) for the Years Ended December 31, 2019, 2018, and 2017	F-7-9
Statements of Cash Flows for the Years Ended December 31, 2019, 2018, and 2017	F-10
Notes to Financial Statements	F-11

(2) Financial Statement Schedules:

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

(3) Exhibits:

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

Exhibit No.	Description of Document
4.3	Schedule identifying Material Terms of Options for the Purchase of Shares of Common Stock (incorporated by reference to Exhibit 4.7 to the Registrant's Annual Report on Form 10-KSB, SEC File No. 000-32353, filed March 20, 2006).
4.4	Form of Warrant to Purchase Common Stock (incorporated by reference to Exhibit 4.1 to the Registrant's Current Report on Form 8-K SEC File No. 001-33038 filed November 13, 2018).
4.5	Form of Warrant to Purchase Common Stock (incorporated by reference to Exhibit 4.1 to the Registrant's Current Report on Form 8-K SEC File No. 001-33038 filed September 13, 2019).
4.6	Form of Warrant to Purchase Common Stock (incorporated by reference to Exhibit 4.1 to the Registrant's Current Report on Form 8-K SEC File No. 001-33038 filed August 1, 2019).
4.7#*	Warrant to Purchase Common Stock issued to The University of Texas M. D. Anderson Cancer Center.
4.8*	Description of Securities Registered Pursuant to Section 12 of the Securities Exchange Act Of 1934, as amended.
10.1+	ZIOPHARM Oncology, Inc. Amended and Restated 2003 Stock Incentive Plan (incorporated by reference to Exhibit 10.1 to the Registrant's Annual Report on Form 10-K SEC File No. 001-33038 filed March 1, 2011).
10.2+	Form of Incentive Stock Option Agreement granted under the Registrant's 2003 Stock Option Plan (incorporated by reference to Exhibit 10.8 to the Registrant's Annual Report on Form 10-KSB, SEC File No. 000-32353, filed March 20, 2006).
10.3+	Form of Restricted Stock Agreement granted under the Registrant's 2003 Stock Option Plan (incorporated by reference to Exhibit 10.1 to the Registrant's Current Report on Form 8-K SEC File No. 001-33038 filed December 18, 2007).
10.4+	ZIOPHARM Oncology, Inc. 2012 Equity Incentive Plan (incorporated by reference to Exhibit 10.1 to the Registrant's Current Report on Form 8-K SEC File No. 001-33038 filed June 26, 2012).
10.5+	Form of Restricted Stock Agreement Granted Under the ZIOPHARM Oncology, Inc. 2012 Equity Incentive Plan (incorporated by reference to Exhibit 10.2 to the Registrant's Current Report on Form 8-K SEC File No. 001-33038 filed June 26, 2012).
10.6+	Form of Option Agreement Granted Under the ZIOPHARM Oncology, Inc. 2012 Equity Incentive Plan (incorporated by reference to Exhibit 10.3 to the Registrant's Current Report on Form 8-K SEC File No. 001-33038 filed June 26, 2012).
10.7	Form of Indemnity Agreement for directors and executive officers (incorporated by reference to Exhibit 99.1 to the Registrant's Current Report on Form 8-K, SEC File No. 001-33038, filed January 31, 2013).
10.8+	Employment Agreement by and between the Registrant and Laurence James Neil Cooper, M.D., Ph.D. dated as of May 5, 2015 (incorporated by reference to Exhibit 10.1 to the Registrant's Current Report on Form 8-K, SEC File No. 001-33038, filed May 7, 2015).
10.9+	Employment Agreement, dated as of April 23, 2019, by and between the Company and David Mauney, M.D. (incorporated by reference to Exhibit 10.1 to the Registrant's Current Report on Form 8-K, SEC File No. 001-33038, filed April 29, 2019).
10.10+	Employment Agreement, dated as of April 23, 2019, by and between the Company and Robert Hadfield (incorporated by reference to Exhibit 10.2 to the Registrant's Current Report on Form 8-K, SEC File No. 001-33038, filed April 29, 2019).

Exhibit No.	Description of Document
10.11+	Employment Agreement, dated as of June 4, 2019, by and between the Company and Sath Shukla (incorporated by reference to Exhibit 10.1 to the Registrant's Current Report on Form 8-K, SEC File No. 001-33038, filed July 24, 2019).
10.12	License Agreement by and among the Registrant, Intrexon Corporation and The University of Texas System Board of Regents on behalf of The University of Texas M.D. Anderson Cancer Center dated as of January 13, 2015 (incorporated by reference to Exhibit 10.5 to the Registrant's Current Report on Form 8-K, SEC File No. 001-33038, filed January 28, 2015).
10.13†	Exclusive License Agreement by and between the Registrant, Precigen, Inc. and Intrexon Corporation, dated October 5, 2018 (incorporated by reference to Exhibit 10.1 to the Registrant's Quarterly Report on Form 10-Q, SEC File No. 001-33038, filed November 9, 2018).
10.14†	License and Collaboration Agreement by and among the Registrant, Intrexon Corporation and ARES TRADING S.A. dated as of March 27, 2015 (incorporated by reference to Exhibit 10.1 to the Registrant's Current Report on Form 8-K, SEC File No. 001-33038, filed April 2, 2015).
10.15	Research and Development Agreement by and among the Registrant, Intrexon Corporation and The University of Texas M.D. Anderson Cancer Center dated as of August 17, 2015 (incorporated by reference to Exhibit 10.1 to the Registrant's Current Report on Form 8-K, SEC File No. 001-33038, filed August 21, 2015).
10.16	Amendment #1 to the Research and Development Agreement by and among the Registrant, Intrexon Corporation and The University of Texas M.D. Anderson Cancer Center dated as of August 30, 2016 (incorporated by reference to Exhibit 10.21 to the Registrant's Annual Report on Form 10-K, SEC File No. 001-33038, filed March 5, 2019).
10.17	Amendment #2 to the Research and Development Agreement by and among the Registrant, Intrexon Corporation and The University of Texas M.D. Anderson Cancer Center dated as of January 17, 2017 (incorporated by reference to Exhibit 10.22 to the Registrant's Annual Report on Form 10-K, SEC File No. 001-33038, filed March 5, 2019).
10.18	Amendment #3 to the Research and Development Agreement by and among the Registrant, Intrexon Corporation and The University of Texas M.D. Anderson Cancer Center dated as of November 14, 2017 (incorporated by reference to Exhibit 10.23 to the Registrant's Annual Report on Form 10-K, SEC File No. 001-33038, filed March 5, 2019).
10.19	Fourth Amendment to Research and Development Agreement, dated September 19, 2019 by and among the Registrant, The University of Texas MD Anderson Cancer Center and Precigen, Inc. (incorporated by reference to Exhibit 10.7 to the Registrant's Quarterly Report on Form 10-Q, SEC File No. 001-33038, filed November 7, 2019).
10.20#*	Fifth Amendment to Research and Development Agreement, dated October 22, 2019 by and among the Registrant and The University of Texas MD Anderson Cancer Center.
10.21#*	2019 Research and Development Agreement, dated October 22, 2019, by and between the Registrant and The University of Texas MD Anderson Cancer Center.
10.22#	Patent License Agreement, dated as of May 28, 2019, by and between the Company and the National Cancer Institute (incorporated by reference to Exhibit 10.3 to the Registrant's Quarterly Report on Form 10-Q, SEC File No. 001-33038, filed August 8, 2019).
10.23#*	Amendment to Patent License Agreement, dated as of January 8, 2020 , by and between the Company and the National Cancer Institute.
10.24#	Cooperative Research and Development Agreement, dated January 9, 2017, by and among the Registrant, the National Cancer Institute, and Intrexon Corporation (incorporated by reference to Exhibit 10.1 to the Registrant's Current Report on Form 8-K SEC File No. 001-33038, filed September 26, 2019).

Exhibit No.	Description of Document
10.25	Amendment #1 to the Cooperative Research and Development Agreement, dated March 23, 2018, by and among the Registrant, National Cancer Institute, Intrexon Corporation and Precigen, Inc (incorporated by reference to Exhibit 10.2 to the Registrant's Current Report on Form 8-K SEC File No. 001-33038, filed September 26, 2019).
10.26#	Amendment #2 to the Cooperative Research and Development Agreement, dated February 1, 2019, by and among the National Cancer Institute, the Registrant and Precigen, Inc (incorporated by reference to Exhibit 10.3 to the Registrant's Current Report on Form 8-K SEC File No. 001-33038, filed September 26, 2019).
10.27	Form of Securities Purchase Agreement, dated November 11, 2018, by and between the Registrant and certain investors (incorporated by reference to Exhibit 10.1 to the Registrant's Current Report on Form 8-K, SEC File No. 001-33038, filed November 13, 2018).
10.28	Form of Registration Rights Agreement, dated November 11, 2018, by and between the Registrant and certain investors (incorporated by reference to Exhibit 10.2 to the Registrant's Current Report on Form 8-K, SEC File No. 001-33038, filed November 13, 2018).
10.29	Form of Securities Purchase Agreement, dated July 26, 2019, by and between the Registrant and certain investors (incorporated by reference to Exhibit 10.1 to the Registrant's Current Report on Form 8-K SEC File No. 001-33038, filed August 1, 2019).
10.30	Form of Registration Rights Agreement, dated July 26, 2019, by and between the Registrant and certain investors (incorporated by reference to Exhibit 10.2 to the Registrant's Current Report on Form 8-K SEC File No. 001-33038, filed August 1, 2019).
10.31	Form of Securities Purchase Agreement, dated September 12, 2019, by and between the Registrant and an investor (incorporated by reference to Exhibit 10.1 to the Registrant's Current Report on Form 8-K SEC File No. 001-33038, filed September 13, 2019).
10.32	Form of Registration Rights Agreement, dated September 12, 2019, by and between the Registrant and an investor (incorporated by reference to Exhibit 10.2 to the Registrant's Current Report on Form 8-K SEC File No. 001-33038, filed September 13, 2019).
21.1*	Subsidiaries of the Registrant.
23.1*	Consent of Independent Registered Public Accounting Firm.
24.1*	Power of Attorney (incorporated by reference to the signature page of this Annual Report on Form 10-K).
31.1*	Certification of Principal 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 Principal Financial 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 Principal 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 Principal Financial 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

Exhibit No.	Description of Document
101.LAB*	XBRL Taxonomy Extension Label Linkbase Document
101.PRE*	XBRL Taxonomy Extension Presentation Linkbase Document

* Filed herewith.
** Furnished herewith.
\+ Indicates management contract or compensatory plan.
† Confidential treatment has been granted by the Securities and Exchange Commission as to certain portions of this document.
# Portions of this document (indicated by "[***]") have been omitted because they are not material and would likely cause competitive harm to Ziopharm Oncology, Inc. if disclosed.

SIGNATURES

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

ZIOPHARM ONCOLOGY, INC.

Date: March 2, 2020

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

Date: March 2, 2020

By: /s/ Satyavrat Shukla
Satyavrat Shukla
Executive Vice President and Chief Financial Officer
(*Principal Financial Officer*)

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

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

Signature	Title	Date
/s/ Laurence J.N. Cooper Laurence J.N. Cooper, M.D., Ph.D.	Chief Executive Officer and Director (*Principal Executive Officer*)	March 2, 2020
/s/ Satyavrat Shukla Satyavrat Shukla	Executive Vice President and Chief Financial Officer (*Principal Financial Officer*)	March 2, 2020
/s/ Kevin G. Lafond Kevin G. Lafond	Senior Vice President Finance, Chief Accounting Officer and Treasurer (*Principal Accounting Officer*)	March 2, 2020
/s/ Christopher Bowden Christopher Bowden	Director	March 2, 2020
/s/ Scott Braunstein Scott Braunstein	Director	March 2, 2020

Table of Contents

Signature	Title	Date
/s/ Elan Ezickson Elan Ezickson	Director	March 2, 2020
/s/ Heidi Hagen Heidi Hagen	Director	March 2, 2020
/s/ Douglas Pagán Douglas Pagán	Director	March 2, 2020
/s/ Scott Tariff Scott Tariff	Director	March 2, 2020

Table of Contents

ZIOPHARM Oncology, Inc.

INDEX TO FINANCIAL STATEMENTS

	Page
Reports of Independent Registered Public Accounting Firm	F-1
Balance Sheets as of December 31, 2019 and 2018	F-5
Statements of Operations for the Years Ended December 31, 2019, 2018, and 2017	F-6
Statements of Changes in Stockholders' Equity (Deficit) for the Years Ended December 31, 2019, 2018, and 2017	F-7-9
Statements of Cash Flows for the Years Ended December 31, 2019, 2018, and 2017	F-10
Notes to Financial Statements	F-11

REPORT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

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

Opinion on the Financial Statements

We have audited the accompanying balance sheets of ZIOPHARM Oncology, Inc. and subsidiaries (the Company) as of December 31, 2019 and 2018, the related statements of operations stockholders' equity (deficit) and cash flows for each of the three years in the period ended December 31, 2019, and the related notes to the financial statements (collectively, the financial statements). In our opinion, the financial statements present fairly, in all material respects, the financial position of the Company as of December 31, 2019 and 2018, and the results of its operations and its cash flows for each of the three years in the period ended December 31, 2019, in conformity with accounting principles generally accepted in the United States of America.

We have also audited, in accordance with the standards of the Public Company Accounting Oversight Board (United States) (PCAOB), the Company's internal control over financial reporting as of December 31, 2019, based on criteria established in Internal Control—Integrated Framework issued by the Committee of Sponsoring Organizations of the Treadway Commission in 2013, and our report dated March 2, 2020 expressed an adverse opinion on the Company's internal control over financial reporting because of a material weakness.

Basis for Opinion

These financial statements are the responsibility of the Company's management. Our responsibility is to express an opinion on the Company's financial statements based on our audits. We are a public accounting firm registered with the PCAOB and are required to be independent with respect to the Company in accordance with U.S. federal securities laws and the applicable rules and regulations of the Securities and Exchange Commission and the PCAOB.

We conducted our audits in accordance with the standards of the PCAOB. Those standards require that we plan and perform the audits to obtain reasonable assurance about whether the financial statements are free of material misstatement, whether due to error or fraud. Our audits included performing procedures to assess the risks of material misstatement of the financial statements, whether due to error or fraud, and performing procedures that respond to those risks. Such procedures included examining, on a test basis, evidence regarding the amounts and disclosures in the financial statements. Our audits also included evaluating the accounting principles used and significant estimates made by management, as well as evaluating the overall presentation of the financial statements. We believe that our audits provide a reasonable basis for our opinion.

Critical Audit Matters

The critical audit matter communicated below are matters arising from the current-period audit of the financial statements that were communicated or required to be communicated to the Company's Audit Committee and that: (1) relate to accounts or disclosures that are material to the financial statements and (2) involved our especially challenging, subjective, or complex judgments. The communication of critical audit matters does not alter in any way our opinion on the financial statements, taken as a whole, and we are not, by communicating the critical audit matters below, providing separate opinions on the critical audit matters or on the accounts or disclosures to which they relate.

Accounting for the Joint Venture

As described in Note 16 to the financial statements, the Company entered into a joint venture with TriArm Therapeutics, Ltd., to launch Eden BioCell, Ltd., to lead clinical development and commercialization of certain Sleeping Beauty-generated CAR-T therapies. The Company contributed certain intellectual property in exchange

for 10,000,000 ordinary shares of Eden BioCell. As a result of the design and purpose of Eden BioCell, management applied significant judgment in determining that Eden BioCell was considered a variable interest entity, or VIE. They , and concluded the equity interest in Eden BioCell would be accounted for under the equity method of accounting as the Company was not the primary beneficiary of the VIE as it did not have the power to direct the activities of the VIE that most significantly impact its performance. The Company determined that the contribution of certain intellectual property should be accounted for as a transfer on nonfinancial assets recognized at fair value. Management determined the intellectual property had a de minimis fair value as a result of the early stage of the technology and the likelihood of clinical success.

We identified the Company's accounting for the joint venture as a critical audit matter because auditing management's judgment around the proper accounting for the transaction required significant audit effort and a high degree of auditor judgment.

Our audit procedures related to the Company's accounting for the joint venture included the following, among others:

- We obtained and read the joint venture agreement, gained an understanding of the purpose and nature of the joint venture and the rights and control provided under the agreement, and evaluated management's documentation.
- We obtained an understanding of the relevant internal controls related to the accounting for the joint venture and tested such internal controls for design and operating effectiveness, including management review controls related to the proper application of the accounting guidance.
- We evaluated the Company's application of relevant accounting guidance and the consistency of management's methods and assumptions used in determining whether Eden BioCell is an equity method investment and whether the Company has control over the joint venture and the fair value determination for the equity method investment.

We have served as the Company's auditor since 2010.

/s/ RSM US LLP

Boston, Massachusetts
March 2, 2020

REPORT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

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

Opinion on the Internal Control Over Financial Reporting

We have audited ZIOPHARM Oncology, Inc. and subsidiaries's (the Company) internal control over financial reporting as of December 31, 2019, based on criteria established in *Internal Control — Integrated Framework* issued by the Committee of Sponsoring Organizations of the Treadway Commission in 2013. In our opinion, because of the effect of the material weakness described below on the achievement of the objectives of the control criteria, the Company has not maintained effective internal control over financial reporting as of December 31, 2019, based on criteria established in *Internal Control — Integrated Framework* issued by the Committee of Sponsoring Organizations of the Treadway Commission in 2013.

We have also audited, in accordance with the standards of the Public Company Accounting Oversight Board (United States) (PCAOB), the financial statements of the Company and our report dated March 2, 2020 expressed an unqualified opinion.

A material weakness is a deficiency, or a combination of deficiencies, in internal control over financial reporting, such that there is a reasonable possibility that a material misstatement of the company's annual or interim financial statements will not be prevented or detected on a timely basis. The following material weakness has been identified and included in management's assessment: Management did not design and maintain effective internal controls relating to the monitoring and oversight of expensing third party clinical trial costs. Specifically, their internal controls were not designed effectively to provide reasonable assurance regarding the accurate and timely evaluation of the amount of third party costs to record. This material weakness was considered in determining the nature, timing and extent of audit tests applied in our audit of the 2019 financial statements, and this report does not affect our report dated March 2, 2020 on those financial statements.

Basis for Opinion

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

We conducted our audit in accordance with the standards of the PCAOB. Those standards require that we plan and perform the audit to obtain reasonable assurance about whether effective internal control over financial reporting was maintained in all material respects. Our audit 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 audit also included performing such other procedures as we considered necessary in the circumstances. We believe that our audit provides a reasonable basis for our opinion.

Definition and Limitations of Internal Control Over Financial Reporting

A company's internal control over financial reporting is a process designed to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles. A company's internal control over financial reporting

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

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

/s/ RSM US LLP

Boston, Massachusetts

March 2, 2020

ZIOPHARM Oncology, Inc.

BALANCE SHEETS

(in thousands, except share and per share data)

	December 31, 2019	December 31, 2018
ASSETS		
Current assets:		
Cash and cash equivalents	$ 79,741	$ 61,729
Receivables	3,330	1,864
Prepaid expenses and other current assets	22,421	20,692
Total current assets	105,492	84,285
Property and equipment, net	1,110	1,097
Deposits	130	128
Right-of-use asset	2,272	—
Other non-current assets	110	9,541
Total assets	$ 109,114	$ 95,051
LIABILITIES, PREFERRED STOCK AND STOCKHOLDERS' EQUITY		
Current liabilities:		
Accounts payable	$ 906	$ 707
Accrued expenses	10,846	8,763
Lease liability - current portion	774	—
Deferred rent - current portion	—	13
Total current liabilities	12,526	9,483
Lease liability - noncurrent portion	1,578	—
Deferred rent - noncurrent portion	—	4
Total liabilities	14,104	9,487
Commitments and contingencies (Note 9)		
Preferred stock, $0.001 par value, 30,000,000 shares authorized		
Series 1 preferred stock, $1,200 stated value; 250,000 designated; 0 shares issued and outstanding at December 31, 2019 and 2018; liquidation value of $0 million at December 31, 2019 and 2018	—	—
Stockholders' equity:		
Common stock, $0.001 par value; 250,000,000 shares authorized; 181,803,320 and 161,066,136 shares issued and outstanding at December 31, 2019 and 2018, respectively	182	161
Additional paid-in capital	778,953	651,732
Accumulated deficit	(684,125)	(566,329)
Total stockholders' equity	95,010	85,564
Total liabilities and stockholders' equity	$ 109,114	$ 95,051

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,		
	2019	2018	2017
Collaboration revenue	$ —	$ 146	$ 6,389
Operating expenses:			
Research and development	38,331	34,134	45,084
General and administrative	19,527	19,918	14,798
Total operating expenses	57,858	54,052	59,882
Loss from operations	(57,858)	(53,906)	(53,493)
Other income, net	813	631	465
Non-cash inducement warrant expense	(60,751)	—	—
Change in fair value of derivative liabilities	—	158	(1,295)
Net loss	$ (117,796)	$ (53,117)	$ (54,323)
Preferred stock dividends	$ —	$ (16,998)	$ (18,938)
Settlement of a related party relationship	$ —	$ 207,361	$ —
Net income (loss) applicable to common stockholders	$ (117,796)	$ 137,246	$ (73,261)
Net income (loss) per share - basic	$ (0.70)	$ 0.96	$ (0.53)
Net income (loss) per share - diluted	$ (0.70)	$ 0.96	$ (0.53)
Weighted average common shares outstanding used to compute basic net income (loss) per share	167,952,114	143,508,674	136,938,264
Weighted average common shares outstanding used to compute diluted net income (loss) per share	167,952,114	143,710,160	136,938,264

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

ZIOPHARM Oncology, Inc.

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

(in thousands, except share and per share data)

	Series 1 Preferred Stock-Mezzanine		Common Stock		Additional Paid In Capital	Accumulated Deficit	Total Stockholders' Equity (Deficit)
	Shares	Amount	Shares	Amount			
Balance at December 31, 2016	106,184	$125,321	132,376,670	$ 132	$580,567	$ (657,997)	$ (77,298)
Cumulative effect adjustment ASU No. 2016-09	—	—	—	—	122	(122)	—
Exercise of stock options	—	—	59,864	1	87	—	88
Stock-based compensation	—	—	—	—	8,454	—	8,454
Issuance of restricted common stock	—	—	907,032	1	(1)	—	—
Repurchase of common stock	—	—	(394,267)	(1)	(2,058)	—	(2,059)
Issuance of common stock, net of commissions and expenses of $2.7 million	—	—	9,708,738	10	47,260	—	47,270
Preferred stock dividends	13,460	18,672	—	—	(18,938)	—	(18,938)
Net loss	—	—	—	—	—	(54,323)	(54,323)
Balance at December 31, 2017	119,644	$143,993	142,658,037	$ 143	$615,493	$ (712,442)	$ (96,806)

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

ZIOPHARM Oncology, Inc.

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

(in thousands, except share and per share data)

	Series 1 Preferred Stock-Mezzanine		Common Stock		Additional Paid In Capital	Accumulated Deficit	Total Stockholders' Equity (Deficit)
	Shares	Amount	Shares	Amount			
Adjustment for implementation of ASU No. 2014-09, Revenue from Contracts with Customers	—	—	—	—	—	(8,131)	(8,131)
Stock-based compensation	—	—	—	—	7,534	—	7,534
Issuance of restricted common stock	—	—	150,321	2	(1)	—	1
Exercise of employee stock options	—	—	104,166	2	240	—	242
Cancelled restricted common stock	—	—	(271,433)	(2)	3	—	1
Repurchase of restricted common stock	—	—	(514,349)	(3)	(1,621)	—	(1,624)
Issuance of warrants and common stock in a private placement, net of commissions and expenses of $2,898	—	—	18,939,394	19	47,082	—	47,101
Preferred stock dividends	11,415	16,775	—	—	(16,998)	—	(16,998)
Settlement of a related party relationship (Note 7)	(131,059)	(160,767)	—	—	—	207,361	207,361
Net loss	—	—	—	—	—	(53,117)	(53,117)
Balance at December 31, 2018	—	$ —	161,066,136	$ 161	$651,732	$ (566,329)	$ 85,564

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

ZIOPHARM Oncology, Inc.

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

(in thousands, except share and per share data)

	Series 1 Preferred Stock-Mezzanine		Common Stock		Additional Paid In Capital	Accumulated Deficit	Total Stockholders' Equity (Deficit)
	Shares	Amount	Shares	Amount			
Stock-based compensation			—	—	6,341	—	6,341
Issuance of restricted common stock			1,519,766	2	998	—	1,000
Exercise of employee stock options			443,051	—	1,219	—	1,219
Cancelled restricted common stock			(74,599)	—	—	—	—
Repurchase of restricted common stock			(225,339)	—	(653)	—	(653)
Issuance of inducement warrants			—	—	60,751		60,751
Issuance of common stock in connection with at the market offering, net of commssions and expenses of $0.1 million			1,271,274	1	6,084		6,085
Warrant exercise, net of commissions and expenses of $1.1 million			17,803,031	18	52,481	—	52,499
Net loss			—	—	—	(117,796)	(117,796)
Balance at December 31, 2019	—	$ —	181,803,320	$ 182	$778,953	$ (684,125)	$ 95,010

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,		
	2019	**2018**	**2017**
Cash flows from operating activities:			
Net loss	$ (117,796)	$ (53,117)	$ (54,323)
Adjustments to reconcile net loss to net cash used in operating activities:			
Depreciation	629	575	369
Stock-based compensation	7,341	7,534	8,454
Non-cash inducement warrant expense	60,751	—	—
Change in fair value of derivative liabilities	—	(158)	1,295
Change in operating assets and liabilities:			
(Increase) decrease in:			
Receivables	(1,466)	(1,845)	2
Prepaid expenses and other current assets	(1,729)	(1,263)	3,992
Deposits	(2)	—	—
Other noncurrent assets	9,431	3,942	(12,991)
Increase (decrease) in:			
Accounts payable	199	(3,709)	4,261
Accrued expenses	1,725	(1,145)	800
Deferred revenue	—	(146)	(6,389)
Deferred rent	—	(125)	(139)
Lease liabilities	63	—	—
Net cash used in operating activities	(40,854)	(49,457)	(54,669)
Cash flows from investing activities:			
Purchases of property and equipment	(284)	(459)	(737)
Net cash used in investing activities	(284)	(459)	(737)
Cash flows from financing activities:			
Proceeds from exercise of stock options	1,219	240	88
Issuance of restricted common stock	—	—	(2,059)
Repurchase of common stock	(653)	(1,622)	—
Proceeds from issuance of common stock, net	—	—	47,270
Proceeds from underwritten financing	—	47,101	—
Issuance of common stock upon exercise of warrants, net	52,499	—	—
Issuance of common stock in connection with an at the market offering, net	6,085	—	—
Cash paid for settlement of related party relationship	—	(5,408)	—
Net cash provided by financing activities	59,150	40,311	45,299
Net decrease in cash and cash equivalents, and restricted cash	18,012	(9,605)	(10,107)
Cash and cash equivalents, and restricted cash, beginning of period	61,729	71,334	81,441
Cash and cash equivalents, and restricted cash, end of period	$ 79,741	$ 61,729	$ 71,334
Supplementary disclosure of cash flow information:			
Bonus paid in common stock	$ 1,000	$ —	$ —
Fixed assets in accrued expenses	$ 358	$ —	$ —
Supplementary disclosure of noncash investing and financing activities:			
Noncash portion of related party relationship settlement	$ —	$ 212,769	$ —
Payment of Series 1 preferred stock dividends in preferred stock	$ —	$ 16,998	$ 18,938

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

ZIOPHARM Oncology, Inc.

NOTES TO FINANCIAL STATEMENTS

1. Organization

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

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

The Company has operated at a loss since its inception in 2003 and has no recurring revenues from operations. The Company anticipates that losses will continue for the foreseeable future. As of December 31, 2019, the Company has approximately $79.7 million of cash and cash equivalents, in addition to an aggregate of approximately $98.0 million of net proceeds that the Company raised in January and February 2020 from an underwritten public offering and its at-the-market facility. Given the Company's current development plans, the Company anticipates its cash resources, along with the proceeds raised from its recent financing activities, will be sufficient to fund its operations into mid-2022, and the Company has no committed sources of additional capital at this time. 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. If adequate additional funds are not available when required, or if the Company is unsuccessful in entering into partnership agreements for further development of our product candidates, management may need to curtail its development efforts and planned operations to conserve cash.

2. Financings

February 2020 Public Offering

On February 5, 2020, the Company entered into an underwriting agreement with Jefferies, as representative of the several underwriters named therein, relating to the issuance and sale of 27,826,086 shares of its common stock. The price to the public in the offering was $3.25 per share, and the underwriters agreed to purchase the shares from the Company pursuant to the underwriting agreement at a purchase price of $3.055 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 4,173,912 shares of common stock at a purchase price of $3.055 per share. The offering was made pursuant to the Company's effective registration statement on Form S-3ASR (File No. 333-232283) previously filed with the SEC, and a prospectus supplement thereunder. The underwriters purchased the 27,826,086 shares on February 5, 2020. The net proceeds from the offering were approximately $85.0 million after deducting underwriting discounts and offering expenses paid by the Company.

At-the-Market Offering

Subsequent to December 31, 2019, the Company sold an aggregate of 2,814,673 shares of its common stock. The offering was made pursuant to the Company's effective registration statement on Form S-3ASR (File No. 333-232283) previously filed with the SEC, and a prospectus supplement thereunder. The net proceeds from the offering were approximately $13.0 million after deducting underwriting discounts and offering expenses payable by the Company.

ZIOPHARM Oncology, Inc.

NOTES TO FINANCIAL STATEMENTS

2. Financings (Continued)

During the year ended December 31, 2019, the Company sold an aggregate of 1,271,274 shares of its common stock. The offering was made pursuant to the Company's effective registration statement on Form S-3ASR (File No. 333-232283) previously filed with the SEC, and a prospectus supplement thereunder. The net proceeds from the offering were approximately $6.1 million after deducting underwriting discounts and offering expenses payable by the Company.

November 2018 Private Placement and 2019 Inducement Warrants

On November 11, 2018, the Company entered into a securities purchase agreement with certain institutional and accredited investors pursuant to which it sold an aggregate of 18,939,394 immediately separable units at a price per unit of $2.64 to such investors, for net proceeds of approximately $47.1 million. Each unit was comprised of (i) one share of the Company's common stock, par value $0.001 per share and (ii) a warrant to purchase one share of common stock. The securities issued by the Company pursuant to the securities purchase agreement and to be issued upon exercise of the warrants were not registered under the Securities Act and may not be offered or sold in the United States absent registration or an applicable exemption from registration requirements. When issuing the units, the Company relied on the private placement exemption from registration provided by Section 4(a)(2) of the Securities Act and by Rule 506 of Registration D, promulgated thereunder and on similar exemptions under applicable state laws and filed a Form D with the SEC on November 19, 2018. On February 7, 2019, the Company filed a registration statement on Form S-3 registering the resale of shares issued pursuant to the securities purchase agreement and the resale of shares that may be issued upon exercise of the warrants.

July 2019 and September 2019 Warrant Exercise

On July 26, 2019 and September 12, 2019, the Company entered into agreements for the exercise of the warrants issued in November 2018 to purchase common stock in a private placement. Pursuant to the terms of the agreements, investors exercised warrants for an aggregate of 17,803,031 shares of common stock, at an exercise price of $3.01 per share. The Company issued new warrants to purchase up to 17,803,031 additional shares of common stock as an inducement for warrant holders to exercise their 2018 warrants early. The new warrants will become exercisable six months following the date of issuance, will expire on the fifth anniversary of the initial exercise date, and have an exercise price of $7.00 (Note 14). Proceeds from the exercise of the warrants, before deducting placement agent fees and other related expenses of $1.1 million were approximately $52.5 million. For the year ended December 31, 2019, the Company also recorded $60.8 million in non-cash inducement warrant expense, which is included in the Company's statement of operations.

May 2017 Offering

On May 11, 2017, the Company sold in an underwritten offering an aggregate of 9,708,738 shares of its common stock to a single investor. The price to the investor in the offering was $5.15 per share, and the underwriters agreed to purchase the shares from the Company pursuant to the underwriting agreement at a purchase price of $4.893 per share. The net proceeds from the offering were approximately $47.3 million after deducting underwriting commissions and estimated offering expenses payable by the Company.

3. Summary of Significant Accounting Policies

Basis of Presentation

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

ZIOPHARM Oncology, Inc.

NOTES TO FINANCIAL STATEMENTS

3. Summary of Significant Accounting Policies (Continued)

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 the financial statements are:

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

Subsequent Events

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

February 2020 Public Offering

On February 5, 2020, the Company entered into an underwriting agreement with Jefferies, as representative of the several underwriters named therein, relating to the issuance and sale of 27,826,086 shares of its common stock. The net proceeds from the offering were approximately $85.0 million after deducting underwriting discounts and offering expenses paid by the Company (see Note 2).

At-the-Market Offering

Subsequent to the balance sheet date, the Company sold an aggregate of 2,814,673 shares of its common stock. The offering was made pursuant to the Company's effective registration statement on Form S-3ASR (File No. 333-232283) previously filed with the SEC, and a prospectus supplement thereunder. The net proceeds from the offering were approximately $13.0 million after deducting underwriting discounts and offering expenses payable by the Company.

Amendment - License Agreement with the National Cancer Institute

On January 8, 2020, we amended the Patent License to expand the TCR library licensed from the NCI to include additional TCRs reactive to mutated KRAS and TP53 neoantigens. Under the amendment to the patent license, we agreed to pay the NCI a cash payment of $600,000 within sixty days of the amendment.

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. The following

ZIOPHARM Oncology, Inc.

NOTES TO FINANCIAL STATEMENTS

3. Summary of Significant Accounting Policies (Continued)

table provides a reconciliation of cash, cash equivalents, and restricted cash within the statement of financial position that sum to the total of the same such amounts shown in the statement of cash flows.

	December 31,		
(in thousands)	**2019**	**2018**	**2017**
Cash and cash equivalents	$79,741	$61,729	$70,946
Restricted cash included in prepaid expenses and other current assets	—	—	388
Total cash, cash equivalents, and restricted cash shown in the statement of cash flows	$79,741	$61,729	$71,334

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.

Long-Lived Assets

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

Operating Segments

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

Warrants

The Company assesses whether warrants issued require accounting as derivatives. The Company determined that the warrants were (1) indexed to the Company's own stock and (2) classified in stockholders' equity in accordance with Financial Accounting Standards Board ("FASB") Accounting Standards Codification ("ASC") Topic 815, *Derivatives and Hedging*. As such, the Company has concluded the warrants meet the scope exception for determining whether the instruments require accounting as derivatives and should be classified in stockholders' equity.

ZIOPHARM Oncology, Inc.

NOTES TO FINANCIAL STATEMENTS

3. Summary of Significant Accounting Policies (Continued)

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, 2019 and 2018 are as follows:

($ in thousands)		Fair Value Measurements at Reporting Date Using		
Description	Balance as of December 31, 2019	Quoted Prices in Active Markets for Identical Assets/Liabilities (Level 1)	Significant Other Observable Inputs (Level 2)	Significant Unobservable Inputs (Level 3)
Cash equivalents	$ 68,031	$ 68,031	$ —	$ —

($ in thousands)		Fair Value Measurements at Reporting Date Using		
Description	Balance as of December 31, 2018	Quoted Prices in Active Markets for Identical Assets/Liabilities (Level 1)	Significant Other Observable Inputs (Level 2)	Significant Unobservable Inputs (Level 3)
Cash equivalents	$ 24,437	$ 24,437	$ —	$ —

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

Revenue Recognition from Collaboration Agreements

The Company adopted Accounting Standards Codification, or ASC Topic 606, *Revenue from Contracts with Customers*, or ASC 606, using the modified retrospective approach on January 1, 2018. The Company completed its assessment and the implementation resulted in a cumulative effect adjustment to accumulated deficit as of January 1, 2018 of approximately $8.1 million and a corresponding increase to the contract liability (formerly deferred revenue). The adjustment to the Company's financial statements due to the adoption of ASC 606 is related to the Company's Ares Trading Agreement (Note 6), which was the Company's sole open revenue contract outstanding at January 1, 2018.

The Company primarily generates revenue through collaboration arrangements with strategic partners for the development and commercialization of product candidates. Commencing January 1, 2018, the Company recognized revenue in accordance with ASC 606 which replaced ASC 605, *Multiple Element Arrangements*, as

ZIOPHARM Oncology, Inc.

NOTES TO FINANCIAL STATEMENTS

3. Summary of Significant Accounting Policies (Continued)

used in historical years. The core principle of ASC 606 is that an entity should recognize revenue to depict the transfer of promised goods and/or services to customers in an amount that reflects the consideration to which the entity expects to be entitled in exchange for those goods and/or services. To determine the appropriate amount of revenue to be recognized for arrangements that the Company determines are within the scope of ASC 606, the Company performs the following steps: (i) identify the contract(s) with the customer, (ii) identify the performance obligations in the contract, (iii) determine the transaction price, (iv) allocate the transaction price to the performance obligations in the contract and (v) recognize revenue when (or as) each performance obligation is satisfied.

The Company recognizes collaboration revenue under certain of the Company's license or collaboration agreements that are within the scope of ASC 606. The Company's contracts with customers typically include promises related to licenses to intellectual property, research and development services and options to purchase additional goods and/or services. If the license to the Company's intellectual property is determined to be distinct from the other performance obligations identified in the arrangement, the Company recognizes revenue from non-refundable, up-front fees allocated to the license when the license is transferred to the licensee and the licensee is able to use and benefit from the license. For licenses that are bundled with other promises, the Company utilizes judgement to assess the nature of the combined performance obligation to determine whether the combined performance obligation is satisfied over time or at a point in time and, if over time, the appropriate method of measuring progress for purposes of recognizing revenue from non-refundable, up-front fees. Contracts that include an option to acquire additional goods and/or services are evaluated to determine if such option provides a material right to the customer that it would not have received without entering into the contract. If so, the option is accounted for as a separate performance obligation. If not, the option is considered a marketing offer which would be accounted for as a separate contract upon the customer's election.

The terms of the Company's arrangements with customers typically include the payment of one or more of the following: (i) non-refundable, up-front payment, (ii) development, regulatory and commercial milestone payments, (iii) future options and (iv) royalties on net sales of licensed products. Accordingly, the transaction price is generally comprised of a fixed fee due at contract inception and variable consideration in the form of milestone payments due upon the achievement of specified events and tiered royalties earned when customers recognize net sales of licensed products. The Company measures the transaction price based on the amount of consideration to which it expects to be entitled in exchange for transferring the promised goods and/or services to the customer. The Company utilizes the most likely amount method to estimate the amount of variable consideration, to predict the amount of consideration to which it will be entitled for its one open contract. Amounts of variable consideration are included in the transaction price to the extent that it is probable that a significant reversal in the amount of cumulative revenue recognized will not occur when the uncertainty associated with the variable consideration is subsequently resolved. At the inception of each arrangement that includes development and regulatory milestone payments, the Company evaluates whether the associated event is considered probable of achievement and estimates the amount to be included in the transaction price using the most likely amount method. Milestone payments that are not within the control of the Company or the licensee, such as those dependent upon receipt of regulatory approval, are not considered to be probable of achievement until the triggering event occurs. At the end of each reporting period, the Company reevaluates the probability of achievement of each milestone and any related constraint, and if necessary, adjusts its estimate of the overall transaction price. Any such adjustments are recorded on a cumulative catch-up basis, which would affect revenue and net loss in the period of adjustment. For arrangements that include sales-based royalties, including milestone payments based upon the achievement of a certain level of product sales, the Company recognizes revenue upon the later of: (i) when the related sales occur or (ii) when the performance obligation to which some or all of the payment has been allocated has been satisfied (or partially satisfied). To date, the Company has not recognized

ZIOPHARM Oncology, Inc.

NOTES TO FINANCIAL STATEMENTS

3. Summary of Significant Accounting Policies (Continued)

any development, regulatory or commercial milestones or royalty revenue resulting from any of its collaboration arrangements. Consideration that would be received for optional goods and/or services is excluded from the transaction price at contract inception.

The Company allocates the transaction price to each performance obligation identified in the contract on a relative standalone selling price basis. However, certain components of variable consideration are allocated specifically to one or more particular performance obligations in a contact to the extent both of the following criteria are met: (i) the terms of the payment relate specifically to the efforts to satisfy the performance obligation or transfer the distinct good or service and (ii) allocating the variable amount of consideration entirely to the performance obligation or the distinct good or service is consistent with the allocation objective of the standard whereby the amount allocated depicts the amount of consideration to which the entity expects to be entitled in exchange for transferring the promised goods or services. The Company develops assumptions that require judgment to determine the standalone selling price for each performance obligation identified in each contract. The key assumptions utilized in determining the standalone selling price for each performance obligation may include forecasted revenues, development timelines, estimated research and development costs, discount rates, likelihood of exercise and probabilities of technical and regulatory success.

Revenue is recognized based on the amount of the transaction price that is allocated to each respective performance obligation when or as the performance obligation is satisfied by transferring a promised good and/or service to the customer. For performance obligations that are satisfied over time, the Company recognizes revenue by measuring the progress toward complete satisfaction of the performance obligation using a single method of measuring progress which depicts the performance in transferring control of the associated goods and/or services to the customer. The Company uses input methods to measure the progress toward the complete satisfaction of performance obligations satisfied over time. The Company evaluates the measure of progress each reporting period and, if necessary, adjusts the measure of performance and related revenue recognition. Any such adjustments are recorded on a cumulative catch-up basis, which would affect revenue and net loss in the period of adjustment.

The Company recognized the upfront payment received in 2015 associated a former open contract as a contract liability upon receipt of payment as it requires deferral of revenue recognition to a future period until the Company performs its obligations under the arrangement. Amounts expected to be recognized as revenue within the twelve months following the balance sheet date were classified in current liabilities. Amounts not expected to be recognized as revenue within the twelve months following the balance sheet date were classified as contract liabilities, net of current portion. The Company determined that there were three performance obligations; the first performance obligation consists of the license and research development services and the other two performance obligations are material rights as it relates to potential future targets that have not yet been identified. As described above, the transaction price of $57.5 million was allocated to the performance obligations based on their relative standalone selling prices.

There were multiple distinct performance obligations, including material rights; thus, the Company allocated the transaction price to each distinct performance obligation based on its relative standalone selling price. The standalone selling price is generally determined based on the prices charged to customers or using expected cost-plus margin. Revenue is recognized by measuring the progress toward complete satisfaction of the performance obligations using an input measure. Furthermore, the Company has not capitalized any contract costs under the guidance in ASC 340-40, *Other Assets and Deferred Costs: Contracts with Customers*.

The Company did not believe that any variable consideration should be included in the transaction price at the date of adoption of ASC 606 on January 1, 2018. Such assessment considered the application of the constraint to

ZIOPHARM Oncology, Inc.

NOTES TO FINANCIAL STATEMENTS

3. Summary of Significant Accounting Policies (Continued)

ensure that estimates of variable consideration would be included in the transaction price only to the extent the Company had a high degree of confidence that revenue would not be reversed in a subsequent reporting period. The Company will re-evaluate the transaction price, including the estimated variable consideration included in the transaction price and all constrained amounts, in each reporting period and as other changes in circumstances occur.

Impact of Topic 606 Adoption

As a result of adopting ASC 606, the Company recorded an $8.1 million adjustment to the opening balance of accumulated deficit in the first quarter of 2018 as a result of the treatment of the up-front consideration received in July 2015 under ASC 605-25 versus ASC 606. Refer below for a summary of the amount by which each financial statement line item was affected by the impact of the cumulative adjustment:

($ in thousands)	Impact of Topic 606 Adoption on the Balance Sheet as of January 1, 2018		
Description	As reported under Topic 606	Adjustments	Balances without adoption of Topic 606
Contract liability, current portion	$ 622	$ (5,767)	$ 6,389
Contract liability, net of current portion	$ 49,037	$ 13,898	$ 35,139
Accumulated deficit	$ (720,573)	$ (8,131)	$ (712,442)

($ in thousands)	Impact of Topic 606 Adoption on the Statement of Operations for the Year Ended December 31, 2018		
Description	As reported under Topic 606	Adjustments	Balances without adoption of Topic 606
Collaboration revenue	$ 146	$ (4,732)	$ 4,878
Net loss	$ (53,117)	$ (4,732)	$ (48,385)
Net income (loss) applicable to common shareholders	$ 137,246	$ (4,732)	$ 141,978
Net income (loss) per share - basic	$ 0.96	$ (0.03)	$ 0.99
Net income (loss) per share - diluted	$ 0.96	$ (0.03)	$ 0.99

($ in thousands)	Impact of Topic 606 Adoption on the Statement of Cash Flows for the Year Ended December 31, 2018		
Description	As reported under Topic 606	Adjustments	Balances without adoption of Topic 606
Net loss	$ (53,117)	$ (4,732)	$ (48,385)
Changes in contract liability	$ —	$ —	$ —

The most significant change above relates to the Company’s collaboration revenue, which to date has been exclusively generated from its collaboration arrangement with Ares Trading and PGEN Therapeutics, a wholly owned subsidiary of Precigen Inc., or Precigen, which was formerly known as Intrexon Corporation (Note 8). Under ASC 605, the Company accounted for the up-front payment over the estimated period of performance of the research and development services which was estimated to be 9 years. In connection with the adoption of ASC 606, the Company uses cost-based input method to measure progress because such method best reflects the

ZIOPHARM Oncology, Inc.

NOTES TO FINANCIAL STATEMENTS

3. Summary of Significant Accounting Policies (Continued)

satisfaction of the performance obligation. In applying the cost-based input method of revenue recognition, the Company uses actual costs incurred relative to the budgeted costs to complete the research programs. These costs consist primarily of internal full-time equivalent effort and third-party contract costs. Revenue is recognized based on actual costs incurred as a percentage of total budgeted costs. As a result, although the performance obligations noted above and identified under ASC 606 were generally consistent with the units of account identified under ASC 605, the timing of the allocation of the transaction price to the identified performance obligations under ASC 606 differed from the allocations of consideration under ASC 605. Accordingly, the transaction price ultimately allocated to each performance obligation under ASC 606 differed from the amounts allocated under ASC 605. Additionally, at December 31, 2018, the contract liability is $0 under both methods of revenue recognition (Note 7). There is no revenue related to the year ended December 31, 2019.

Research and Development Costs

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

Income Taxes

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

The Company accounts for uncertain tax positions using a “more-likely-than-not” threshold for recognizing and resolving uncertain tax positions. The evaluation of uncertain tax positions is based on factors including, but not limited to, changes in tax law, the measurement of tax positions taken or expected to be taken in tax returns, the effective settlement of matters subject to audit, new audit activity and changes in facts or circumstances related to a tax position. The Company evaluates this tax position on an annual basis. The Company also accrues for potential interest and penalties, related to unrecognized tax benefits in income tax expense (Note 11).

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, 2019, 2018, and 2017 and did not capitalize any such costs

ZIOPHARM Oncology, Inc.

NOTES TO FINANCIAL STATEMENTS

3. Summary of Significant Accounting Policies (Continued)

on the balance sheets. The Company recognized $4.0 million, $3.0 million, and $2.5 million of compensation expense related to stock options during the years ended December 31, 2019, 2018, and 2017, respectively. In the years ended December 31, 2019, 2018, and 2017, the Company recognized $2.3 million, $4.5 million, and $6.0 million of compensation expense, respectively, related to restricted stock (Note 14). The total compensation expense relating to vesting of stock options and restricted stock awards for the years ended December 31, 2019, 2018, and 2017 was $6.3 million, $7.5 million, and $8.5 million, respectively. The following table presents share-based compensation expense included in the Company's Statements of Operations:

	Year ended December 31,		
(in thousands)	**2019**	**2018**	**2017**
Research and development	$1,461	$1,683	$2,401
General and administrative	4,880	5,851	6,053
Share based employee compensation expense before tax	$6,341	$7,534	$8,454
Income tax benefit	—	—	—
Net share based employee compensation expense	$6,341	$7,534	$8,454

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 2019, 2018, and 2017 was approximately $2.47, $1.64, and $3.94 per share, respectively. Assumptions regarding volatility, expected term, dividend yield and risk-free interest rate are required for the Black-Scholes model. The volatility assumption is based on the Company's historical experience. The risk-free interest rate is based on a U.S. treasury note with a maturity similar to the option award's expected life. The expected life represents the average period of time that options granted are expected to be outstanding. The Company calculated expected term using the simplified method described in SEC Staff Accounting Bulletin, or SAB, No. 107 and No. 110 as it continues to meet the requirements promulgated in SAB No. 110. The assumptions for volatility, expected life, dividend yield and risk-free interest rate are presented in the table below:

	2019	**2018**	**2017**
Weighted average risk-free interest rate	1.39 - 2.53%	2.55 - 3.06%	1.85 - 2.27%
Expected life in years	5.75 - 6.25	6	6
Expected volatility	71.39 - 85.00%	80.75 - 84.71%	80.31 - 81.03%
Expected dividend yield	0	0	0

Net Income (Loss) Per Share

Basic net loss per share is computed by dividing net income (loss) by the weighted average number of common shares outstanding for the period. Diluted earnings (loss) per share is computed using the weighted-average number of common shares outstanding during the period, plus the dilutive effect of outstanding options and warrants, using the treasury stock method and the average market price of the Company's common stock during the applicable period.

	For the Year Ended December 31,		
in thousands, except share and per share data	2019	2018	2017
Basic			
Net loss	$(117,796)	$ (53,117)	$(54,323)
Preferred stock dividends	—	(16,998)	(18,938)
Settlement of a related party relationship	—	207,361	—

ZIOPHARM Oncology, Inc.

NOTES TO FINANCIAL STATEMENTS

3. Summary of Significant Accounting Policies (Continued)

in thousands, except share and per share data	For the Year Ended December 31, 2019	2018	2017
Net income / (loss) applicable to common shareholders	$ (117,796)	$ 137,246	$ (73,261)
Weighted-average common shares outstanding	167,952,114	143,508,674	136,938,264
Earnings per share, basic	$ (0.70)	$ 0.96	$ (0.53)
Diluted			
Net Loss	$ (117,796)	$ (53,117)	$ (54,323)
Preferred stock dividends	—	(16,998)	(18,938)
Precigen license transaction	—	207,361	—
Net income / (loss) applicable to common shareholders	$ (117,796)	$ 137,246	$ (73,261)
Weighted-average common shares outstanding	167,952,114	143,508,674	136,938,264
Effect of dilutive securities			
Stock options	—	201,362	—
Unvested restricted common stock	—	124	—
Warrants	—	—	—
Dilutive potential common shares	—	201,486	—
Shares used in calculating diluted earnings per share	167,952,114	143,710,160	136,938,264
Earnings per share, diluted	$ (0.70)	$ 0.96	$ (0.53)

Certain shares related to some of the Company's outstanding common stock options, unvested restricted stock, preferred stock, and warrants have not been included in the computation of diluted net earnings (loss) per share for the years ended December 31, 2019, 2018 and 2017 as the result would be antidilutive. Such potential common shares at December 31, 2019, 2018, and 2017 consist of the following:

	December 31, 2019	2018	2017
Stock options	6,872,879	5,075,723	4,352,135
Unvested restricted stock	939,636	681,946	1,808,559
Preferred stock	—	—	34,134,524
Warrants	22,272,727	18,939,394	—
	30,085,242	24,697,063	40,295,218

During the year ended December 31, 2018, the Company and PGEN, entered into a License Agreement to replace all existing agreements between the companies that provides the Company with certain exclusive and non-exclusive rights to technology controlled by PGEN. The License Agreement was dated October 5, 2018. In consideration of the Company entering into the License Agreement, Precigen agreed to forfeit and return to the

ZIOPHARM Oncology, Inc.

NOTES TO FINANCIAL STATEMENTS

3. Summary of Significant Accounting Policies (Continued)

Company all shares of the Company's Series 1 Preferred Stock held by or payable to Precigen as of the date of the License Agreement (Note 7).

New Accounting Pronouncements

In August 2018, the FASB issued ASU No. 2018-13, *Fair Value Measurement (Topic 820): Disclosure Framework—Changes to the Disclosure Requirements for Fair Value Measurement*, or ASU 2018-03. The guidance in this ASU modify the disclosure requirements on fair value measurements in Topic 820, Fair Value Measurement. Under the new guidance, transfers between asset classes and the valuation related to level 3 assets is modified. The new standard is effective for annual reporting periods beginning after December 15, 2019, including interim reporting periods within each annual reporting period. The Company is currently evaluating the impact of the adoption of this ASU on the financial statements.

In June 2018, the FASB issued ASU No. 2018-07, *Compensation—Stock Compensation (Topic 718): Improvements to Nonemployee Share-Based Payment Accounting*, or ASU 2018-07. The guidance in this ASU expand the scope of Topic 718 to include share-based payment transactions for acquiring goods and services from nonemployees. The new standard was effective for annual reporting periods beginning after December 15, 2018, including interim reporting periods within each annual reporting period. The Company adopted this ASU on January 1, 2019. The adoption did not have a material impact on the Company's financial statements.

In February 2016, the FASB issued ASU No. 2016-02, *Leases (Topic 842)*, which requires lessees to recognize a right-of-use asset and lease liability for most lease arrangements. The Company adopted ASU No. 2016-02, on January 1, 2019 using the effective date method, in which it did not restate prior periods. Upon adoption, the Company elected the package of practical expedients permitted under the transition guidance within Topic 842 which, among other things, allowed it to carry forward the historical lease classification. The Company does not allocate consideration in its leases to lease and non-lease components and does not record leases on its balance sheets with terms of 12 months or less. Refer to Note 8—*Leases* for further details.

In May 2017, the FASB issued ASU No. 2017-09, *Compensation—Stock Compensation* (Topic 718): *Scope of Modification Accounting*, or ASU 2017-09, to clarify when to account for a change to the terms or conditions of a share-based payment award as a modification. Under this new guidance, modification accounting is required if the fair value, vesting conditions, or classification of the award changes as a result of the change in terms or conditions. ASU 2017-09 is effective for annual reporting periods beginning after December 15, 2017, including interim reporting periods within each annual reporting period. The Company adopted this standard on January 1, 2018. The adoption did not have any impact on the Company's financial statements.

ZIOPHARM Oncology, Inc.

NOTES TO FINANCIAL STATEMENTS

4. Property and Equipment, net

Property and equipment, net, consists of the following:

(in thousands)	December 31, 2019	2018
Office and computer equipment	$ 1,436	$ 1,249
Software	1,030	1,030
Leasehold improvements	1,892	1,839
Research and development equipment	1,195	1,182
Capital in-process	389	—
	5,942	5,300
Less: accumulated depreciation	(4,832)	(4,203)
Property and equipment, net	$ 1,110	$ 1,097

Depreciation charged to the statement of operations for the years ended December 31, 2019, 2018, and 2017 was $629 thousand, $575 thousand, and $369 thousand, respectively.

5. Accrued Expenses

Accrued expenses consist of the following:

(in thousands)	December 31, 2019	2018
Clinical services	$ 5,247	$3,003
Employee compensation	1,910	1,786
Preclinical services	1,147	1,247
Professional services	991	745
Manufacturing services	586	1,164
Accrued vacation	489	363
Payroll taxes and benefits	284	349
Other consulting services	192	106
Total	$10,846	$8,763

6. Related Party Transactions

Collaborations with Precigen/ PGEN

During the year ended December 31, 2018, the Company and PGEN entered into an Exclusive License Agreement (Note 7).

During the year ended December 31, 2018, the Company issued an aggregate of 11,415 shares of Series 1 preferred stock to Precigen, the holder of all of the outstanding shares of the Company's Series 1 preferred stock, as monthly dividend payments. The Company recorded such shares of Series 1 preferred stock at a fair value of $18.9 million, which is a component of temporary equity and recorded a loss on the change of the derivative liabilities in the amount of $1.3 million. See Notes 3 and 13 for additional discussion regarding the accounting for and valuation of these derivative financial instruments.

ZIOPHARM Oncology, Inc.

NOTES TO FINANCIAL STATEMENTS

6. Related Party Transactions (Continued)

During the years ended December 31, 2019, 2018, and 2017, the Company expensed $3.0 million, $8.1 million, and $21.4 million, respectively, for services performed by Precigen. As of December 31, 2019, and 2018, the Company recorded $0.1 million and $1.9 million, respectively, in current liabilities on its balance sheet for amounts due to Precigen.

Collaboration with PGEN and MD Anderson

On January 13, 2015, the Company, together with Precigen, entered into the MD Anderson License with MD Anderson (which Precigen subsequently assigned to PGEN). Pursuant to the MD Anderson License, the company, together with PGEN, hold an exclusive, worldwide license to certain technologies owned and licensed by MD Anderson including technologies relating to novel CAR T-cell therapies, non-viral gene transfer systems, genetic modification and/or propagation of immune cells and other cellular therapy approaches, Natural Killer, or NK Cells, and TCRs, arising from the laboratory of Laurence Cooper, M.D., Ph.D., who became the Company's Chief Executive Officer in May 2015 and was formerly a tenured professor of pediatrics at MD Anderson and is now currently a visiting scientist under that institution's policies. In partial consideration for entering into the MD Anderson License, the Company issued MD Anderson an aggregate of 11,722,163 shares of common stock for which the Company incurred a $67.3 million charge recorded in 2015.

During the year ending December 31, 2019, the Company did not make any payments to MD Anderson, and the total aggregate payments in connection with this agreement are $41.9 million. The net balance of cash resources on hand at MD Anderson available to offset expenses and future costs is $20.3 million, which is included in prepaid expenses and other current assets. The classification is based on management's current estimate of plans to utilize the prepaid balance and is subject to revision on a quarterly basis.

7. Settlement of a Related Party Relationship

Exclusive License Agreement with PGEN Therapeutics

On October 5, 2018, the Company entered into the license agreement with PGEN. As between the Company and PGEN, the terms of the License Agreement replace and supersede the terms of: (a) that certain Exclusive Channel Partner Agreement by and between the Company and Precigen, dated January 6, 2011, as amended by the First Amendment to Exclusive Channel Partner Agreement effective September 13, 2011, the Second Amendment to the Exclusive Channel Partner Agreement effective March 27, 2015, and the Third Amendment to Exclusive Channel Partner Agreement effective June 29, 2016, which was subsequently assigned by Precigen to PGEN; (b) certain rights and obligations pursuant to that certain License and Collaboration Agreement effective March 27, 2015 between ZIOPHARM, Precigen and ARES TRADING Trading S.A., or Ares Trading, a subsidiary of Merck KGaA, or Merck, as assigned by Precigen to PGEN, or the Ares Trading Agreement; (c) that certain License Agreement between the Company, Precigen, and MD Anderson, with an effective date of January 13, 2015, or the MD Anderson License, which was subsequently assigned by Precigen and assumed by PGEN effective as of January 1, 2018; and (d) that certain Research and Development Agreement between the Company, Precigen and MD Anderson with an effective date of August 17, 2015, or the Research and Development Agreement, and any amendments or statements of work thereto.

Pursuant to the terms of the License Agreement, PGEN has granted the Company exclusive, worldwide rights to research, develop and commercialize (i) products utilizing PGEN's RheoSwitch® gene switch, or RTS®, for the treatment of cancer, referred to as IL-12 Products, (ii) CAR products directed to (A) CD19 for the treatment of cancer, referred to as CD19 Products, and (B) a second target for the treatment of cancer, subject to the rights of

ZIOPHARM Oncology, Inc.

NOTES TO FINANCIAL STATEMENTS

7. Settlement of a Related Party Relationship (Continued)

Ares Trading to pursue such target under the Ares Trading Agreement, and (iii) T-cell receptor, or TCR, products designed for neoantigens for the treatment of cancer. PGEN has also granted the Company an exclusive, worldwide, royalty-bearing, sub-licensable license for certain patents relating to the *Sleeping Beauty* technology to research, develop and commercialize TCR products for both neoantigens and shared antigens for the treatment of cancer, referred to as TCR Products.

The Company is solely responsible for all aspects of the research, development and commercialization of the exclusively licensed products for the treatment of cancer. The Company is required to use commercially reasonable efforts to develop and commercialize IL-12 Products and CD19 Products and after a two-year period, the TCR Products.

PGEN has also granted the Company an exclusive, worldwide, royalty-bearing, sub-licensable license to research, develop and commercialize products utilizing an additional construct that expresses RTS IL-12 for the treatment of cancer, referred to as Gorilla IL-12 Products.

In consideration of the licenses and other rights granted by PGEN, we will pay PGEN an annual license fee of $100 thousand and we have agreed to reimburse PGEN for certain historical costs of the licensed programs up to $1.0 million, payable quarterly. The Company determined that the fair value of this program was $1.0 million and this was expensed in accordance with ASC 730, Research and Development during the year ended December 31, 2018. The Company recorded a liability for $0.1 million and $1.0 million for the years ended December 31, 2019 and 2018, respectively, and has included these amounts in accrued expenses on the balance sheet.

The agreement also calls for an annual license fee of $100 thousand as long as the agreement is effective. The Company will also make milestone payments totaling up to an additional $52.5 million for each exclusively licensed program upon the initiation of later stage clinical trials and upon the approval of exclusively licensed products in various jurisdictions. In addition, the Company will pay PGEN tiered royalties ranging from low-single digit to high-single digit on the net sales derived from the sales of any approved IL-12 Products and CAR Products. The Company will also pay PGEN royalties ranging from low-single digit to mid-single digit on the net sales derived from the sales of any approved TCR Products, up to a maximum royalty amount of $100.0 million in the aggregate. The Company will also pay PGEN 20% of any sublicensing income received by the Company relating to the licensed products.

The Company is responsible for all development costs associated with each of the licensed products, other than Gorilla IL-12 Products. The Company and PGEN will share the development costs and operating profits for Gorilla IL-12 Products, with the Company responsible for 80% of the development costs and receiving 80% of the operating profits, and PGEN responsible for the remaining 20% of the development costs and receiving 20% of the operating profits.

PGEN will pay the Company royalties ranging from low-single digits to mid-single digits on the net sales derived from the sale of PGEN’s CAR products, up to $50.0 million.

In consideration of the Company entering into the License Agreement, Precigen forfeited and returned to the Company all shares of the Company’s Series 1 preferred stock held by or payable to Precigen as of the date of the License Agreement. In addition, PGEN is required to transfer all of Ziopharm’s rights and obligations under the Ares Trading Agreement to Precigen (or its’ affiliate). As a result, Ziopharm shall not be responsible for any remaining obligations under the Merck Agreement. Additionally, Precigen forfeited and returned to the Company

ZIOPHARM Oncology, Inc.

NOTES TO FINANCIAL STATEMENTS

7. Settlement of a Related Party Relationship (Continued)

all shares of the Company's Series 1 preferred stock held by or payable to Precigen as of the date of the License Agreement.

The Company determined that this transaction represented a capital transaction between related parties. The Company fair valued the preferred stock and the derivative liability on the date of the transaction, noting a total fair value of $163.3 million. The relinquishment of the Ziopharm's obligation under the Ares Trading Agreement was also considered part of the overall capital transaction. The Company recognized an additional credit to accumulated deficit of $49.5 million as a result of the relief of the obligation under the Ares Trading Agreement (Note 7). The total amount of the settlement was $212.8 million.

The Company incurred approximately $7.4 million of transaction advisory costs with third-party vendors, of which $5.4 million was considered a direct cost associated with the Series 1 preferred stock extinguishment and is also included as part of the consideration transferred. The remaining $2.0 million of transaction costs were recognized as an expense during the year ended December 31, 2018.

The Company recognized a net credit to accumulated deficit of $207.3 million, calculated as the difference in the carrying value of the Series 1 preferred stock, derivative liability, and contract liability, and the consideration transferred of $5.4 million, in connection with the transaction. This amount is included in net income available to common shareholders in the calculation of earnings per share for the year ended December 31, 2018 (Note 3).

8. Leases

Operating Leases

The Company adopted FASB ASU No. 2016-02, *Leases (Topic 842)* on January 1, 2019 using the effective date method, in which it did not restate prior periods. Upon adoption, the Company elected the package of practical expedients permitted under the transition guidance within Topic 842 which, among other things, allowed it to carry forward the historical lease classification. The Company does not allocate consideration in its leases to lease and non-lease components and does not record leases on its balance sheets with terms of 12 months or less.

The Company uses its estimated incremental borrowing rate, which is derived from information available at the lease commencement date, in determining the present value of lease payments. The Company's incremental borrowing rate represents the rate of interest that it would have to pay to borrow over a similar term an amount equal to the lease payments in a similar economic environment. The Company considers publicly available data for instruments with similar terms and characteristics when determining its incremental borrowing rates.

The adoption of Topic 842 resulted in recognition of approximately $1.6 million of right-of-use assets and $1.6 million of lease liabilities on the Company's balance sheets on January 1, 2019. The adoption did not have a material impact on the Company's statements of operations or accumulated deficit. The Company will review the classification of newly entered leases as either an operating or a finance lease and recognize a related right-of-use asset and lease liabilities on its balance sheets upon commencement.

In June 2012, the Company entered into a master lease for the Company's corporate office headquarters in Boston, which was originally set to expire in August 2016, but renewed through August 31, 2021. As of December 31, 2019, and December 31, 2018, a total security deposit of $0.1 million is included in deposits on the Company's balance sheet. On January 30, 2018, the Company entered into a lease agreement for office space in Houston at MD Anderson. Under the terms of the MD Anderson Lease, the Company leases approximately

ZIOPHARM Oncology, Inc.

NOTES TO FINANCIAL STATEMENTS

8. Leases (Continued)

two hundred and ten square feet and are required to make rental payments at an average monthly rate of approximately $1.0 thousand through April 2021. All future rent expense incurred in Houston, will be deducted from the Company's prepayments at MD Anderson.

On March 12, 2019, the Company entered into a lease agreement for office space in Houston. Under the terms of the First Houston Lease agreement, the Company leases approximately one thousand and thirty-eight square feet and is required to make rental payments at an average monthly rate of approximately $2.0 thousand through April 2021. On October 15, 2019, the Company entered into a lease agreement for additional office space in Houston. Under the terms of the Second Houston Lease, the Company leases approximately eight thousand four hundred and forty-three square feet and is initially required to make rental payments of approximately $17.0 thousand through February 2027, subject to an annual base rent increase of approximately 3.0% throughout the term.

The components of lease expense were as follows:

(in thousands)	Year Ended December 31, 2019
Operating lease cost	$ 772
Total lease cost	$ 772
Weighted-average remaining lease term (years)	4.42
Weighted-average discount rate	8.00%

Cash paid for amounts included in the measurement of the lease liabilities were $0.7 million for the year-ended December 31, 2019. The Company recognized new operating lease assets obtained in exchange for operating lease liabilities of $1.2 million for the year-ended December 31, 2019.

As of December 31, 2019, the maturities of the Company's operating lease liabilities were as follows (in thousands):

Maturity of Lease Liabilities	Operating Leases
2020	$ 925
2021	701
2022	213
2023	220
2024	226
Thereafter	514
Total lease payments	$ 2,799
Less: Imputed Interest and Adjustments	(447)
Present value of lease payments	$ 2,352

Disclosures related to periods prior to adoption of the New Lease Standard

Prior to the adoption of ASC 842, the Company recorded rent expense on a straight-line basis over the term of the lease under ASC 840. Total rent expense was approximately $0.7 million and $0.7 million for the years ended December 31, 2018 and 2017, respectively.

ZIOPHARM Oncology, Inc.

NOTES TO FINANCIAL STATEMENTS

8. Leases (Continued)

For comparative purposes, the Company's aggregate future minimum non-cancellable commitments under operating leases as of December 31, 2018 were as follows:

2019	723
2020	736
2021	488
Future minimum lease payments, net	$1,947

9. Commitments and Contingencies

License Agreements

Exclusive License Agreement with PGEN

On October 5, 2018, the Company entered into an exclusive license agreement with PGEN. Refer to Note 7—Settlement of a Related Party Relationship for further details.

License Agreement and Research and Development Agreements—The University of Texas MD Anderson Cancer Center

On January 13, 2015, ZIOPHARM, together with Precigen, entered into the MD Anderson License with MD Anderson (which Precigen subsequently assigned to PGEN). Pursuant to the MD Anderson License, the Company, together with PGEN, holds an exclusive, worldwide license to certain technologies owned and licensed by MD Anderson including technologies relating to novel CAR T-cell therapies, non-viral gene transfer systems, genetic modification and/or propagation of immune cells and other cellular therapy approaches, Natural Killer, or NK Cells, and TCRs, arising from the laboratory of Laurence Cooper, M.D., Ph.D., who became the Company's Chief Executive Officer in May 2015 and was formerly a tenured professor of pediatrics at MD Anderson and is now currently a visiting scientist under that institution's policies.

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

Pursuant to the Research and Development Agreement, the Company, PGEN and MD Anderson have agreed to form a joint steering committee that will oversee and manage the new and ongoing research programs. Under the License Agreement with PGEN, ZIOPHARM and PGEN agreed that PGEN would no longer participate on the joint steering committee after the date of the License Agreement. As provided under the MD Anderson License, the Company provided funding for research and development activities in support of the research programs under the Research and Development Agreement for a period of three years and in an amount of no less than $15.0 million and no greater than $20.0 million per year. On November 14, 2017, the Company entered into an amendment to the Research and Development Agreement extending its term until April 15, 2021.

On October 22, 2019, the Company entered into the 2019 Research and Development Agreement, or the 2019 Agreement, with The University of Texas M.D. Anderson Cancer Center, or MD Anderson, pursuant to which the parties agreed to collaborate with respect to the Company's *Sleeping Beauty* immunotherapy program, which uses non-viral gene transfer to stably express and clinically evaluate neoantigen-specific TCRs in T cells. Under the 2019 Agreement, the parties will, among other things, collaborate on programs to expand the Company's TCR library and conduct clinical trials.

ZIOPHARM Oncology, Inc.

NOTES TO FINANCIAL STATEMENTS

9. Commitments and Contingencies (Continued)

The Company will own all intellectual property developed under the 2019 Agreement and will retain all rights to intellectual property for oncology products manufactured using non-viral gene transfer technologies under the Agreement, including the Company's *Sleeping Beauty* technology. The Company has granted MD Anderson an exclusive license for such intellectual property outside the field of oncology and to develop and commercialize autologous TCR products manufactured using viral gene transfer technologies, and a non-exclusive license for allogeneic TCR products manufactured using viral-based technologies.

The Company has agreed, beginning on January 1, 2021, to reimburse MD Anderson up to a total of $20.0 million for development costs under the 2019 Agreement. In addition, the Company will pay MD Anderson royalties on net sales of its TCR products at rates in the low single digits. The Company is required to make performance-based payments upon the successful completion of clinical and regulatory benchmarks relating to its TCR products. The aggregate potential benchmark payments are $36.5 million, of which only $3.0 million will be due prior to the first marketing approval of the Company's TCR products. The royalty rates and benchmark payments owed to MD Anderson may be reduced upon the occurrence of certain events. The Company also agreed that it will sell the Company's TCR products to MD Anderson at preferential prices and will sell its TCR products in Texas exclusively to MD Anderson for a limited period of time following the first commercial sale of the Company's TCR products.

In connection with the execution of the 2019 Agreement, the Company issued MD Anderson a warrant to purchase 3,333,333 shares of common stock. Refer to Note 10 – *Warrants* for further details.

During the year ended December 31, 2019, the Company made no payments to MD Anderson compared to $2.7 million during the year ended December 31, 2018. The decrease in cash paid to MD Anderson during the year ended December 31, 2019 as compared to the same period in the prior year is a result of the final quarterly payment being made to MD Anderson in January 2018 and the result of approved expenditures incurred by the Company being deducted from the existing prepaid expense. The net balance of cash resources on hand at MD Anderson available to offset expenses and future costs is $20.3 million, which is included in prepaid expenses and other current assets on the Company's balance sheet at December 31, 2019.

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

ZIOPHARM Oncology, Inc.

NOTES TO FINANCIAL STATEMENTS

9. Commitments and Contingencies (Continued)

License Agreement with the National Cancer Institute

On May 28, 2019, the Company entered into a patent license agreement, or the Patent License, with the National Cancer Institute, or the NCI. Pursuant to the Patent License, the Company holds an exclusive, worldwide license to certain intellectual property to develop and commercialize patient-derived (autologous), peripheral blood T-cell therapy products engineered by transposon-mediated gene transfer to express TCRs reactive to mutated KRAS, TP53 and EGFR. In addition, pursuant to the Patent License, the Company holds an exclusive, worldwide license to certain intellectual property for manufacturing technologies to develop and commercialize autologous, peripheral blood T-cell therapy products engineered by non-viral gene transfer to express TCRs, as well as a non-exclusive, worldwide license to certain additional manufacturing technologies.

Pursuant to the terms of the Patent License, the Company is required to pay the NCI a cash payment in the aggregate amount of $1.5 million payable in $0.5 million installments within sixty days, six-months, and the twelve-month anniversary of the effective date of the agreement for the Patent License. The Company also reimbursed the NCI for past patent expenses in the aggregate amount of approximately $46 thousand. Under the amendment to the patent license signed in January 2020, we agreed to pay the NCI a cash payment of $600,000 within sixty days of the amendment. For the year-ended December 31, 2019, the Company made payments under the Patent License of $1.0 million. At December 31, 2019, the Company included the remaining $0.5 million for the Patent License as accrued expenses on the Company's balance sheet. At December 31, 2019, the Company included a prepayment of $0.3 million related to the Patent License as prepaid expenses and other current assets on the Company's balance sheet.

The terms of the Patent License also require the Company to pay the NCI minimum annual royalties in the amount of $0.3 million, which amount will be reduced to $0.1 million once the aggregate minimum annual royalties paid by the Company equals $1.5 million. The first minimum annual royalty payment is payable on the date that is eighteen months following the date of the Patent License.

The Company is also required to make performance-based payments upon successful completion of clinical and regulatory benchmarks relating to the licensed products. The aggregate potential benchmark payments are $4.3 million, of which aggregate payments of $3.0 million are due only after marketing approval in the United States or in Europe, Japan, Australia, China or India. The first benchmark payment of $0.1 million will be due upon the initiation of the Company's first sponsored phase 1 clinical trial of a licensed product or licensed process in the field of use licensed under the Patent License.

In addition, the Company is required to pay the NCI one-time benchmark payments following aggregate net sales of licensed products at certain net sales up to $1.0 billion. The aggregate potential amount of these benchmark payments is $12.0 million. The Company must also pay the NCI royalties on net sales of products covered by the Patent License at rates in the low to mid-single digits depending upon the technology included in a licensed product. To the extent the Company enters into a sublicensing agreement relating to a licensed product, the Company is required to pay the NCI a percentage of all consideration received from a sublicensee, which percentage will decrease based on the stage of development of the licensed product at the time of the sublicense.

The Patent License will expire upon expiration of the last patent contained in the licensed patent rights, unless terminated earlier. The NCI may terminate or modify the Patent License in the event of a material breach, including if the Company does not meet certain milestones by certain dates, or upon certain insolvency events that remain uncured following the date that is 90 days following written notice of such breach or insolvency event. The Company may terminate the Patent License, or any portion thereof, in the Company's sole discretion at any time upon 60 days' written notice to the NCI. In addition, the NCI has the right to: (i) require the

ZIOPHARM Oncology, Inc.

NOTES TO FINANCIAL STATEMENTS

9. Commitments and Contingencies (Continued)

Company to sublicense the rights to the product candidates covered by the Patent License upon certain conditions, including if the Company is not reasonably satisfying required health and safety needs and (ii) terminate or modify the Patent License, including if the Company is not satisfying requirements for public use as specified by federal regulations.

Cooperative Research and Development Agreement (CRADA) with the National Cancer Institute

On January 10, 2017, the Company announced the signing of the CRADA with the NCI for the development of adoptive cell transfer, or ACT,-based immunotherapies genetically modified using the *Sleeping Beauty* transposon/transposase system to express TCRs for the treatment of solid tumors. The principal goal of the CRADA is to develop and evaluate ACT for patients with advanced cancers using autologous peripheral blood lymphocytes, or PBL, genetically modified using the non-viral *Sleeping Beauty* system to express TCRs that recognize neoantigens expressed within a patient's cancer. Research conducted under the CRADA will be at the direction of Steven A. Rosenberg, M.D., Ph.D., Chief of the Surgery Branch at the NCI, in collaboration with the Company's researchers and PGEN researchers. During the year ended December 31, 2019 and 2018, the Company made payments of $2.5 million, each year. In February 2019, the Company extended the CRADA with the NCI for two years, committing an additional $5.0 million to this program.

Exclusive Channel Partner Agreement with PGEN for the Cancer Programs

From 2011 to 2018, the Company was party to various arrangements with Precigen (now PGEN) in which the Company used PGEN's technology to research and develop cancer treatments in return for various future profit sharing and royalty arrangements. These agreements were modified or terminated by the License Agreement described in Note 7.

Ares Trading License and Collaboration Agreement

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

PGEN was entitled to receive $5.0 million from Ares Trading, payable in equal quarterly installments over two years for each identified product candidate, which will be used to fund discovery work. The Company was responsible for costs exceeding the quarterly installments and all other costs of the preclinical research and development. For the year ended December 31, 2019, the Company incurred no expense under the Ares Trading Agreement. For the year ended December 31, 2018, the Company has expensed $0.1 million under the Ares Trading Agreement, respectively. For the year ended December 31, 2017, the Company expensed $1.6 million under the Ares Trading agreement.

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

Under the License Agreement, PGEN agreed to perform all future obligations of the Company under the Ares Trading Agreement other than certain payment obligations. Accordingly, the Company recognized the remaining deferred revenue as part of the settlement of related party relationships as described in Note 7.

ZIOPHARM Oncology, Inc.

NOTES TO FINANCIAL STATEMENTS

9. Commitments and Contingencies (Continued)

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

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

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

Collaboration Agreement with Solasia Pharma K.K.

On March 7, 2011, the Company entered into a License and Collaboration Agreement with Solasia which was amended on July 31, 2014 to include an exclusive worldwide license. Pursuant to the License and Collaboration Agreement, the Company granted Solasia an exclusive license to develop and commercialize darinaparsin in both intravenous and oral forms and related organic arsenic molecules, in all indications for human use

As consideration for the license, the Company is 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, as defined in the agreement, will receive a portion of all milestone and royalty payments made by Solasia to the Company in accordance with the terms of the license agreement with the Licensors.

10. Warrants

In connection with the Company's November 2018 private placement which provided net proceeds of approximately $47.1 million, the Company issued warrants to purchase an aggregate of 18,939,394 shares of common stock which became exercisable six months after the closing of the private placement. The warrants have an exercise price of $3.01 per share and have a five-year term. The relative fair value of the warrants was estimated at $18.4 million using a Black-Scholes model with the following assumptions: expected volatility of 71%, risk free interest rate of 2.99%, expected life of five years and no dividends.

ZIOPHARM Oncology, Inc.

NOTES TO FINANCIAL STATEMENTS

10. Warrants (Continued)

The Company assessed whether the both the 2019 and 2018 warrants required accounting as derivatives. The Company determined that the warrants were (1) indexed to the Company's own stock and (2) classified in stockholders' equity in accordance with Financial Accounting Standards Board ("FASB") Accounting Standards Codification ("ASC") Topic 815, *Derivatives and Hedging*. As such, the Company has concluded the warrants meet the scope exception for determining whether the instruments require accounting as derivatives and should be classified in stockholders' equity.

On July 26, 2019 and September 12, 2019, the Company entered into agreements with existing investors for the exercise of previously issued warrants to purchase common stock in a private placement. Pursuant to the terms of the agreements, investors exercised their 2018 warrants for an aggregate of 17,803,031 shares of common stock, at an exercise price of $3.01 per share. The warrants exercised were originally issued by the Company in a private placement that closed in November 2018 (Note 2). Proceeds from the warrant exercise, after deducting placement agent fees and other related expenses of $1.1 million were approximately $52.5 million. The Company issued participating investors new warrants to purchase up to 17,803,031 additional shares of common stock as an inducement for the warrant holders to exercise their 2018 warrants early. The 2019 warrants will become exercisable six months following the date of issuance, will expire on the fifth anniversary of the initial exercise date, and have an exercise price of $7.00. The 2019 warrants were valued using a Black-Scholes valuation model and resulted in a $60.8 million non-cash charge in the Company's statement of operations.

On October 22, 2019, the Company entered into the 2019 Agreement with MD Anderson. In connection with the execution of the 2019 Agreement, the Company issued MD Anderson a warrant to purchase 3,333,333 shares of common stock. The warrant has an initial exercise price of $0.001 per share and grant date fair value of $14.5 million. The warrant expires on December 31, 2026 and vests upon the occurrence of certain clinical milestones. The Company will recognize expense on the warrant in the same manner as if the Company paid cash for services to be rendered. For the year ended December 31, 2019, the Company did not recognize any expense related to the warrant.

ZIOPHARM Oncology, Inc.

NOTES TO FINANCIAL STATEMENTS

11. 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, 2019 and 2018 are as follows:

(in thousands)	December 31, 2019	December 31, 2018
Deferred tax assets:		
Net operating loss carryforwards	$ 124,115	$ 106,430
Start-up and organizational costs	30,480	33,977
Research and development credit carryforwards	35,130	33,684
Stock compensation	1,087	990
Capitalized acquisition costs	4,501	5,160
Lease liability	626	—
Depreciation	176	132
Other	1,186	920
	197,301	181,293
Less valuation allowance	(196,696)	(181,293)
Total deferred tax assets	605	—
Deferred tax liabilities:		
Right of use asset	(605)	—
Total deferred tax liabilities	$ (605)	$ —
Net deferred taxes	$ —	$ —

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, 2019, the Company has aggregate net operating loss carryforwards for federal tax purposes of approximately $470 million, of which $342 million is available to offset future federal taxable income to the extent permitted under the Internal Revenue Code, or IRC, expiring in varying amounts through 2039 and approximately $128 million can be carried forward indefinitely. The Company also has approximately $404 million of state net operating loss carryforwards available to offset future state taxable income, expiring at various dates through 2039. Additionally, the Company has approximately $35.0 million of research and development credits at December 31, 2019, expiring in varying amounts through 2039, which may be available to reduce future taxes.

In March 2016, the FASB issued ASU No. 2016-09, "Improvements to Employee Share-Based Payment Accounting" (ASU 2016-09), which is intended to simplify several aspects of accounting for share-based payment transactions, including the income tax effects, statutory withholding requirements, forfeitures, and classification on the statement of cash flows. ASU 2016-09 is effective for annual reporting periods after December 15, 2016, including interim reporting periods within each annual reporting period. The Company adopted this standard on January 1, 2017. The update revises requirements in the following areas: minimum statutory withholding, accounting for income taxes, and forfeitures. Prior to adoption, the Company recognized share-based compensation, net of estimated forfeitures, over the vesting period of the grant. Upon adoption of ASU 2016-09, the Company elected to change its accounting policy to recognize forfeitures as they occur. The new forfeiture policy election was adopted using a modified retrospective approach with a cumulative effect adjustment of $122 thousand recorded to retained earnings as of January 1, 2017. The update requires the

ZIOPHARM Oncology, Inc.

NOTES TO FINANCIAL STATEMENTS

11. Income Taxes (Continued)

Company to recognize the income tax effect of awards in the income statement when the awards vest or are settled without triggering a liability. The income tax related items had no effect on the current period presentation and the Company maintains a full valuation allowance against its deferred tax assets. As a result, an accumulated excess tax benefit of 10.2 million was recognized as a deferred tax asset with a full valuation allowance against it. Additionally, the Company continued to estimate the number of awards expected to be vested. The adoption had no material impact on the Company's financial statements for the 2017 tax year or the interim periods within.

In May 2014, the FASB issued an accounting standard update which provides for new revenue recognition guidance, superseding nearly all prior revenue recognition guidance. The new revenue standard outlines a single comprehensive model for accounting for revenue from contracts with customers and requires more detailed revenue disclosures.

The Company adopted the new revenue standard on January 1, 2018 and as a result of the adoption increased deferred revenue by $8.1 million and decreased retained earnings by the same amount. Previously the Company had recorded revenue of $15.9 million and had deferred revenue of $41.5 million at December 31, 2017. The increase in the deferred revenue represented the recapture of revenue that was previously recorded and taxed. There was no impact to tax as the increase to the deferred tax asset was fully offset by the Company's full valuation allowance.

Under the IRC Section 382, certain substantial changes in the Company's ownership may limit the amount of net operating loss carryforwards that can be utilized in any one year to offset future taxable income.

Section 382 of the IRC provides limits to which a corporation that has undergone a change in ownership (as defined) can utilize any net operating loss, or NOL, and general business tax credit carryforwards it may have. The Company commissioned an analysis to determine whether Section 382 could limit the use of its carryforwards in this manner. After completing the analysis, it was determined an ownership change had occurred in February 2007. As a result of this change, the Company's NOL's and general business tax credits from February 23, 2007 and prior would be completely limited under IRC Section 382. The deferred tax assets related to NOL's and general business credits have been reduced by $11.2 million and $636 thousand, respectively, as a result of the change. The Company updated the IRC Section 382 analysis through December 31, 2018. There was no change in ownership at this time.

The Company has provided a valuation allowance for the full amount of these net deferred tax assets, since it is more likely than not that these future benefits will not be realized. However, these deferred tax assets may be available to offset future income tax liabilities and expenses. The valuation allowance increased by $15.4 million in 2019 primarily due to net operating loss carryforwards and the increase in research and development credits.

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

ZIOPHARM Oncology, Inc.

NOTES TO FINANCIAL STATEMENTS

11. Income Taxes (Continued)

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

	Year Ended December 31,		
(in thousands)	**2019**	**2018**	**2017**
Federal income tax at statutory rates	21%	21%	34%
State income tax, net of federal tax benefit	3%	4%	4%
Non-cash inducement warrant expense	-11%	0%	0%
Research and development credits	1%	2%	3%
Stock compensation	0%	-1%	-1%
Research and development true-up	0%	0%	-7%
Officers compensation	0%	-1%	-2%
Other	-1%	-2%	-3%
Federal rate change	0%	3%	-124%
Change in valuation allowance	-13%	-26%	96%
Effective tax rate	0%	0%	0%

The Company adopted ASC740, “Accounting for Uncertain Tax Positions” on January 1, 2007. ASC 740 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. There were no adjustments to its uncertain tax positions in the years ended December 31, 2019, 2018, and 2017.

The Company has not recognized any interest and penalties in the statement of operations because of the Company’s net operating losses and tax credits that are available to be carried forward. When necessary, the 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 2019.

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

ZIOPHARM Oncology, Inc.

NOTES TO FINANCIAL STATEMENTS

12. Preferred Stock and Stockholders' Equity (Deficit)

On April 26, 2006, the date of the Company's annual stockholders meeting that year, the shareholders approved the adoption of an Amended and Restated Certificate of Incorporation pursuant to which the Company has 280,000,000 shares of authorized capital stock, of which 250,000,000 shares are designated as common stock (par value $0.001 per share), and 30,000,000 shares are designated as preferred stock (par value $0.001 per share).

Common Stock

February 2020 Public Offering

On February 5, 2020, the Company entered into an underwriting agreement with Jefferies, as representative of the several underwriters named therein, relating to the issuance and sale of 27,826,086 shares of its common stock. The price to the public in the offering was $3.25 per share, and the underwriters agreed to purchase the shares from the Company pursuant to the underwriting agreement at a purchase price of $3.055 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 4,173,912 shares of common stock at a purchase price of $3.055 per share. The offering was made pursuant to the Company's effective registration statement on Form S-3ASR (File No. 333-232283) previously filed with the SEC, and a prospectus supplement thereunder. The underwriters purchased the 27,826,086 shares on February 5, 2020. The net proceeds from the offering were approximately $85.0 million after deducting underwriting discounts and offering expenses paid by the Company.

At-the-Market Offering

During the year ended December 31, 2019, the Company sold an aggregate of 1,271,274 shares of its common stock. The offering was made pursuant to the Company's effective registration statement on Form S-3ASR (File No. 333-232283) previously filed with the SEC, and a prospectus supplement thereunder. The net proceeds from the offering were approximately $6.1 million after deducting underwriting discounts and offering expenses payable by the Company.

Also, subsequent to December 31, 2019, the Company sold an aggregate of 2,814,673 shares of our common stock. The offering was made pursuant to the Company's effective registration statement on Form S-3ASR (File No. 333-232283) previously filed with the SEC, and a prospectus supplement thereunder. The net proceeds from the offering were approximately $13.0 million after deducting underwriting discounts and offering expenses payable by the Company.

November 2018 Private Placement and 2019 Inducement Warrants

On November 11, 2018, the Company entered into a securities purchase agreement with certain institutional and accredited investors, pursuant to which the Company agreed to issue and sell to the Investors an aggregate of 18,939,394 immediately separable units, with each unit being composed of (i) one share of the Company's common stock, par value $0.001 per share, and (ii) a warrant to purchase one share of common stock, at a price per unit of $2.64, for net proceeds of approximately $47.1 million.

May 2017 Offering

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

ZIOPHARM Oncology, Inc.

NOTES TO FINANCIAL STATEMENTS

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

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

Preferred Stock

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

On June 29, 2016, the Company entered into amendments to certain agreements with Precigen (now PGEN) (Note 7). In consideration for the execution and delivery of these amendments the Company issued to Precigen 100,000 shares of its newly designated Series 1 preferred stock. Each share of the Company's Series 1 preferred stock had a stated value of $1,200, subject to appropriate adjustment in the event of any stock dividend, stock split, combination or other recapitalization. The Series 1 preferred stock had certain rights, preferences, privileges and obligations, including dividend rights, conversion rights, consent rights with respect to certain Company actions, and rights to preferential payments in the event of any voluntary or involuntary liquidation, dissolution or winding up of the Company or a change of control or sale, lease, transfer or exclusive license of all or substantially all of the Company's assets prior to the conversion of the Series 1 preferred stock.

On October 5, 2018, the Company and PGEN entered into the License Agreement to replace all existing agreements between the companies, which provides the Company with certain exclusive and non-exclusive rights to technology controlled by PGEN. In consideration of the Company entering into the License Agreement, Precigen forfeited and returned to the Company all shares of the Company's Series 1 preferred stock held by or payable to Precigen as of the date of the License Agreement (Notes 7 and 12).

13. Derivative Financial Instruments

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

On October 5, 2018, the Company entered into the License Agreement with PGEN. In partial consideration for the termination of the former agreements, the Company and PGEN agreed that Precigen would forfeit all outstanding shares of the Series 1 preferred stock held by Precigen, including any accrued dividends and related financial instruments. Thus, upon closing of the transaction, these derivative financial instruments were no longer outstanding (Note 7).

ZIOPHARM Oncology, Inc.

NOTES TO FINANCIAL STATEMENTS

13. Derivative Financial Instruments (Continued)

The change in the derivative liability for the years ended December 31, 2019, 2018 and 2017 consists of the following:

	Fair Value
Balance, December 31, 2016	$ 862
Dividends	267
Change in fair value	1,295
Balance, December 31, 2017	$ 2,424
Dividends	223
Change in fair value	(158)
Settlement of a related party relationship	(2,489)
Balance, December 31, 2018	$ —
Dividends	—
Change in fair value	—
Balance, December 31, 2019	$ —

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

	December 31, 2018
Risk-free interest rate	2.50 - 3.13%
Expected dividend rate	0
Expected volatility	77.6 - 82.4%
Preferred stock conversion limit - percentage of outstanding common stock	19.90%
Preferred conversion floor price	$1.00

14. Stock Option Plan

The Company adopted the 2012 Equity Incentive Plan, or the "2012 Plan," in May 2012. Including subsequent increases, the Company had reserved 14.0 million shares for issuance. At December 31, 2019, there are 5,842,879 shares reserved for issuance and 2,503,508 available for future grant.

As of December 31, 2019 the Company had outstanding options to its employees to purchase up to 4,550,071 shares of the Company's common stock, to its directors to purchase up to 1,282,808 shares of the Company's common stock, as well as options to consultants in connection with services rendered to purchase up to 10,000 shares of the Company's common stock.

ZIOPHARM Oncology, Inc.

NOTES TO FINANCIAL STATEMENTS

14. Stock Option Plan (Continued)

Stock options to employees generally vest ratably in either quarterly or annual installments over three years, commencing on the first anniversary of the grant date and have contractual terms of ten years. Stock options to directors generally vest ratably over one or two 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 1,030,000 additional shares for issuance under options granted outside of the 2003 and 2012 Plans.

Proceeds from the option exercises during the years ended December 31, 2019, 2018, and 2017 amounted to $1.2 million, $0.2 million and $0.1 million respectively. The intrinsic value of these options amounted to $1.1 million, $0.1 million and $0.2 million for years ended December 31, 2019, 2018 and 2017, respectively.

Transactions under the 2012 Plan for the years ending December 31, 2019, 2018, and 2017 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, 2016	3,465,335	$ 5.07		
Granted	688,800	5.27		
Exercised	(180,000)	3.67		
Cancelled	(122,000)	6.64		
Outstanding, December 31, 2017	3,852,135	5.12		
Granted	1,744,950	2.35		
Exercised	(104,167)	2.30		
Cancelled	(215,833)	5.72		
Outstanding, December 31, 2018	5,277,085	4.24		
Granted	2,880,691	3.40		
Exercised	(581,105)	3.30		
Cancelled	(1,733,792)	4.21		
Outstanding, December 31, 2019	5,842,879	$ 3.21	8.07	$ 7,482
Options exercisable, December 31, 2019	2,765,357	$ 4.39	6.70	$ 3,603
Options exercisable, December 31, 2018	3,099,935	$ 5.15	4.93	$ 88
Options available for future grant at December 31, 2019	2,503,508			

In September 2017, the Company granted 500,000 inducement stock options, with an exercise price of $6.16 per share, which vests ratably in annual installments over three years, commencing on the first anniversary of the grant date and has a contractual term of ten years. The grant date fair value was $2.2 million.

On July 22, 2019, August 19, 2019, and November 21, 2019, the Company granted 400,000, 65,000, and 65,000 shares of its common stock, with exercise prices of $5.60, $5.18, and $4.59, respectively. The options vest ratably, over four years, commencing with one quarter on the first anniversary of the grant date and then quarterly thereafter. The options have a contractual term of ten years. These options were granted outside of the 2012 Plan and therefore, are not included in the table above. The grant date fair value was $1.5 million, $231 thousand, and $193 thousand, respectively. As of December 31, 2019, all 1,030,000 options are outstanding.

ZIOPHARM Oncology, Inc.

NOTES TO FINANCIAL STATEMENTS

14. Stock Option Plan (Continued)

At December 31, 2019, total unrecognized compensation costs related to non-vested stock options outstanding amounted to $9.0 million. The cost is expected to be recognized over a weighted-average period of 1.78 years.

Restricted Stock

In January 2019, the Company issued 947,108 shares of restricted stock to its employees, which vest ratably in annual installments over three years, commencing on the first anniversary of the grant date. In September 2019, the Company issued 15,000 shares of restricted stock to its employees, which vest ratably in annual installments over four years, commencing with one-quarter on the first anniversary of the grant date and then quarterly thereafter. In December 2018, the Company issued 30,000 shares of restricted stock to its employees, which vest ratably in annual installments over three years, commencing on the first anniversary of the grant date. In December 2017, the Company issued 838,000 shares of restricted stock to its employees, which vest ratably in annual installments over three years, commencing on the first anniversary of the grant date. In December 2019, the Company issued 111,230 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 2018, the Company issued 120,321 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 2017, the Company issued 69,032 shares of restricted stock to its non-employee directors, which vest in their entirety on the one-year anniversary of the grant date.

In January 2019, one of the Company's executives received 446,428 shares of restricted stock in lieu of their annual cash bonus. The shares were immediately vested.

In the year ended December 31, 2019, the Company repurchased 225,339 shares at average prices ranging from $2.24 to 4.72 to cover payroll taxes. In the year ended December 31, 2018, the Company repurchased 514,349 shares at average prices ranging from $1.70 to 4.41 to cover payroll taxes. In the year ended December 31, 2017, the Company repurchased 394,269 shares at average prices ranging from $4.14 to $7.12 to cover payroll taxes. A summary of the status of restricted stock as of December 31, 2019, 2018 and 2017 is as follows:

	Number of Shares	Weighted-Average Grant Date Fair Value
Non-vested, December 31, 2016	1,680,492	$ 7.49
Granted	907,032	4.14
Vested	(778,965)	7.66
Cancelled	—	—
Non-vested, December 31, 2017	1,808,559	5.74
Granted	150,321	1.87
Vested	(1,005,377)	6.62
Cancelled	(271,433)	5.00
Non-vested, December 31, 2018	682,070	3.47
Granted	1,519,766	2.44
Vested	(1,187,601)	2.82
Cancelled	(74,599)	3.41
Non-vested, December 31, 2019	939,636	$ 2.93

As of December 31, 2019, there was $2.7 million of total unrecognized stock-based compensation expense related to non-vested restricted stock arrangements. The expense is expected to be recognized over a weighted-average period of 1.29 years.

ZIOPHARM Oncology, Inc.

NOTES TO FINANCIAL STATEMENTS

15. 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 $404 thousand, $329 thousand, and $90 thousand to this plan during the years ended December 31, 2019, 2018, and 2017, respectively.

16. Joint Venture

On December 18, 2018, the Company entered into a Framework Agreement with TriArm Therapeutics, Ltd., or TriArm, whereby the parties will launch Eden BioCell, Ltd., or Eden BioCell, to lead clinical development and commercialization of certain Sleeping Beauty-generated CAR-T therapies as set forth in a separate license agreement.

On January 3, 2019, Eden BioCell was incorporated in Hong Kong as a private company. Eden BioCell, the Company and TriArm entered into a Share Subscription Agreement on January 23, 2019, where the Company and TriArm agreed to contribute certain intellectual property, services and cash (only with respect to TriArm) to Eden BioCell to subscribe for a certain number of newly issued ordinary shares in the share capital of Eden BioCell. On the closing date, upon the issuance and subscription of the shares, in respect of the aforementioned consideration, 10,000,000 ordinary shares were issued to the Company and 10,000,000 ordinary shares were issued to TriArm.

The closing of the transaction occurred on July 5, 2019. The Framework Agreement and Share Subscription Agreements were each respectively amended to be effective as of this date. Upon consummation of the joint venture, Eden BioCell and the Company also entered into a license agreement, pursuant to which the Company licensed the rights to Eden BioCell for third-generation *Sleeping Beauty*-generated CAR-T therapies targeting the CD19 antigen for the territory of China (including Macau and Hong Kong), Taiwan and Korea. Eden BioCell will be responsible for certain milestone and royalty payments to related to the Company's license agreements with MD Anderson and PGEN, Inc. (Note 7). TriArm entered into a Master Services Agreement with Eden BioCell and contributed $10.0 million of cash on the closing date. TriArm also committed to contribute an additional $25.0 million to Eden BioCell over time through the achievement of specified milestones. TriArm and the Company each received a 50% equity interest in the joint venture in exchange for their contributions to Eden BioCell.

As of July 5, 2019, as a result of the design and purpose of Eden BioCell, the Company determined that Eden BioCell was considered a variable interest entity, or VIE, and concluded that it is not the primary beneficiary of the VIE as it did not have the power to direct the activities of the VIE that most significantly impact its performance. Rather, the Company accounts for the equity interest in Eden BioCell under the equity method of accounting as it has the ability to exercise significant influence over the operations of Eden BioCell.

The Company determined that Eden BioCell was not a customer and therefore, accounted for the transaction as the transfer of nonfinancial assets to be recognized at their fair value on the contribution date. The fair value of the intellectual property contributed to Eden BioCell had a de minimis value due to the early stage of the technology and the likelihood of clinical success. Due to the de minimis fair value of the intellectual property contributed, the Company did not record a gain or loss on this transaction and recognized a value of $0 for the equity-method investment.

ZIOPHARM Oncology, Inc.

NOTES TO FINANCIAL STATEMENTS

17. Selected Quarterly Information (Unaudited)
(in thousands, except per share amounts)

Year Ended December 31, 2019	First Quarter	Second Quarter	Third Quarter	Fourth Quarter
Revenue	$ —	$ —	$ —	$ —
Total operating expenses	13,621	14,753	13,448	16,036
Loss from operations	(13,621)	(14,753)	(13,448)	(16,036)
Non-cash inducement warrant expense	—	—	(60,751)	—
Net income (loss) applicable to common shareholders	(13,434)	(14,620)	(73,996)	(15,746)
Net income (loss) per share, basic	$ (0.08)	$ (0.09)	$ (0.43)	$ (0.09)
Net income (loss) per share, diluted	$ (0.08)	$ (0.09)	$ (0.43)	$ (0.09)

Year Ended December 31, 2018	First Quarter	Second Quarter	Third Quarter	Fourth Quarter
Revenue	$ 146	$ —	$ —	$ —
Total operating expenses	16,342	12,378	12,570	12,762
Loss from operations	(16,196)	(12,378)	(12,570)	(12,762)
Preferred stock dividends	(5,120)	(5,462)	(6,074)	(342)
Settlement of a related party relationship	—	—	—	207,361
Net income (loss) applicable to common shareholders	(21,140)	(17,493)	(18,659)	194,538
Net income (loss) per share, basic	$ (0.15)	$ (0.12)	$ (0.13)	$ 1.29
Net income (loss) per share, diluted	$ (0.15)	$ (0.12)	$ (0.13)	$ 1.29

CERTAIN CONFIDENTIAL INFORMATION CONTAINED IN THIS DOCUMENT, MARKED BY [*****], HAS BEEN OMITTED BECAUSE ZIOPHARM ONCOLOGY, INC. HAS DETERMINED THE INFORMATION (I) IS NOT MATERIAL AND (II) WOULD LIKELY CAUSE COMPETITIVE HARM TO ZIOPHARM ONCOLOGY, INC. IF PUBLICLY DISCLOSED.

THIS WARRANT AND THE SECURITIES ISSUABLE UPON EXERCISE OF THIS WARRANT HAVE NOT BEEN REGISTERED UNDER THE SECURITIES ACT OF 1933, AS AMENDED (THE "SECURITIES ACT"), OR THE SECURITIES LAWS OF ANY STATE OR OTHER JURISDICTION. THIS WARRANT AND THE SECURITIES ISSUABLE UPON EXERCISE OF THIS WARRANT MAY NOT BE SOLD OR OFFERED FOR SALE, PLEDGED OR HYPOTHECATED EXCEPT PURSUANT TO AN EFFECTIVE REGISTRATION STATEMENT UNDER THE SECURITIES ACT OR PURSUANT TO AN EXEMPTION FROM REGISTRATION THEREUNDER, IN EACH CASE IN ACCORDANCE WITH ALL APPLICABLE SECURITIES LAWS OF THE STATES OR OTHER JURISDICTIONS, AND IN THE CASE OF A TRANSACTION EXEMPT FROM REGISTRATION, SUCH WARRANTS AND THE SECURITIES ISSUABLE UPON EXERCISE OF SUCH WARRANTS MAY ONLY BE TRANSFERRED IF THE TRANSFER AGENT FOR SUCH WARRANTS AND THE SECURITIES ISSUABLE UPON EXERCISE OF SUCH WARRANTS HAS RECEIVED DOCUMENTATION SATISFACTORY TO IT THAT SUCH TRANSACTION DOES NOT REQUIRE REGISTRATION UNDER THE SECURITIES ACT.

ZIOPHARM ONCOLOGY, INC.

WARRANT TO PURCHASE COMMON STOCK

No. CSW-1 **October 22, 2019 ("Issuance Date")**

Void After the Expiration Date

THIS CERTIFIES THAT, for value received, The Board of Regents of The University of Texas System (the "***Holder***"), on behalf of The University of Texas M.D. Anderson Cancer Center ("***MD Anderson***"), or its permitted assigns, is entitled to subscribe for and purchase at the Exercise Price from Ziopharm Oncology, Inc. (the "***Company***") up to three million three hundred thirty-three thousand three hundred thirty-three (3,333,333) shares of common stock, $0.001 par value per share, of the Company (the "***Common Stock***"), all subject to the terms, conditions and adjustments set forth below in this Warrant.

This Warrant is being issued pursuant to the terms of the 2019 Research and Development Agreement, dated as of October 22, 2019, by and between the Company and the Holder (the "***R&D Agreement***"). If any term or provision of this Warrant conflicts with any term or provision of the R&D Agreement, the terms and provisions of this Warrant shall control.

1. DEFINITIONS. As used herein, the following terms shall have the following respective meanings:

(a) "***Business Day***" means any day other than Saturday, Sunday, a federal holiday or other day on which commercial banks in Boston, Massachusetts are closed to the public.

(b) "***Commission***" means the United States Securities and Exchange Commission.

(c) "***Effectiveness Date***" means the date the Registration Statement has been declared effective by the Commission.

(d) "***Effectiveness Period***" has the meaning set forth in Section 18.1 hereof.

(e) "***Exercise Period***" shall mean the period commencing at 12:00:01 a.m., Boston, Massachusetts time, on the Issuance Date and ending at 11:59:59 p.m., Boston, Massachusetts time, on the Expiration Date, unless sooner terminated as provided herein.

(f) "***Exercise Price***" shall mean $0.001 per share of Common Stock, subject to adjustment pursuant to Section 6 below.

(g) "***Exercise Shares***" shall mean the shares of Common Stock issuable upon exercise of this Warrant, subject to adjustment pursuant to the terms herein, including but not limited to, adjustment pursuant to Section 6 below.

(h) "***Exchange Act***" has the meaning set forth in Section 4.4 hereof.

(i) "***Expiration Date***" means 11:59:59 p.m., Boston, Massachusetts time, on December 31, 2026.

(j) "***Filing Date***" means the sixtieth (60th) Business Day following a written request from Holder; *provided*, *that* any such request shall only occur after this Warrant has been exercised in full or in part in accordance with Section 3.2 and payment of the Exercise Price was made; *provided*, *however*, that if the Filing Date falls on a day that is not a Business Day, then the Filing Date shall be extended to the next Business Day.

(k) "***Prospectus***" means any prospectus included in a Registration Statement (including, without limitation, a prospectus that includes any information previously omitted from a prospectus filed as part of an effective registration statement in reliance upon Rule 430A promulgated under the Securities Act), as amended or supplemented by any prospectus supplement, with respect to the terms of the offering of any portion of the Registrable Securities covered by a Registration Statement, and all other amendments and supplements to any such Prospectus, including post-effective amendments, and all material incorporated by reference in such Prospectus.

(l) "***Registrable Securities***" means shares of Common Stock issued or issuable to the Holder upon exercise of the Warrants; *provided*, *however*, that the applicable Holder has completed and delivered to the Company a questionnaire in the form as may reasonably be requested by the Company from time to time; *provided*, *further*, that such securities shall no longer be deemed Registrable Securities if (i) such securities have been sold pursuant to a Registration Statement, (ii) such securities have been sold in compliance with Rule 144, or (ii) all such securities may be sold without limitation or restriction pursuant to Rule 144.

(m) "***Registration Statement***" means the registration statements and any additional registration statements contemplated by this Agreement, including (in each case) the related Prospectus, amendments and supplements to such registration statement or Prospectus, including pre- and post-effective amendments, all exhibits thereto, and all material incorporated by reference in such registration statement. "Registration Statement" shall include the Company's existing automatic Registration Statement on Form S-3 filed on June 21, 2019 (File no. 333-232283) if the Company elects to file a post-effective amendment or a prospectus supplement pursuant to such Registration Statement that would be deemed to be part of such existing automatic Registration Statement in accordance with Rule 430B under the Securities Act and would permit the sale and distribution of all the Registrable Securities (an "***ASR Pro Supp***").

(n) "***Rule 144***" means Rule 144 promulgated by the Commission pursuant to the Securities Act, as such Rule may be amended from time to time, or any similar rule or regulation hereafter adopted by the Commission having substantially the same effect as such Rule.

(o) "***Rule 415***" means Rule 415 promulgated by the Commission pursuant to the Securities Act, as such Rule may be amended from time to time, or any similar rule or regulation hereafter adopted by the Commission having substantially the same effect as such Rule.

(p) "***Securities Act***" means the Securities Act of 1933, as amended, and related regulations and guidance promulgated by the Commission.

2. DURATION OF WARRANT. The rights represented by this Warrant may be exercised in whole or in part at any time or times during the Exercise Period, subject to the vesting schedule set forth in Section 3.1. If not exercised at or before the Expiration Date, this Warrant shall become void, and all rights of the Holder under this Warrant shall cease.

3. VESTING SCHEDULE; EXERCISE.

3.1 Vesting Schedule. The Exercise Shares shall vest and become exercisable as set forth below, provided that on each vesting date, the R&D Agreement has not been earlier terminated in accordance with its terms. Upon termination of the R&D Agreement, vesting of the Exercise Shares shall cease and this Warrant shall thereafter remain exercisable during the Exercise Period for up to that number of Exercise Shares as were vested as of the effective time of such termination.

(a) [***]

3.2 Exercise. The rights represented by this Warrant may be exercised in whole or in part at any time, subject to the terms of Section 2 and as further specified herein, during the Exercise Period, so long as the Exercise Shares for which this Warrant is being exercised are then vested and exercisable hereunder in accordance with Section 3.1, by delivery by the Holder of the following to the Company at its address set forth above (or at such other address as it may designate by notice in writing to the Holder):

(a) An executed Notice of Exercise in the form attached hereto as Exhibit A;

(b) Payment of the Exercise Price either in cash or by wire transfer of immediately available funds; provided, however, that, for so long as the R&D Agreement is in effect, the Holder may, at its option in writing in the Notice of Exercise, elect to offset the Exercise Price against any amounts then owed to the Holder from the Company; and

(c) This Warrant.

For the avoidance of doubt, this Warrant may not be exercised for any Exercise Shares that have not vested in accordance with Section 3.1. Upon the exercise of the rights represented by this Warrant, a book-entry statement for the Exercise Shares so purchased, registered in the name of the Holder or persons affiliated with the Holder, if the Holder so designates, shall be delivered to the Holder within a reasonable time after the rights represented by this Warrant shall have been so exercised.

The person in whose name any book-entry statements for Exercise Shares are to be delivered upon exercise of this Warrant shall be deemed to have become the holder of record of such shares of Common Stock purchased on the date on which this Warrant was surrendered and payment of the Exercise Price was made, irrespective of the date of delivery of such book-entry statement, except that, if the date of such surrender and payment is a date when the stock transfer books of the Company are closed, such person shall be deemed to have become the holder of such shares at the close of business on the next succeeding date on which the stock transfer books are open.

4. COVENANTS OF THE COMPANY.

4.1 Covenants as to Exercise Shares. The Company covenants and agrees that all Exercise Shares that may be issued upon the exercise of the rights represented by this Warrant will, upon issuance, be validly issued and outstanding, fully paid and nonassessable, and free from all taxes, liens and charges with respect to the issuance thereof. The Company further covenants and agrees that the Company will at all times during the Exercise Period, have authorized and reserved, free from preemptive rights, a sufficient number of shares of its Common Stock to provide for the exercise of the rights represented by this Warrant. If at any time during the Exercise Period the number of authorized but unissued shares of Common Stock shall not be sufficient to permit exercise of this Warrant, the Company will take such corporate action as may, in the opinion of its counsel, be necessary to increase its authorized but unissued shares of Common Stock to such number of shares as shall be sufficient for such purposes.

4.2 Delivery of New Warrant. Unless the purchase rights represented by this Warrant shall have expired or shall have been fully exercised, the Holder shall, at the time of delivery of the Exercise Shares being issued in accordance with Section 3.2, surrender this Warrant to the Company pursuant to Section 3.2(c) and promptly after such surrender, the Company shall deliver to the Holder a new Warrant evidencing the rights of the Holder to purchase the unexpired and unexercised Exercise Shares called for by this Warrant. Such new Warrant shall in all other respects be identical to this Warrant.

4.3 Notices of Record Date. In the event of any taking by the Company of a record of the holders of any class of securities for the purpose of determining the holders thereof

who are entitled to receive any dividend (other than a cash dividend which is the same as cash dividends paid in previous quarters) or other distribution, the Company shall mail to the Holder, at least ten (10) days prior to the date specified herein, a notice specifying the date on which any such record is to be taken for the purpose of such dividend or distribution.

4.4 Rule 144. As long as any Holder owns any Registrable Securities, the Company covenants to use its commercially reasonable efforts to timely file (or obtain extensions in respect thereof and file within the applicable grace period) all reports required to be filed by the Company after the date hereof pursuant to Section 13(a) or 15(d) of the Securities Exchange Act of 1934, as amended (the "***Exchange Act***"). The Company further covenants that it will take such further action as any Holder may reasonably request, all to the extent required from time to time to enable such person to sell the Registrable Securities without registration under the Securities Act within the limitation of the exemptions provided by Rule 144 promulgated under the Securities Act, including providing any legal opinions relating to such sale pursuant to Rule 144. Upon the request of any Holder, the Company shall deliver to such Holder a written certification of a duly authorized officer as to whether it has complied with such requirements.

5. REPRESENTATIONS OF HOLDER.

5.1 Acquisition of Warrant for Personal Account. The Holder represents and warrants that it is acquiring the Warrant and the Exercise Shares solely for its account for investment and not with a view to or for sale or distribution of said Warrant or Exercise Shares or any part thereof. The Holder also represents that the entire legal and beneficial interests of the Warrant and Exercise Shares the Holder is acquiring is being acquired for, and will be held for, its account only.

5.2 Information and Sophistication. The Holder hereby: (i) acknowledges that it has received all the information it has requested from the Company and it considers necessary or appropriate for deciding whether to acquire this Warrant and the Exercise Shares, (ii) represents that it has had an opportunity to ask questions and receive answers from the Company regarding the financial condition of the Company and the risks associated with the acquisition of this Warrant and the Exercise Shares and (iii) further represents that it has such knowledge and experience in financial and business matters that it is capable of evaluating the merits and risk of this investment.

5.3 Ability to Bear Economic Risk. The Holder acknowledges that investment in the securities of the Company involves a high degree of risk, and represents that it is able, without materially impairing its financial condition, to hold the Exercise Shares for an indefinite period of time and to suffer a complete loss of its investment.

5.4 Securities Are Not Registered.

(a) The Holder understands that the Warrant and the Exercise Shares have not been registered under the Securities Act of 1933, as amended (the "***Act***") on the basis that no distribution or public offering of the stock of the Company is to be effected. The Holder realizes that the basis for the exemption may not be present if, notwithstanding its representations, the Holder has a present intention of acquiring the securities for a fixed or determinable period in the future, selling (in connection with a distribution or otherwise), granting any participation in, or otherwise distributing the securities. The Holder has no such present intention.

(b) The Holder recognizes that the Warrant and the Exercise Shares must be held indefinitely unless they are subsequently registered on a Registration Statement or an exemption from such registration is available. The Holder recognizes that the Company has no obligation to comply with any exemption from such registration.

(c) The Holder is aware that neither the Warrant nor the Exercise Shares may be sold pursuant to Rule 144 adopted under the Securities Act unless certain conditions are met, which may include, among other things, the existence of a public market for the shares, the availability of certain current public information about the Company and the resale following the required holding period under Rule 144. The Holder is aware that the conditions for resale set forth in Rule 144 may not occur in the foreseeable future.

5.5 Disposition of Warrant and Exercise Shares.

(a) The Holder further agrees not to make any disposition of all or any part of the Warrant or Exercise Shares in any event unless and until:

(i) The Company shall have received a letter secured by the Holder from the Commission stating that no action will be recommended to the Commission with respect to the proposed disposition;

(ii) There is then in effect a Registration Statement covering such proposed disposition and such disposition is made in accordance with said registration statement; or

(iii) The Holder shall have notified the Company of the proposed disposition and shall have furnished the Company with a detailed statement of the circumstances surrounding the proposed disposition, and if reasonably requested by the Company, the Holder shall have furnished the Company with an opinion of counsel, reasonably satisfactory to the Company, for the Holder to the effect that such disposition will not require registration of such Warrant or Exercise Shares under the Securities Act or any applicable state securities laws.

(b) The Holder understands and agrees that all certificates and/or book entry-statements evidencing the shares to be issued to the Holder may bear the following legend:

> THESE SECURITIES HAVE NOT BEEN REGISTERED UNDER THE SECURITIES ACT OF 1933, AS AMENDED (THE “SECURITIES ACT”), OR THE SECURITIES LAWS OF ANY STATE OR OTHER JURISDICTION. THESE SECURITIES MAY NOT BE SOLD OR OFFERED FOR SALE, PLEDGED OR HYPOTHECATED EXCEPT PURSUANT TO AN EFFECTIVE REGISTRATION STATEMENT UNDER THE SECURITIES ACT OR PURSUANT TO AN EXEMPTION FROM REGISTRATION THEREUNDER, IN EACH CASE IN ACCORDANCE WITH ALL APPLICABLE SECURITIES LAWS OF THE STATES OR OTHER JURISDICTIONS, AND IN THE CASE OF A TRANSACTION EXEMPT FROM REGISTRATION, SUCH

SECURITIES MAY ONLY BE TRANSFERRED IF THE TRANSFER AGENT FOR SUCH WARRANTS AND THE SECURITIES ISSUABLE UPON EXERCISE OF SUCH WARRANTS HAS RECEIVED DOCUMENTATION SATISFACTORY TO IT THAT SUCH TRANSACTION DOES NOT REQUIRE REGISTRATION UNDER THE SECURITIES ACT.

5.6 Accredited Investor Status. The Holder is an "accredited investor" as defined in Regulation D promulgated under the Securities Act.

5.7 Brokers and Finders. No person will have, as a result of the issuance of this Warrant, any valid right, interest or claim against or upon the Company or the Holder for any commission, fee or other compensation pursuant to any agreement, arrangement or understanding entered into by or on behalf of the Holder.

6. ADJUSTMENT OF EXERCISE PRICE AND NUMBER OF EXERCISE SHARES. In the event of changes in the outstanding Common Stock of the Company by reason of stock dividends, split-ups, recapitalizations, reclassifications, combinations or exchanges of shares, separations, reorganizations, liquidations, or the like, the number and class of shares available under the Warrant in the aggregate and the Exercise Price shall be correspondingly adjusted to give the Holder of the Warrant, on exercise for the same aggregate Exercise Price, the total number, class, and kind of shares as the Holder would have owned had the Warrant been exercised prior to the event and had the Holder continued to hold such shares until after the event requiring adjustment; *provided*, *however*, that such adjustment shall not be made with respect to, and this Warrant shall terminate if not exercised prior to, the events set forth in Section 8 below. The form of this Warrant need not be changed because of any adjustment in the number of Exercise Shares subject to this Warrant.

7. FRACTIONAL SHARES. No fractional shares shall be issued upon the exercise of this Warrant as a consequence of any adjustment pursuant hereto. All Exercise Shares (including fractions) issuable upon exercise of this Warrant may be aggregated for purposes of determining whether the exercise would result in the issuance of any fractional share. If, after aggregation, the exercise would result in the issuance of a fractional share, the Company shall, in lieu of issuance of any fractional share, pay the Holder otherwise entitled to such fraction a sum in cash equal to the product resulting from multiplying the then current fair market value of an Exercise Share by such fraction.

8. EARLY TERMINATION. In the event of, at any time during the Exercise Period, any capital reorganization, or any reclassification of the capital stock of the Company (other than a change in par value or from par value to no par value or no par value to par value or as a result of a stock dividend or subdivision, split-up or combination of shares), or the consolidation or merger of the Company with or into another corporation (other than a merger solely to effect a reincorporation of the Company into another state), or the sale or other disposition of all or substantially all the properties and assets of the Company in its entirety to any other person, the Company shall provide to the Holder twenty (20) days advance written notice of such reorganization, reclassification, consolidation, merger or sale or other disposition of the Company's assets, and this Warrant shall terminate unless exercised prior to the occurrence of such reorganization, reclassification, consolidation, merger or sale or other disposition of the Company's assets.

9. NO STOCKHOLDER RIGHTS. Except as otherwise specifically provided herein, the Holder, solely in such person's capacity as a Holder of this Warrant, shall not be entitled to vote or receive dividends or be deemed the holder of capital stock of the Company for any purpose, nor shall anything contained in this Warrant be construed to confer upon the Holder, solely in such person's capacity as the Holder of this Warrant, any of the rights of a stockholder of the Company or any right to vote, give or withhold consent to any corporate action (whether any reorganization, issue of stock, reclassification of stock, consolidation, merger, conveyance or otherwise), receive notice of meetings, receive dividends or subscription, or otherwise, prior to the issuance to the Holder of the Warrant Shares which such person is then entitled to receive upon the due exercise of this Warrant. In addition, nothing contained in this Warrant shall be construed as imposing any liabilities on the Holder to purchase any securities (upon exercise of this Warrant or otherwise) or as a stockholder of the Company, whether such liabilities are asserted by the Company or by creditors of the Company.

10. TRANSFER AND ASSIGNMENT OF WARRANT. During such time as any of the Exercise Shares remain unvested, this Warrant shall not be assigned or transferred by Holder, whether by operation of law or otherwise. Following such time as all of the Exercise Shares have vested and become exercisable in accordance with Section 3.1 above, and subject to applicable laws, the restriction on transfer set forth in this Warrant (including the foregoing sentence), and any restrictions applicable to the transfer of shares set forth in the Company's charter or bylaws or in the R&D Agreement, as each may be amended from time to time, this Warrant and all rights hereunder (including registration rights pursuant to Section 18) shall be freely transferable, by the Holder in person or by duly authorized attorney, upon: (i) delivery of this Warrant and an executed version of the form of assignment attached hereto as Exhibit B to any transferee designated by the Holder within ten (10) days of the date of such transfer or assignment; and (ii) execution and delivery of an investment letter in the form and substance satisfactory to the Company pursuant to which the transferee or assignee, among other things, shall agree with the Company to be bound by all of the provisions of this Warrant. The rights to transfers and assignment shall apply to the Holders (and to subsequent) successors and assigns. This Warrant and the rights evidenced hereby shall be binding upon and shall inure to the benefit of the parties hereto and the successors of the Company and the successors and permitted assigns of the Holder. Such successors and/or permitted assigns of the Holder shall be deemed to be a Holder for all purposes hereunder.

11. NO THIRD-PARTY BENEFICIARIES. This Warrant is for the sole benefit of the Company and the Holder and their respective successors and, in the case of the Holder, permitted assigns and nothing herein, express or implied, is intended to or shall confer upon any other person any legal or equitable right, benefit or remedy of any nature whatsoever, under or by reason of this Warrant.

12. LOST, STOLEN, MUTILATED OR DESTROYED WARRANT. If this Warrant is lost, stolen, mutilated or destroyed, the Company may, on such terms as to indemnity or otherwise as it may reasonably impose (which shall, in the case of a mutilated Warrant, include the surrender thereof), issue a new Warrant of like denomination and tenor as the Warrant so lost, stolen, mutilated or destroyed. Any such new Warrant shall constitute an original contractual obligation of the Company, whether or not the allegedly lost, stolen, mutilated or destroyed Warrant shall be at any time enforceable by anyone.

13. WAIVERS. No waiver by either party of any default with respect to any provision, condition or requirement of this Warrant shall be deemed to be a continuing waiver in the future or a waiver of any other provision, condition or requirement hereof, nor shall any delay or omission of any party to exercise any right hereunder in any manner impair the exercise of any such right accruing to it thereafter.

14. AMENDMENT. This Warrant and any term hereof may be changed, waived, discharged or terminated only by an instrument in writing signed by the Company and the Holder.

15. NOTICES, ETC. All notices required or permitted hereunder shall be in writing and shall be deemed effectively given: (a) upon personal delivery to the party to be notified, (b) when sent by confirmed telex or facsimile if sent during normal business hours of the recipient, if not, then on the next business day, (c) five (5) days after having been sent by registered or certified mail, return receipt requested, postage prepaid, (d) one (1) day after deposit with a nationally recognized overnight courier, specifying next day delivery, with written verification of receipt, or (e) when sent by email upon receipt of an acknowledgment by return email by the recipient as to receipt, which acknowledgment shall not be unreasonably delayed or withheld by the recipient. All communications shall be sent to the Company at the physical address or email listed on the signature page and to the Holder at M. D. Anderson Cancer Center, Strategic Industry Ventures, 7007 Bertner Avenue, 1MC9.2216, Houston, Texas 77030-3907, Attention: Larry Hope, Director, New Ventures and Business Development, or [***] or at such other physical address or email address as the Company or the Holder may designate by ten (10) days advance written notice to the other parties hereto.

16. ACCEPTANCE. Receipt of this Warrant by the Holder shall constitute acceptance of and agreement to all of the terms and conditions contained herein.

17. GOVERNING LAW. This Warrant and all rights, obligations and liabilities hereunder shall be governed by the laws of the State of Delaware.

18. REGISTRATION RIGHTS.

18.1 Registration Obligations; Filing Date Registration. The Company shall use reasonable best efforts to prepare and file with the Commission on or prior to the Filing Date a Registration Statement covering the resale of the Registrable Securities as would permit the sale and distribution of all the Registrable Securities from time to time pursuant to Rule 415 in the manner reasonably requested by the Holder. The Registration Statement shall be on Form S-3 (except if the Company is not then eligible to register for resale the Registrable Securities on Form S-3, in which case the Company shall undertake to register the Registrable Securities on Form S-3 as soon as practicable following the availability of such form). The Registration Statement shall contain the "Plan of Distribution" section in the form reasonably acceptable to the Company and the Holder. The Company shall use reasonable best efforts to cause the Registration Statement filed by it to be declared effective under the Securities Act as promptly as practicable after the filing thereof but in any event on or prior to the Effectiveness Date, and to keep such Registration

Statement continuously effective under the Securities Act until the earlier of (i) such date as all Registrable Securities covered by such Registration Statement have ceased to be Registrable Securities or (ii) the date that is two (2) years following the Effectiveness Date (the "***Effectiveness Period***"). If an ASR Pro Supp is not used to comply with this Section 18.1, then by 4:00 p.m., New York City time, on the Business Day following the Effectiveness Date, the Company shall file with the Commission in accordance with Rule 424 under the Securities Act the final prospectus to be used in connection with sales pursuant to such Registration Statement. For the avoidance of doubt, the Company may elect, in its sole discretion, to satisfy its obligations pursuant to this Warrant by filing an ASR Pro Supp on or prior to the Filing Date in lieu of a new Registration Statement, in which case the Company shall have satisfied its obligations pursuant to this Section 18.1 in full, and such ASR Pro Supp shall constitute a "Registration Statement" for all purposes hereof, with such necessary changes in the details of the provisions hereof as are necessitated by the context, including, without limitation, to take into account that the ASR Pro Supp is a Prospectus filed after the effectiveness of a Registration Statement and not a newly filed Registration Statement.

18.2 Registration Expenses. All reasonable fees and expenses incident to the performance of or compliance with this Section 18 by the Company (excluding underwriters' discounts and commissions and all fees and expenses of legal counsel, accountants and other advisors for the Holder except as specifically provided below), except as and to the extent specified in this Section 18.2, shall be borne by the Company whether or not a Registration Statement is filed by the Company or becomes effective and whether or not any Registrable Securities are sold pursuant to a Registration Statement. The fees and expenses referred to in the foregoing sentence shall include, without limitation, (i) all registration and filing fees (including, without limitation, fees and expenses (A) with respect to filings required to be made with the Nasdaq Stock Market, LLC and each other securities exchange or market on which Registrable Securities are required hereunder to be listed, (B) with respect to filings required to be made by the Company with the Financial Industry Regulatory Authority and (C) in compliance with state securities or Blue Sky laws by the Company or with respect to Registrable Securities); (ii) messenger, telephone and delivery expenses; (iii) fees and disbursements of counsel for the Company; (iv) Securities Act liability insurance, if the Company so desires such insurance; and (v) fees and expenses of all other persons retained by the Company in connection with the consummation of the transactions contemplated by this Warrant, including, without limitation, the Company's independent public accountants. In addition, the Company shall be responsible for all of its internal expenses incurred in connection with the consummation of the transactions contemplated by this Warrant (including, without limitation, all salaries and expenses of its officers and employees performing legal or accounting duties), the expense of any annual audit, the fees and expenses incurred in connection with the listing of the Registrable Securities on any securities exchange as required hereunder. In no event shall the Company be responsible for any underwriting, broker or similar fees or commissions of the Purchaser or, except to the extent provided for above or in the related transaction documents, any legal fees or other costs of the Holder.

18.3 Survival. Notwithstanding anything herein to the contrary, this Section 18 shall survive until the end of the Effectiveness Period; *provided*, *however*, that the terms set forth in Section 18.2 shall remain in effect in accordance with their terms.

(*Signature Page Follows*)

IN WITNESS WHEREOF, the Company has caused this Warrant to be executed by its duly authorized officer as of October 22, 2019.

ZIOPHARM ONCOLOGY, INC.

By: /s/ Robert Hadfield
Name: Robert Hadfield
Title: General Counsel

Address: One First Avenue
Parris Building #34
Navy Yard Plaza
Boston, MA 02129
Attn: Robert Hadfield
Email: [***]

EXHIBIT A

NOTICE OF EXERCISE

TO: ZIOPHARM ONCOLOGY, INC.

(1) The undersigned hereby elects to purchase shares of common stock, par value $0.001 per share (the "Common Stock"), of Ziopharm Oncology, Inc. (the "Company") pursuant to the terms of the attached Warrant, and [tenders herewith payment of the exercise price in full, together with all applicable transfer taxes, if any/elects to offset payments owed to the undersigned pursuant to the R&D Agreement, as defined in the Warrant].

(2) Please issue a book-entry statement representing said shares of Common Stock of the Company in the name of the undersigned or in such other name as is specified below:

_____

(Name)

_____

_____

(Address)

(3) The undersigned represents that (i) the aforesaid shares of Common Stock are being acquired for the account of the undersigned for investment and not with a view to, or for resale in connection with, the distribution thereof and that the undersigned has no present intention of distributing or reselling such shares; (ii) the undersigned is aware of the Company's business affairs and financial condition and has acquired sufficient information about the Company to reach an informed and knowledgeable decision regarding its investment in the Company; (iii) the undersigned is experienced in making investments of this type and has such knowledge and background in financial and business matters that the undersigned is capable of evaluating the merits and risks of this investment and protecting the undersigned's own interests; (iv) the undersigned understands that the shares of Common Stock issuable upon exercise of this Warrant have not been registered under the Securities Act of 1933, as amended (the "***Securities Act***"), by reason of a specific exemption from the registration provisions of the Securities Act, which exemption depends upon, among other things, the bona fide nature of the investment intent as expressed herein, and, because such securities have not been registered under the Securities Act, they must be held indefinitely unless subsequently registered under the Securities Act or an exemption from such registration is available; (v) the undersigned is aware that the aforesaid shares of Common Stock may not be sold pursuant to Rule 144 adopted under the Securities Act unless certain conditions are met and until the undersigned has held the shares for the amount of time prescribed by Rule 144; and (vi) the undersigned agrees not to make any disposition of all or any part of the aforesaid shares of Common Stock unless and until there is then in effect a Registration Statement covering such proposed disposition and such disposition is made in accordance with said registration statement, or the undersigned has provided the Company with an opinion of counsel satisfactory to the Company, stating that such registration is not required.

(4) No Exercise Shares subject to the attached Warrant may be exercised prior to the vesting of such Exercise Shares in accordance with Section 3 of such Warrant.

(Date)	(Signature)
	(Print name)

EXHIBIT B

ASSIGNMENT FORM

[To assign the foregoing Warrant, execute this form and supply required information. Do not use this form to purchase shares.]

FOR VALUE RECEIVED, the foregoing Warrant and all rights evidenced thereby are hereby assigned in full to:

Name: _____
(Please Print)

Address: _____
(Please Print)

Email Address: _____
(Please Print)

Date of Transfer/Assignment: _____, 20 __

Date of this Form: _____, 20 __

Holder's
Signature: _____

Holder's
Address: _____

NOTE: The signature to this Assignment Form must correspond with the name as it appears on the face of the Warrant, without alteration or enlargement or any change whatever. Officers of corporations and those acting in a fiduciary or other representative capacity should file proper evidence of authority to assign the foregoing Warrant.

Pursuant to the requirements of Section 10 of the Warrant, attached hereto is a copy of the Warrant so transferred or assigned to the person or entity first named above.

DESCRIPTION OF THE REGISTRANT'S SECURITIES REGISTERED PURSUANT TO SECTION 12 OF THE SECURITIES EXCHANGE ACT OF 1934

The following description sets forth certain material terms and provisions of the securities of Ziopharm Oncology, Inc. (the "Company" "we," "us," and "our") that are registered under Section 12 of the Securities Exchange Act of 1934, as amended. This description also summarizes relevant provisions of Delaware law. The following summary does not purport to be complete and is subject to, and is qualified in its entirety by reference to, the applicable provisions of Delaware law and our amended and restated certificate of incorporation and our amended and restated bylaws, copies of which are incorporated by reference as an exhibit to the Annual Report on Form 10-K of which this Exhibit 4.6 is a part, and are incorporated by reference herein. We encourage you to read our certificate of incorporation, our bylaws and the applicable provisions of Delaware law for additional information.

General

Our authorized capital stock consists of 280,000,000 shares, comprised of 250,000,000 shares of common stock, par value $0.001 per share, and 30,000,000 shares of preferred stock, par value $0.001 per share.

Our common stock is listed on The Nasdaq Stock Market LLC under the trading symbol "ZIOP."

Common Stock

Voting Rights. The holders of our common stock are entitled to one vote for each outstanding share of common stock owned by such stockholder on every matter properly submitted to the stockholders for their vote. Stockholders are not entitled to vote cumulatively for the election of directors. Because of this, the holders of a majority of the shares of common stock entitled to vote in any election of directors can elect all of the directors standing for election, if they should so choose. At any meeting of the stockholders, a quorum as to any matter shall consist of a majority of the votes entitled to be cast on the matter, except where a larger quorum is required by law, by our certificate of incorporation or by our bylaws.

Dividend Rights. Holders of our common stock are entitled to receive ratably dividends and other distributions of cash or any other right or property as may be declared by our board of directors out of our assets or funds legally available for such dividends or distributions. The dividend rights of holders of common stock are subject to the dividend rights of the holders of any series of preferred stock that may be issued and outstanding from time to time.

Liquidation Rights. In the event of any voluntary or involuntary liquidation, dissolution or winding up of our affairs, holders of our common stock would be entitled to share ratably in our assets that are legally available for distribution to stockholders after payment of liabilities. If we have any preferred stock outstanding at such time, the holders of such preferred stock may be entitled to distribution and/or liquidation preferences that require us to pay the applicable distribution to the holders of preferred stock before paying distributions to the holders of common stock.

Rights and Preferences. Holders of our common stock have no preemptive, conversion or subscription rights, and there are no redemption or sinking fund provisions applicable to our common stock. The rights, preferences and privileges of the holders of common stock are subject to, and may be adversely affected by, the rights of the holders of shares of any series of our preferred stock that we may designate and issue in the future.

The transfer agent and registrar for our common stock is American Stock Transfer & Trust Company.

The transfer agent and registrar for any series of preferred stock will be set forth in the applicable prospectus supplement.

Preferred Stock

Pursuant to our amended and restated certificate of incorporation, our board of directors has the authority, without stockholder approval, subject to limitations prescribed by law, to provide for the issuance of up to 30,000,000 shares of preferred stock in one or more series, and by filing a certificate pursuant to the applicable law of the State of Delaware, to establish from time to time the number of shares to be included in each such series, and to fix the designation, powers, preferences and rights of the shares of each series and any qualifications, limitations or restrictions thereof, and to increase or decrease the number of shares of any such series, but not below the number of shares of such series then outstanding.

We will fix the designations, voting powers, preferences and rights of the preferred stock of each series, as well as the qualifications, limitations or restrictions thereof, in the certificate of designation relating to that series. We will file as an exhibit to the registration statement of which this prospectus is a part, or will incorporate by reference from reports that we file with the Commission, the form of any certificate of designation that describes the terms of the series of preferred stock we are offering before the issuance of that series of preferred stock. This description will include:

- the title and stated value;
- the number of shares offered;
- the liquidation preference per share;
- the purchase price per share;
- the dividend rate(s), period(s) and/or payment date(s) or method(s) of calculation for dividends;
- whether dividends are cumulative or non-cumulative and, if cumulative, the date from which dividends will accumulate;
- our right, if any, to defer payment of dividends and the maximum length of any such deferral period;
- the procedures for any auction and remarketing, if any;
- the provisions for a sinking fund, if any;
- the provision for redemption or repurchase, if applicable, and any restrictions on our ability to exercise those redemption and repurchase rights;
- any listing of the preferred stock on any securities exchange or market;
- the terms and conditions, if applicable, upon which the preferred stock will be convertible into common stock, including the conversion price (or manner of calculation) and conversion period;
- whether the preferred stock will be exchangeable into debt securities, and, if applicable, the exchange price, or how it will be calculated, and the exchange period;
- voting rights, if any, of the preferred stock;
- preemptive rights, if any;
- restrictions on transfer, sale or other assignment, if any;
- whether interests in the preferred stock will be represented by depositary shares;
- a discussion of any material and/or special U.S. federal income tax considerations applicable to the preferred stock;
- the relative ranking and preferences of the preferred stock as to dividend rights and rights upon the liquidation, dissolution or winding up of our affairs;
- any limitations on issuance of any class or series of preferred stock ranking senior to or on a parity with the class or series of preferred stock as to dividend rights and rights upon liquidation, dissolution or winding up of our affairs; and
- any other specific terms, preferences, rights, limitations or restrictions of the preferred stock.

Our board of directors could authorize the issuance of shares of preferred stock with terms and conditions that could have the effect of discouraging a takeover or other transaction that might involve a premium price for holders of the shares or which holders might believe to be in their best interests. The issuance of preferred stock could adversely affect the voting power, conversion or other rights of holders of common stock and reduce the likelihood that common stockholders will receive dividend payments and payments upon liquidation.

The laws of the state of Delaware, the state of our incorporation, provide that the holders of preferred stock will have the right to vote separately as a class on any proposal involving fundamental changes in the rights of holders of such preferred stock. This right is in addition to any voting rights that may be provided for in the applicable certificate of designation.

CERTAIN CONFIDENTIAL INFORMATION CONTAINED IN THIS DOCUMENT, MARKED BY [*****], HAS BEEN OMITTED BECAUSE ZIOPHARM ONCOLOGY, INC. HAS DETERMINED THE INFORMATION (I) IS NOT MATERIAL AND (II) WOULD LIKELY CAUSE COMPETITIVE HARM TO ZIOPHARM ONCOLOGY, INC. IF PUBLICLY DISCLOSED.

Fifth Amendment to Research and Development Agreement

This **Fifth Amendment to Research and Development Agreement** (this "**Fifth Amendment**") is made as of October 22, 2019 (the "**Fifth Amendment Effective Date**"), by and among THE UNIVERSITY OF TEXAS M. D. ANDERSON CANCER CENTER ("**UTMDACC**"), a member institution of THE UNIVERSITY OF TEXAS SYSTEM ("**SYSTEM**"), and ZIOPHARM ONCOLOGY, INC., a Delaware corporation ("**ZIOPHARM**").

WHEREAS, UTMDACC are ZIOPHARM are parties to that certain Research and Development Agreement, dated August 17, 2015, as previously amended (the "**MDACC Research Agreement**"); and

WHEREAS, UTMDACC and ZIOPHARM have a mutual interest in amending the MDACC Research Agreement as follows with respect to payment for the funding of RESEARCH PROGRAMS, permitting the use of funds allocated under the MDACC Research Agreement to another agreement and extending the TERM of the MDACC Research Agreement.

NOW, THEREFORE, in consideration of the foregoing premises and of other valuable consideration, the receipt and sufficiency of which are hereby acknowledged, the parties hereto hereby agree as of the Fifth Amendment Effective Date as follows:

1. A new subsection (F) shall be placed after Subsection (E) under Section 5.2 and shall read:

"(F) ZIOPHARM, at its sole discretion, shall have the option to use up [***] of funds previously committed under this AGREEMENT to fund [***]

2. A new subsection (G) shall be placed after Subsection (F) under Section 5.2 and shall read:

(G) "Under the terms of this AGREEMENT and the 2019 Research and Development Agreement by and between ZIOPHARM and UTMDACC dated October 22, 2019 ("**2019 AGREEMENT**"), ZIOPHARM's funding commitment to the DEVELOPMENT COSTS under this AGREEMENT may be used to fund the "DEVELOPMENT COSTS" as defined and agreed under the 2019 AGREEMENT, as well as any expenditures incurred and actually paid by ZIOPHARM in support of the TCR-T PROGRAM (as defined in the 2019 AGREEMENT), including rent for the LEASED FACILITY (as defined in the 2019 AGREEMENT) and any amounts paid to third party contractors and/or any build-out costs for the LEASED FACILITY. ZIOPHARM shall provide UTMDACC with all documentation substantiating all such expenditures as reasonably requested by UTMDACC.

3. Section 9.1, TERM OF THE AGREEMENT is hereby deleted and replaced with the following:

"9.1 TERM OF THE AGREEMENT. The term of this AGREEMENT (the "TERM") shall commence on the EFFECTIVE DATE and expire on December 31, 2026, unless earlier terminated pursuant to this Section 9 or as otherwise provided in this AGREEMENT, or extended pursuant to mutual written agreement."

4. This Fifth Amendment amends the terms of the MDACC Research Agreement as expressly provided above, and the MDACC Research Agreement, as so amended and including all of its other terms and provisions that are not amended, remains in full force and effect.

5. Capitalized terms used but not defined herein shall have the meanings set forth in the MDACC Research Agreement. The validity, performance, construction, and effect of this Fifth Amendment shall be governed by and construed under the substantive laws of the State of New York, without regard to conflicts of law rules that would cause the application of the laws of another jurisdiction. This Fifth Amendment may be executed in counterparts, all of which taken together shall be regarded as one and the same instrument.

{Signature page follows}

IN WITNESS WHEREOF, the parties have caused this Fifth Amendment to be duly executed by their respective authorized officers as of the date first above written.

The University of Texas
M.D. Anderson Cancer Center

By: /s/ Ben Melson
Name: Ben Melson
Title: Senior Vice President and Chief Financial Officer

Ziopharm Oncology, Inc.

By: /s/ Robert Hadfield
Name: Robert Hadfield
Title: General Counsel

Exhibit 10.21

CONFIDENTIAL

CERTAIN CONFIDENTIAL INFORMATION CONTAINED IN THIS DOCUMENT, MARKED BY [*****], HAS BEEN OMITTED BECAUSE ZIOPHARM ONCOLOGY, INC. HAS DETERMINED THE INFORMATION (I) IS NOT MATERIAL AND (II) WOULD LIKELY CAUSE COMPETITIVE HARM TO ZIOPHARM ONCOLOGY, INC. IF PUBLICLY DISCLOSED.

2019 RESEARCH AND DEVELOPMENT AGREEMENT

This 2019 RESEARCH AND DEVELOPMENT AGREEMENT (the "**AGREEMENT**") is entered into as of October 22, 2019 (the "**EFFECTIVE DATE**") by and among THE UNIVERSITY OF TEXAS M. D. ANDERSON CANCER CENTER ("**UTMDACC**"), a member institution of THE UNIVERSITY OF TEXAS SYSTEM ("**SYSTEM**"), and ZIOPHARM ONCOLOGY, INC., a Delaware corporation ("**ZIOPHARM**").

RECITALS

A. WHEREAS, UTMDACC (represented by THE BOARD OF REGENTS ("**BOARD**") of the SYSTEM, an agency of the State of Texas), INTREXON CORPORATION, a Virginia corporation, ("**INTREXON**") and ZIOPHARM are parties to that certain LICENSE AGREEMENT, dated January 13, 2015 (such agreement, the "**LICENSE AGREEMENT**", and such date, the "**LICENSE EFFECTIVE DATE**");

B. WHEREAS, UTMDACC, INTREXON and ZIOPHARM were originally parties to that certain Research and Development Agreement, dated August 17, 2015, as amended from time to time ("**2015 R&D AGREEMENT**") and pursuant to an amendment effective as of October 5, 2018 by and among UTMDACC, INTREXON and ZIOPHARM, INTREXON has withdrawn from further participation under the 2015 R&D Agreement; and

C. WHEREAS, UTMDACC and ZIOPHARM desire to enter into a new research and development agreement relating to ZIOPHARM's immunotherapy program to use non-viral gene transfer to stably express and clinically evaluate neoantigen-specific TCRs in T-cells.

NOW, THEREFORE, in consideration of the mutual covenants and promises herein contained, the parties agree as follows:

1. TCR-T PROGRAM. UTMDACC and ZIOPHARM shall collaborate with respect to the research, development, regulatory, manufacture and other activities in connection with ZIOPHARM's immunotherapy program to use non-viral gene transfer to stably express and clinically evaluate antigen-specific TCRs in T cells pursuant to research and development plans to be prepared by the JSC (as defined in Section 2.1 below) and agreed upon by the parties from time to time after the EFFECTIVE DATE, which development plans may be amended from time to time by the parties. The collaborative activities to be conducted under the AGREEMENT will be referred to as the **TCR-T PROGRAM**"; and the development plans for the TCR-T PROGRAM will be referred to, collectively as the "**TCR-T PROGRAM DEVELOPMENT PLAN**". Each of UTMDACC and ZIOPHARM shall conduct the activities assigned to it with respect to such TCR-T

PROGRAM in the TCR-T PROGRAM DEVELOPMENT PLAN and furnish the facilities, know-how, materials, compositions and technical skills in connection with such activities, as set forth in the TCR-T PROGRAM DEVELOPMENT PLAN. The costs and expenses incurred by UTMDACC in connection with its activities under the TCR-T PROGRAM DEVELOPMENT PLAN, either at UTMDACC or in collaboration with a third party, in each case in furtherance of the TCR-T PROGRAM DEVELOPMENT PLAN, shall be deemed "**DEVELOPMENT COSTS**" and funded by ZIOPHARM in accordance with Section 4. For clarity and notwithstanding anything to the contrary in this AGREEMENT, UTMDACC's agreement or consent shall only be required for the portion of the TCR-T PROGRAM DEVELOPMENT PLAN that constitutes UTMDACC RESEARCH ACTIVITIES (as defined in Section 2.1) or UTMDACC CLINICAL TRIAL (as defined in Section 2.3), and shall not be required for other programs and activities, including those conducted by ZIOPHARM or their third party collaborators, even though such activities may be conducted in the LEASED FACILITY.

2. CONDUCT OF TCR-T PROGRAM.

2.1 THE JSC; PRINCIPAL INVESTIGATOR; GOVERNANCE. Notwithstanding any other provision of this AGREEMENT to the contrary, each party's members to the JSC under the 2015 R&D AGREEMENT shall be initially appointed to the JSC under this AGREEMENT and, for so long as the 2015 R&D AGREEMENT is in effect, the parties shall endeavor to hold all regularly scheduled meetings of the JSC under this AGREEMENT on the same days as the regularly scheduled meetings of the JSC under the 2015 R&D AGREEMENT.

(a) For and on behalf of ZIOPHARM, the JSC or its designee(s) will direct the activities and oversee the DEVELOPMENT COSTS for the TCR-T PROGRAM, and may reasonably delegate such responsibilities to one or more delegate(s) approved by ZIOPHARM. Subject to UTMDACC's conflict of interest policies, one or more principal investigator(s) within UTMDACC for the performance of the non-clinical, if required, and clinical activities under the TCR-T PROGRAM or subsets thereof shall be appointed as follows. Such principal investigators so nominated by the JSC and approved by the UTMDACC shall be deemed "**PRINCIPAL INVESTIGATORS**". In the event UTMDACC decides not to approve any of such nominees by JSC, it shall notify the JSC of such decision and the reasons therefor, and the JSC may nominate a different individual to UTMDACC for its approval. The parties shall use commercially reasonable best efforts to appoint such PRINCIPAL INVESTIGATORS within **[***]** days after the initial nomination by the JSC. For clarity, ZIOPHARM shall have the sole discretion to engage any principal investigator(s) outside UTMDACC. If for any reason any PRINCIPAL INVESTIGATOR at UTMDACC becomes unavailable or cannot conduct or complete any of the TCR-T PROGRAM assigned to such PRINCIPAL INVESTIGATOR, UTMDACC shall promptly notify ZIOPHARM in writing. UTMDACC in conjunction with the JSC will propose a successor to assume the roles and responsibilities of such PRINCIPAL INVESTIGATOR, and ZIOPHARM shall have the right to accept or reject the appointment of such successor at its sole discretion. In the event ZIOPHARM accepts such new appointment, such successor shall become a "**PRINCIPAL INVESTIGATOR**" and, at ZIOPHARM's request, the parties will discuss and amend the TCR-T PROGRAM

DEVELOPMENT PLAN as necessary, taking into consideration the expertise and capacity of such new appointment. If ZIOPHARM rejects the appointment of such proposed successor, then ZIOPHARM will have the right to terminate the TCR-T PROGRAM assigned to such PRINCIPAL INVESTIGATOR. The activities of all the TCR-T PROGRAM to be conducted by UTMDACC through its faculty employees and/or staff employees shall be referred to as the "**UTMDACC RESEARCH ACTIVITIES**".

(b) The parties will establish a joint steering committee ("**JSC**"), which will be responsible for management and oversight of all aspects of the TCR-T PROGRAM. Each party will retain the rights, powers and discretion granted to it under this AGREEMENT and no such rights, powers, or discretion will be delegated to or vested in the JSC unless such delegation or vesting of rights is expressly provided for in this AGREEMENT or the parties expressly so agree in writing. The JSC will not have the power to amend, modify or waive compliance with this AGREEMENT.

(c) ZIOPHARM shall have two (2) members of the JSC, and UTMDACC shall have one (1) member. The initial members of the JSC will be designated by the parties within **[***]** days of the EFFECTIVE DATE. The JSC may elect to include additional members subject to approval of the JSC. The chair of the JSC will be one of the representatives of ZIOPHARM. Each party may remove and fill vacancies for the JSC representative(s) that it appoints. If a member of the JSC is unable to attend a meeting, said member may appoint, in writing, a proxy to participate and vote in said member's stead, *provided, however, that* such proxy has the equivalent scientific and medical expertise and the authority to make decisions with respect to the applicable portion of the TCR-T PROGRAM during such meeting. Non-voting members of the JSC may be invited to attend to facilitate decision-making and administration, *provided, however, that* such non-voting member is bound by written obligation of confidentiality at least as stringent as those contained in this AGREEMENT.

(d) Each member of the JSC shall be entitled to **[***]** vote on all matters subject to the determination of the JSC. Decisions of the JSC will be reached by a **[***]** vote, *provided, however, that* no action may lawfully be taken at any meeting unless at least one representative of each party (including for this purpose any proxy representative appointed as provided below) is present at the meeting, *provided further that* each party will ensure that at least one representative of such party (or its proxy representative) is present at each regular and/or special JSC meeting properly called to action.

(e) The JSC shall: (a) define and develop strategies to accomplish the objectives of the TCR-T PROGRAM, (b) subject to UTMDACC's consent and available funding with respect to any UTMDACC RESEARCH ACTIVITIES, determine appropriate facilities and staffing and such other resources as may be needed to carry out the TCR-T PROGRAM, (c) monitor progress and expenditures for the TCR-T PROGRAM, and (d) seek to resolve any disputes between the parties relating to the TCR-T PROGRAM.

(f) The JSC may establish and delegate authority granted to it under this AGREEMENT to such other committees, teams, groups or auditors as it deems necessary

or appropriate to carry out the responsibilities of the JS C with respect to any the TCR-T PROGRAM including the safe, effective and efficient conduct of related or supporting project; *provided, however, that* the JSC will remain ultimately responsible for management and oversight of the TCR-T PROGRAM regardless of any such delegation.

(g) The JSC may meet in such a manner and at such intervals as it deems appropriate, *provided, however, that* the JSC shall meet a minimum of **[***]** times per year, *provided, further, that* in-person meetings shall take place in Houston, Texas, unless otherwise agreed by UTMDACC and ZIOPHARM. For clarity, the JSC is not required to hold any in-person meetings. The chair of the JSC, or its designee, shall circulate the agenda for each meeting at least **[***]** business days in advance and shall preside personally at each meeting or through the JSC chair's designee.

(h) The JSC shall keep written minutes of its meetings which shall reflect its actions and decisions. The intent of the parties is that minutes shall be agreed and signed by a JSC representative of each party within **[***]** calendar days following the applicable JSC decision.

(i) At least quarterly, the JSC shall prepare for the TCR-T PROGRAM a written status report detailing achievements, progress against objectives and timelines and a statement of actual versus budgeted expenditures. From time to time during the course of the TCR-T PROGRAM, each party, upon reasonable request, will provide the other party and the JSC with a written summary of the results of its activities related to the TCR-T PROGRAM, and, if determined to be appropriate by the JSC, a final written report within **[***]** days of the completion or termination of the TCR-T PROGRAM. All reports submitted under this Section 2.1 will describe the activities taken in furtherance of the TCR-T PROGRAM by the reporting party, any results achieved and any sole or joint intellectual property conceived, reduced to practice, developed or created in connection with or in performance of the TCR-T PROGRAM by the reporting party, in the level of detail and format agreed by the JSC. The JSC shall also have the right to supervise, monitor and provide input with respect to the acceptable clinical trial reporting with respect to any CLINICAL TRIAL, including but not limited to: reporting on regulatory interactions, CMC - Batch Records, translational data, regular clinical reports, IBD and access to IND copies.

(j) To the extent reasonably practicable, UTMDACC shall notify and consult with ZIOPHARM prior to taking any administrative action that would adversely affect, delay and/or discontinue any activities under the TCR-T PROGRAM (including any UTMDACC-INVOLVED CLINICAL TRIALS, as defined below). UTMDACC shall use commercially reasonable best efforts to conclude any such action in a manner sufficient to resume any adversely affected, delayed or discontinued activities as rapidly as reasonably possible. In the event the conduct of the affected TCR-T PROGRAM has not been resumed within **[***]** days following the initiation of a delay, ZIOPHARM, upon delivery of written notice to UTMDACC, shall be relieved from its obligation to fund the TCR-T PROGRAM at UTMDACC (and such amount will be deducted from ZIOPHARM's total funding obligation under Article 5) during the continued period of delay. The foregoing sentence shall not apply to a discontinuation of the TCR-T PROGRAM due to the implementation of a PERMISSIBLE DEVIATION, as defined in Section 2.3 below.

2.2 PERFORMANCE AND CONTROL OF TCR-T PROGRAM. UTMDACC and the PRINCIPAL INVESTIGATORS shall conduct the UTMDACC RESEARCH ACTIVITIES in accordance with the TCR-T PROGRAM DEVELOPMENT PLAN and in accordance with the laws of any jurisdiction applicable to any of the parties hereto, including all applicable statutes, enactments, acts of legislature, laws, ordinances, rules, regulations, notifications, guidelines policies, directions, directives and orders of any statutory authority, tribunal, board, or court having competent jurisdiction, or any applicable central or state government or local authority or other governmental entity of competent jurisdiction, including without limitation, if and where applicable, any of the foregoing that govern human subjects research, patient consent or authorization, privacy or use of information, and the like, all regulations and industry codes (including any modification or re-enactment thereto) applicable to the relevant party's activities or interactions under this AGREEMENT (including when applicable, the Health Insurance Portability and Accountability Act of 1966 and any regulations and official guidance promulgated thereunder ("**HIPAA**") as amended by the Health Information Technology for Economic and Clinical Health Act and the US Physician Payment Sunshine Act, and current Good Manufacturing Practices ("**GMP**") and Good Clinical Practices, International Conference on Harmonization/Good Clinical Practice guidelines, UTMDACC's policies and standards, and applicable requirements and official guidance of relevant regulatory authority, all of which may be in effect from time to time an applicable to conduct under this AGREEMENT) ("**APPLICABLE LAWS**"). In addition, at ZIOPHARM's request and cost, UTMDACC shall, in a timely manner, reasonably cooperate with ZIOPHARM and provide ZIOPHARM with reasonable assistance in connection with the preparation, filing and maintenance of regulatory filings and documentations, including documentation relating to the manufacturing activities conducted by UTMDACC under this AGREEMENT. With the exception of CLINICAL TRIALS (as defined in Section 2.3), and to the extent reasonably practicable, UTMDACC and the PRINCIPAL INVESTIGATORS shall segregate and treat as confidential under Section 14 of this AGREEMENT the conduct and records of the TCR-T PROGRAM from those of any other work performed by or in the laboratories or other facilities of UTMDACC, *provided, however, that*, among other things, UTMDACC and PRINCIPAL INVESTIGATORS shall not be required to establish any separate patient medical record system for any CLINICAL TRIALS conducted as part of the TCR-T PROGRAM. UTMDACC shall not utilize any other third party funding in connection with the conduct of any of the activities under the TCR-T PROGRAM, including but not limited to government grants or personnel paid by such third party funding, without the express prior written approval of ZIOPHARM.

2.3 CLINICAL STUDIES WITHIN THE TCR-T PROGRAM.

(a) UTMDACC shall be the initial site of ZIOPHARM's first clinical trial of its TCR-T Program in the United States, *provided, however, that* any existing or future clinical trial of the National Cancer Institute that is supported by, or conducted in collaboration with, ZIOPHARM shall be exempted from this first clinical trial ("**FIRST TRIAL**"). UTMDACC shall conduct such FIRST TRIAL (as well as any related

long-term follow-ups, animal studies and laboratory-based protocols as determined by the JSC) with one (1) or more ZIOPHARM-approved PRINCIPAL INVESTIGATORS in accordance with the terms and conditions of this AGREEMENT and in compliance with all APPLICABLE LAWS. ZIOPHARM shall have the right to approve appropriate PRINCIPAL INVESTIGATOR(S) for the FIRST TRIAL such that all funding directed to such FIRST TRIAL shall not create fiscal or other conflicts of interest. In addition, such funding shall be accounted for as "clinical" work. Notwithstanding the foregoing with respect to the FIRST TRIAL and in the event either party desires to initiate any new clinical trial within the TCR-T PROGRAM, ZIOPHARM (either by itself or through its designee) shall have the first right to assume the role of the regulatory sponsor for the FIRST TRIAL and each such new clinical trial and the holder of the IND for the FIRST TRIAL and any such new clinical trial (each, a "**NEW CLINICAL TRIAL**" and together with the FIRST TRIAL, the "**CLINICAL TRIALS**"). If ZIOPHARM elects not to assume such regulatory sponsorship, then UTMDACC may do so as agreed by the parties (the party that assumes the role of regulatory sponsor for a CLINICAL TRIAL is referred to as the "**SPONSOR**"). Each CLINICAL TRIAL for which UTMDACC is the SPONSOR shall be deemed a "**UTMDACC CLINICAL TRIAL**" and each CLINICAL TRIAL for which ZIOPHARM or a designee of ZIOPHARM is the SPONSOR shall be deemed a "**ZIOPHARM CLINICAL TRIAL**." UTMDACC CLINICAL TRIALS and ZIOPHARM CLINICAL TRIALS conducted at UTMDACC as a clinical trial site are collectively referred to as "**UTMDACC-INVOLVED CLINICAL TRIALS**"). If UTMDACC or ZIOPHARM desires to: (1) change the PRINCIPAL INVESTIGATOR for any UTMDACC-INVOLVED CLINICAL TRIAL, (2) modify or change the protocol(s), IND(s), Appendix M documents for IBC submission or the enrollment criteria of any UTMDACC-INVOLVED CLINICAL TRIALS, or (3) conduct any UTMDACC CLINICAL TRIALS at sites other than UTMDACC, then the parties will discuss in good faith the manner in which such additional activities shall be conducted. For clarity, ZIOPHARM shall have the sole discretion to conduct any and all ZIOPHARM CLINICAL TRIALS that are not UTMDACC-INVOLVED CLINICAL TRIALS. ZIOPHARM shall also be permitted to assign informational ZIOPHARM clinical research associate(s) at its cost to monitor any UTMDACC-INVOLVED CLINICAL TRIALS, *provided, however, that* such clinical research associate(s) will be subject to all written guidelines, policies, procedures, rules, and regulations, including all premises' rules, applicable to UTMDACC facilities, and will be subject to an obligation of confidentiality consistent with the obligations of confidentiality required of ZIOPHARM hereunder. The costs and expenses incurred in connection with the conduct at UTMDACC of any portion of the FIRST TRIAL or NEW CLINICAL TRIALS that is a UTMDACC-INVOLVED CLINICAL TRIAL under this Section 2.3 shall be deemed DEVELOPMENT COSTS, regardless of whether UTMDACC is the SPONSOR or holds the IND(s) for such trials. Notwithstanding the foregoing, for any UTMDACC-INVOLVED CLINICAL TRIAL, UTMDACC may implement any deviations from a protocol that are required by APPLICABLE LAW or the IRB, or that are necessary to protect the safety, rights or welfare of study subjects ("**PERMISSIBLE DEVIATIONS**"). UTMDACC will promptly notify ZIOPHARM of any PERMISSIBLE DEVIATION in writing, including providing any necessary supporting documentation, and to the extent reasonably possible and appropriate will do so prior to implementation. If ZIOPHARM does not agree with the implementation of any of the PERMISSIBLE DEVIATIONS, ZIOPHARM at its sole discretion may immediately terminate the applicable UTMDACC-INVOLVED CLINICAL TRIAL.

(b) With regard to any UTMDACC-INVOLVED CLINICAL TRIAL, UTMDACC and its medical staff, including a PRINCIPAL INVESTIGATOR, shall be responsible for the conduct of the study in accordance with UTMDACC's human subject research protection program and policies and shall ensure that such CLINICAL TRIAL does not interfere with the clinical care of any research subjects and the treating physician will have sole authority over such clinical care, and nothing in this AGREEMENT will prevent such medical staff from taking any action which is, in the reasonable medical judgment of such medical staff, in a research subject's best interest. Each party is responsible for ensuring that its principal investigator with respect to any CLINICAL TRIAL and all of its employees and agents working on any such CLINICAL TRIAL are (i) properly informed as to the procedures and other relevant information specified in and relating to the applicable CLINICAL TRIAL protocol and related agreements, and (ii) in compliance with this AGREEMENT and all APPLICABLE LAWS and regulations including the investigator responsibilities described in 21 C.F.R. Part 312 of the regulations of the United States Food and Drug Administration ("**FDA**") in their performance of any activities associated with the conduct of any CLINICAL TRIAL.

(c) Subject to APPLICABLE LAWS and the regulatory oversight of the applicable IRB, the parties shall collaboratively and expeditiously prepare a mutually acceptable informed consent form, any authorization or other document required under APPLICABLE LAWS, and appropriate patient recruitment materials as necessary for each UTMDACC-INVOLVED CLINICAL TRIAL. All such materials and any changes thereto will be subject to the approval of the applicable CRC, IRB, IBC, UTMDACC, and the JSC, and the parties shall implement any changes mandated by the CRC, IRB and IBC, *provided, however, that* ZIOPHARM at its sole discretion may terminate the applicable CLINICAL TRIAL immediately if it disagrees with any such mandated changes by the CRC, IRB or IBC. Subject to APPLICABLE LAWS, ZIOPHARM (either by itself or through its designee) will be responsible for filing and maintaining these materials with any governmental authorities and for obtaining any required approvals from any governmental authorities for ZIOPHARM CLINICAL TRIALS and UTMDACC shall make such filing for any and all UTMDACC CLINICAL TRIALS. For any and all CLINICAL TRIALS, the applicable PRINCIPAL INVESTIGATOR will be responsible for filing and maintaining materials related to IRB and IBC for each CLINICAL TRIAL, which materials shall be subject to the prior written approval of ZIOPHARM. Upon approval, ZIOPHARM (either by itself or through its designee) and/or UTMDACC, as applicable, will distribute these materials to the CLINICAL TRIAL sites. The informed consent of each subject participating in a CLINICAL TRIAL will be obtained prospectively using an IRB/EC approved informed consent process. Subject to APPLICABLE LAWS and the regulatory oversight of the applicable IRB and IBC, UTMDACC will be responsible for ensuring that each UTMDACC-INVOLVED CLINICAL TRIAL is in compliance with APPLICABLE LAWS regarding the consenting of human subjects who are participating in any such UTMDACC-INVOLVED CLINICAL TRIAL, and ZIOPHARM (either by itself or through its designee) will be responsible for ensuring that each site other than UTMDACC that is participating in a ZIOPHARM CLINICAL TRIAL is in compliance with APPLICABLE LAWS regarding the consenting of human subjects who are participating in any such ZIOPHARM CLINICAL TRIAL.

(d) Subject to prior review and comment by ZIOPHARM, each UTMDACC-INVOLVED CLINICAL TRIAL will be registered by UTMDACC on a public registry in a manner consistent with the requirements of the International Committee of Medical Journal Editors. UTMDACC will provide ZIOPHARM with a proposed copy of any such registry at least **[*******]** business days prior to submission and will consider ZIOPHARM's comments with respect thereto in good faith.

(e) Specifically, and without limiting the generality of Section 6.2, each party agrees to prepare, maintain and retain complete, accurate and legible written records, accounts, notes, reports and data relating to its role in the performance of each CLINICAL TRIAL for which it is the SPONSOR ("**STUDY RECORDS**"). STUDY RECORDS will be retained in a safe and secure manner for at least **[*******]** years following the later of (i) the approval of the relevant new drug application, (ii) withdrawal of the relevant IND or (iii) as required by APPLICABLE LAWS and regulations including FDA requirements under 21 CFR §312.57. Before UTMDACC destroys any STUDY RECORDS, UTMDACC will notify ZIOPHARM and will either transfer the STUDY RECORDS to ZIOPHARM to the extent such transfer is permitted by APPLICABLE LAWS or arrange with ZIOPHARM for the continued maintenance of such records at an off-site storage site at ZIOPHARM's cost and expense.

(f) From and after the EFFECTIVE DATE, and to the extent permitted by APPLICABLE LAWS, ZIOPHARM (either by itself or through its designee) will be solely responsible for all IND applications and other filings required by the FDA and any other in-country regulatory submissions and approvals (each an "**RA**") required to conduct each ZIOPHARM CLINICAL TRIAL. Prior to commencement of any CLINICAL TRIAL, and to the extent permitted by APPLICABLE LAWS, ZIOPHARM (either by itself or through its designee) will prepare and submit to the appropriate governmental authorities any RAs required under the APPLICABLE LAWS. Unless otherwise agreed upon by the parties, or as otherwise directed by the JSC or to the extent otherwise required by APPLICABLE LAWS, ZIOPHARM (either by itself or through its designee) will be the sponsor of any RA and will be responsible for satisfying all sponsor obligations and other requirements of applicable governmental authorities except for sponsor obligations for any UTMDACC-INVOLVED CLINICAL TRIAL, which shall remain the responsibility of UTMDACC. UTMDACC agrees to cooperate with ZIOPHARM (and its designee) to provide any other documents and information required by APPLICABLE LAWS and regulations or that ZIOPHARM (or its designee) reasonably requests in connection with the preparation, filing and maintenance of any RA.

(g) The JSC shall be responsible for ensuring that all CLINICAL TRIAL investigators collect, assess and report adverse events according to the procedures outlined in the applicable CLINICAL TRIAL protocol and as required by APPLICABLE LAWS, acting through the party that is the SPONSOR of the applicable CLINICAL TRIAL to do so. Each party that acts as SPONSOR of a CLINICAL TRIAL under this AGREEMENT will be responsible for the reporting of adverse events to the other parties,

but in no event more than one (1) business day following a determination of a suspected unexpected serious adverse event, and ZIOPHARM will (to the extent permitted by APPLICABLE LAWS and except as UTMDACC may otherwise be required by APPLICABLE LAWS to do so) report all such adverse events to appropriate government authorities as required by APPLICABLE LAWS. Each party further agrees that it will, in a timely manner consistent with APPLICABLE LAWS and the terms of all applicable CLINICAL TRIAL protocols and related documents, provide ZIOPHARM and the other parties hereto with all relevant information it obtains regarding the safety and/or the toxicity of any STUDY PRODUCT (as defined in Section 2.4).

(h) ZIOPHARM shall reimburse UTMDACC for the cost of providing necessary medical treatment to a study subject for any injuries directly resulting from the administration of the STUDY PRODUCT in a CLINICAL TRIAL conducted at UTMDACC to a study subject as set forth in the applicable protocol and consent as part of his/her participation in such CLINICAL TRIAL to the extent such injury is not due to the natural progression of the underlying disease or condition of such study subject, unless UTMDACC's negligence or misconduct causes the injury. Any costs reimbursed by ZIOPHARM under this Section 2.3(h) shall be deemed DEVELOPMENT COSTS under Section 4.

(i) UTMDACC and ZIOPHARM will promptly notify each other upon identifying any aspect of a UTMDACC-INVOLVED CLINICAL TRIAL protocol, including information discovered during site monitoring visits, or the study results that may adversely affect the safety, well-being, or medical care of the study subjects, or that may affect the willingness of subjects to continue participation in such CLINICAL TRIAL, influence the conduct of such CLINICAL TRIAL, or that may alter the IBC's and IRB's approval to continue such CLINICAL TRIAL. For each such CLINICAL TRIAL, UTMDACC shall promptly notify the IBC and IRB of any such events. When the safety or medical care of any study subject enrolled in such CLINICAL TRIAL could be directly affected by study results, then notwithstanding any other provision of this Agreement, UTMDACC will send such study subject a written communication about the results. To the extent appropriate under the circumstances, any such written communication will be subject to prior, timely review and comment by ZIOPHARM.

(j) Unless otherwise agreed by ZIOPHARM, all UTMDACC-INVOLVED CLINICAL TRIALS will be overseen and the results reviewed by an independent data monitoring committee ("**DMC**") established and supported and paid for by ZIOPHARM. The JSC will review and approve the DMC's membership and procedures. ZIOPHARM will assume responsibility for setting up and supporting all DMC meetings. The JSC will be notified of any DMC meetings. A representative from each party will be invited to attend all sessions of the DMC meetings. All DMC sessions reports related to any UTMDACC-INVOLVED CLINICAL TRIAL will be made available to the JSC.

(k) ZIOPHARM will promptly determine whether to accept or reject a major DMC recommendation for a CLINICAL TRIAL such as a recommendation to close a CLINICAL TRIAL. Should ZIOPHARM accept a major DMC recommendation,

ZIOPHARM will promptly communicate that decision to the members of the DMC and the JSC. In the event when ZIOPHARM does not elect to accept for implementation a major DMC recommendation, ZIOPHARM will promptly communicate that decision to the members of the DMC and the JSC with its rationale. If UTMDACC does not agree with ZIOPHARM's decision, UTMDACC, after consultation, as appropriate, with ZIOPHARM about alternative changes, if any, may terminate the applicable UTMDACC-INVOLVED CLINICAL TRIAL, *provided, however, that* UTMDACC shall notify ZIOPHARM in writing prior to such termination and, to the extent requested by ZIOPHARM, and as permitted by and to the extent consistent with APPLICABLE LAWS, instead of terminating such UTMDACC-INVOLVED CLINICAL TRIAL, transfer the trial to another site designated by ZIOPHARM. With respect to any UTMDACC CLINICAL TRIAL, if ZIOPHARM notifies UTMDACC that it wishes to assume the SPONSORSHIP for any such UTMDACC CLINICAL TRIAL, UTMDACC shall, as permitted by and to the extent consistent with APPLICABLE LAWS, instead of terminating such UTMDACC CLINICAL TRIAL, transfer to ZIOPHARM (or its designee) the SPONSORSHIP for any such UTMDACC CLINICAL TRIAL. The parties will work together to effect a prompt and orderly transfer of the CLINICAL TRIAL to another site and as applicable, the SPONSORSHIP for the CLINICAL TRIAL to ZIOPHARM or its designee. For the sake of clarity, in the event of a disagreement, UTMDACC shall have no obligation to continue a UTMDACC-INVOLVED CLINICAL TRIAL at UTMDACC and UTMDACC will have the right to suspend the CLINICAL TRIAL pending the transfer of the CLINICAL TRIAL and the SPONSORSHIP as contemplated herein.

(l) Notwithstanding anything to the contrary in this AGREEMENT, UTMDACC shall take appropriate corrective action including to terminate or suspend patient enrollment for any UTMDACC-INVOLVED CLINICAL TRIAL (i) for health, safety or regulatory reasons, or (ii) if a PRINCIPAL INVESTIGATOR is no longer employed by UTMDACC, or (iii) if a PRINCIPAL INVESTIGATOR is no longer able to perform his or her obligations, or (iv) if ZIOPHARM breaches its obligations under this AGREEMENT with respect to such CLINICAL TRIAL and fails to cure such breach within thirty (30) business days of receiving written notice from UTMDACC of such breach, *provided, however, that* before terminating or suspending enrollment for the UTMDACC-INVOLVED CLINICAL TRIAL on the basis of (ii) or (iii) above, at the request of ZIOPHARM, UTMDACC working with the JSC will make a good faith effort to: (a) find a substitute researcher who is ready, willing and able to assume the role of PRINCIPAL INVESTIGATOR and complete such UTMDACC-INVOLVED CLINICAL TRIAL and who is acceptable to ZIOPHARM; or (b) to the extent requested by ZIOPHARM, and as permitted by and to the extent consistent with APPLICABLE LAWS, instead of terminating such UTMDACC-INVOLVED CLINICAL TRIAL, transfer the trial to another site designated by ZIOPHARM and in conjunction therewith in the case of a UTMDACC CLINICAL TRIAL, transfer the SPONSORSHIP for such CLINICAL TRIAL to ZIOPHARM (or its designee).

2.4 MANUFACTURE, USE AND SUPPLY OF STUDY PRODUCT.

(a) Unless otherwise agreed, ZIOPHARM will be responsible for producing or otherwise obtaining and supplying gene and cell products and other study agents used in each CLINICAL TRIAL to be appropriately formulated and in sufficient quantities to complete the applicable CLINICAL TRIAL. Such products, together with any materials and/or components purchased by or on account of ZIOPHARM or supplied by or on behalf of ZIOPHARM for use to manufacture such products, as well as any manufacturing intermediaries, will be referred to collectively as the "**STUDY PRODUCT**". ZIOPHARM will be responsible for ensuring that all STUDY PRODUCTS will be properly labeled in accordance with the CLINICAL TRIAL protocol and APPLICABLE LAWS and will instruct UTMDACC with respect to such labelling requirements for any STUDY PRODUCT manufactured by UTMDACC.

(b) Unless otherwise agreed, UTMDACC will (i) use any STUDY PRODUCT only to conduct the CLINICAL TRIAL for which it was supplied and for no other purpose, (ii) not transfer any STUDY PRODUCT to anyone other than persons expressly authorized to receive them under this AGREEMENT, and (iii) not modify, replicate, make derivatives of or reverse engineer STUDY PRODUCT owned by or exclusively licensed to ZIOPHARM without ZIOPHARM's prior written consent, which consent shall be in ZIOPHARM's sole discretion. UTMDACC will store and handle STUDY PRODUCT in a secure manner to prevent access or use by unauthorized persons, and will observe such reasonable safety measures as are customarily employed by UTMDACC with respect to other similar materials.

(c) Upon completion of a CLINICAL TRIAL or TCR-T PROGRAM, UTMDACC or the applicable study site will destroy, or at ZIOPHARM's request and cost, return to ZIOPHARM any unused STUDY PRODUCT. ZIOPHARM will provide UTMDACC with specific return and destruction procedures for STUDY PRODUCT used in CLINICAL TRIALS.

(d) *Use of UTMDACC's Cell Processing Facility.*

(i) During the TERM, at ZIOPHARM's request and cost, UTMDACC agrees to produce, at its cell processing facility (**[*******]**) and/or at the cell processing facility funded by ZIOPHARM, any human cellular and tissue based STUDY PRODUCT and/or components used to manufacture the STUDY PRODUCT ("**HCT STUDY PRODUCTS**") for any CLINICAL TRIALS under the oversight of the JSC; *provided, however, that* UTMDACC will only be **[*******]** to manufacture HCT STUDY PRODUCTS for which it determines in its reasonable discretion that it has the existing ability, capacity, facilities, equipment, resources, and expertise to do so, giving **[*******]** (at a minimum no less than any **[*****] of [*****]**) to the use of its resources for the manufacturing of HCT STUDY PRODUCTS for use in the TCR-T PROGRAM in such determination. If UTMDACC is unable to manufacture a product for ongoing or planned clinical trial it will promptly provide written notification to ZIOPHARM of such inability, together with an explanation for the reason thereof. In the event there are manufacturing activities ongoing pursuant to this Section 2.4 at the end of the TERM, UTMDACC agrees to, at its election: (A) negotiate with ZIOPHARM the terms and conditions under which UTMDACC will continue to conduct such manufacturing activities on behalf of ZIOPHARM; or (B) cooperate with ZIOPHARM to, at ZIOPHARM's cost and expense, effect an orderly transition of such manufacturing activities to ZIOPHARM or its designee.

(ii) The terms for production of any HCT STUDY PRODUCTS produced by UTMDACC, including pricing, manufacturing and release specifications, and quality control and quality assurance testing, will be agreed upon by the parties in writing prior to the commencement of manufacturing. All costs and expenses incurred by UTMDACC in connection with the production of such HCT STUDY PRODUCTS as agreed to by the parties shall be included in the DEVELOPMENT COSTS and funded by ZIOPHARM in accordance with Section 4, *provided, however, that* such costs and expenses shall be at a rate that is no greater than that used for any internal programs of UTMDACC.

(iii) UTMDACC agrees to maintain all required GMP documentation concerning the production services with respect to the HCT STUDY PRODUCTS manufactured by UTMDACC, including documentation of all production and quality control testing, standard operating procedures, training records, batch records, logs and such other matters as may be required by APPLICABLE LAWS or by the specifications prescribed by ZIOPHARM ("**PRODUCTION DATA**"). All PRODUCTION DATA will be maintained by UTMDACC in a secure location and access will be limited to authorized UTMDACC and ZIOPHARM personnel (including consultants and advisors), auditors and governmental authorities; *provided, however, that* at ZIOPHARM's request and cost, and subject to reasonable confidentiality restrictions, copies of such PRODUCTION DATA will be made available to potential third party manufacturers. Based on its prior experience with similar products, UTMDACC will develop a schedule for production, testing and delivery of the each HCT STUDY PRODUCTS and once agreed upon by the parties, UTMDACC agrees to produce, test and deliver the HCT STUDY PRODUCTS in accordance with the production schedule and pricing agreed upon by the parties, subject to any default in payment by ZIOPHARM or events of FORCE MAJEURE.

(iv) For the avoidance of doubt, ZIOPHARM will retain (i) ownership of all know-how, data and other intellectual property owned by or independently developed by ZIOPHARM and (ii) control of all intellectual property licensed to ZIOPHARM from third parties, in each case, that is made available to UTMDACC in connection with the manufacture of any HCT STUDY PRODUCTS ("**ZIOPHARM MANUFACTURING IP**"). UTMDACC shall have no right to (x) use, or (y) disclose to any third party any ZIOPHARM MANUFACTURING IP except for purposes of carrying out CLINICAL TRIALS, as expressly permitted by this AGREEMENT or as otherwise expressly agreed in writing by ZIOPHARM.

(e) ZIOPHARM shall, at its sole election, have the right to manufacture STUDY PRODUCT and/or HCT STUDY PRODUCTS for use under this AGREEMENT at any site and at any time it deems appropriate. At ZIOPHARM's request and if agreed by UTMDACC (*provided, however, that* UTMDACC has the existing ability, capacity, facilities, equipment, resources and expertise to do so, giving reasonable priority to the use of its resources for the manufacturing of HCT STUDY PRODUCTS for use in the TCR-T

PROGRAM in such determination), UTMDACC will manufacture (including formulating and/or assembling) and supply STUDY PRODUCT (other than the HCT STUDY PRODUCTS) on behalf of ZIOPHARM, and such manufacturing and supply shall be subject to the terms and conditions to be agreed by the parties.

(f) UTMDACC agrees to reasonably assist ZIOPHARM in the establishment of manufacturing facilities for ZIOPHARM and, at ZIOPHARM's request and cost, shall deliver to ZIOPHARM (or its designee), all data, reports, standard operating procedures, analyses, reagents, vectors, cell lines (such as feeder cells) and other information directly relating to the manufacture of HCT STUDY PRODUCTS that exists at UTMDACC and is then reasonably available and transferable, subject to any third party confidentiality obligations. If at any time during the TERM, ZIOPHARM identifies particular documents, data or information directly relating to the manufacture of HCT STUDY PRODUCTS that exists at UTMDACC, is then owned or licensed by ZIOPHARM and is reasonably available and transferable and that was not previously delivered to ZIOPHARM, UTMDACC shall promptly provide such data and information to ZIOPHARM subject to any third party confidentiality obligations, upon ZIOPHARM's request and expense, and such expense shall be included in the DEVELOPMENT COSTS and funded by ZIOPHARM in accordance with Section 4. As applicable with good practices, the transfer of biologic materials and vectors shall be by the use of qualified shippers.

(g) During the TERM, UTMDACC shall expeditiously provide ZIOPHARM and designee(s) with reasonable access, at agreed times during ordinary administrative business hours, to UNIVERSITY PERSONNEL (as defined in Section 5.7) knowledgeable regarding the manufacture of HCT STUDY PRODUCTS for the purpose of assisting ZIOPHARM with technology transfer to a manufacturing facility. The assistance may be rendered by teleconference or in-person meetings in Houston, at ZIOPHARM's expense, and such expense shall be included in the DEVELOPMENT COSTS and funded by ZIOPHARM in accordance with Section 4.

(h) Prior to the commencement of any CLINICAL TRIAL that includes STUDY PRODUCTS supplied by UTMDACC, the parties will enter into an appropriate quality agreement that will, among other things, provide that ZIOPHARM shall have the right, at its own cost, to immediately inspect any facility at UTMDACC where manufacturing and/or supply of any STUDY PRODUCT is conducted, and to audit, review and copy the records maintained therein in connection with such manufacture and supply.

2.5 STUDY DATA; SPECIMENS.

(a) "**STUDY DATA**" means all analyzed data, results and other data generated by or on behalf of any party in the course of performing a CLINICAL TRIAL or other research study performed in furtherance of a TCR-T PROGRAM, including, but not limited to the case report forms (but not including original medical records). All STUDY DATA generated by **[*******]** (either **[*******]** or **[*******]** with **[*******]**) will be referred to as "**JOINT STUDY DATA**" and all STUDY DATA generated solely by ZIOPHARM (either by itself or through its affiliates, subcontractors and/or sub-licensees, but not **[*******]**) will be referred to as "**ZIOPHARM STUDY DATA**".

(b) The parties agree that all JOINT STUDY DATA will be **[***]** between the parties in a manner consistent with APPLICABLE LAWS and the requirements of oversight bodies such as institutional review boards or ethics committees. **[***]** Unless otherwise agreed in writing, JOINT STUDY DATA will be **[***]** and ZIOPHARM STUDY DATA will be **[***]** owned by ZIOPHARM. UTMDACC and ZIOPHARM shall have the right to publish the STUDY DATA, subject to Section 8.1 below.

(c) UTMDACC agrees that until publication of the results of an applicable study as permitted under this AGREEMENT, UTMDACC will have the limited right to use the JOINT STUDY DATA solely for internal research, academic and patient care purposes, and that it will not disclose any JOINT STUDY DATA to any other person or entity except: (a) as necessary, in UTMDACC's reasonable medical judgment, for the medical care of any research subject, (b) as necessary for protection of UTMDACC's interests against lawsuits, allegations of scientific misconduct, conflict of interest actions, patent infringement and interference proceedings, (c) for purposes of publication or public presentation as permitted under this AGREEMENT, (d) as required by APPLICABLE LAWS and regulations including laws and regulations of the FDA relating to licensure of study products, and (e) with respect to [***] subject to confidentiality restrictions as provided herein and other applicable legal requirements with respect to such data. For clarity, ZIOPHARM will have unlimited right to disclose and use any ZIOPHARM STUDY DATA solely owned by ZIOPHARM and any JOINT STUDY DATA, and UTMDACC will have the right to use and disclose ZIOPHARM STUDY DATA solely in furtherance of the UTMDACC RESEARCH ACTIVITIES (including publication in accordance with Section 8.1 below) and for no other purpose, except that UTMDACC will have no restrictions upon its right to use and disclose ZIOPHARM STUDY DATA pursuant to the rules of CONFIDENTIAL INFORMATION contained in Section 14.

(d) The parties will mutually agree upon a development plan under this AGREEMENT in connection with UTMDACC's provision of access to [***] ("**UTMDACC SPECIMENS**"), on commercially reasonable terms (not to exceed UTMDACC's cost plus **[*****] percent ([***]%)), to be used by ZIOPHARM [***]. As between UTMDACC and ZIOPHARM, and subject to the rights, if any of study subjects and third parties, all UTMDACC SPECIMENS shall **[***]**; provided that, for the avoidance of doubt, any INVENTIONS resulting from ZIOPHARM's use of such UTMDACC SPECIMENS shall be determined in accordance with Section 5. ZIOPHARM shall use any such UTMDACC SPECIMENS solely to perform the TCR-T PROGRAM in accordance with the TCR-T PROGRAM DEVELOPMENT PLAN under this AGREEMENT and for no other purpose, and in compliance with all APPLICABLE LAWS. ZIOPHARM shall not sell, transfer, disclose or otherwise provide access to the UTMDACC SPECIMENS to any person or entity without the prior written consent of UTMDACC (other than to Ziopharm's subcontractors, consultants and collaboration partners conducting activities on behalf of ZIOPHARM in connection with the TCR-T PROGRAM). Upon completion of the TCR-T PROGRAM or earlier upon UTMDACC's

written request, ZIOPHARM shall return any remaining UTMDACC SPECIMENS to UTMDACC or destroy the UTMDACC SPECIMENS and certify such destruction in writing (provided, that if ZIOPHARM or its subcontractors, consultants and collaboration partners are actively using any such UTMDACC SPECIMENS to perform the TCR-T PROGRAM in accordance with the TCR-T PROGRAM DEVELOPMENT PLAN under this AGREEMENT, ZIOPHARM shall be permitted to retain such UTMDACC SPECIMENS for so long as needed to complete such on-going activities).

(e) As between UTMDACC and ZIOPHARM, and subject to the rights, if any, of study subjects and third parties, all tissue samples and biological materials that are derived from any TCR-T PROGRAM ("**STUDY MATERIALS**") will be the property of **[*******]** unless otherwise expressly agreed upon by the parties. For clarity, STUDY MATERIALS do not include STUDY PRODUCT or UTMDACC SPECIMENS. STUDY MATERIALS may be used by the parties as expressly authorized by the JSC.

(f) As reasonably requested by ZIOPHARM, UTMDACC will provide access to materials and specimens from UTMDACC's vivarium, and to the extent necessary to perform the TCR-T PROGRAM in accordance with the TCR-T PROGRAM DEVELOPMENT PLAN under this AGREEMENT will purchase and maintain specimens on ZIOPHARM's behalf, in each case on commercially reasonable terms (not to exceed UTMDACC's [***].

2.6 ZIOPHARM MATERIALS. To the extent ZIOPHARM provides any tangible chemical and/or biological materials to UTMDACC in connection with the TCR-T PROGRAM (the "**ZIOPHARM MATERIALS**"), title to such ZIOPHARM MATERIALS shall remain with ZIOPHARM at all times. UTMDACC and the PRINCIPAL INVESTIGATORS shall use the ZIOPHARM MATERIALS solely to perform the TCR-T PROGRAM in accordance with the TCR-T PROGRAM DEVELOPMENT PLAN under this AGREEMENT and for no other purpose, and in compliance with ZIOPHARM's instructions and all APPLICABLE LAWS. UTMDACC and PRINCIPAL INVESTIGATOR shall not sell, transfer, disclose or otherwise provide access to the ZIOPHARM MATERIALS to any person or entity without the prior written consent of ZIOPHARM. UTMDACC and PRINCIPAL INVESTIGATOR shall not reverse engineer or otherwise attempt to determine the structure, composition or individual components of the ZIOPHARM MATERIALS, or alter, modify, improve or otherwise make or test any derivatives of the ZIOPHARM MATERIALS. Upon completion of the TCR-T PROGRAM or earlier upon ZIOPHARM's request, UTMDACC and PRINCIPAL INVESTIGATOR shall, according to ZIOPHARM's instructions and at ZIOPHARM's cost, return the ZIOPHARM MATERIALS to ZIOPHARM or destroy the ZIOPHARM MATERIALS and certify such destruction in writing.

3. FACILITIES; PERSONNEL; THIRD PARTY AGREEMENTS.

3.1 LEASE OF UTMDACC FACILITIES. In connection with this AGREEMENT and the 2015 R&D AGREEMENT, the parties have entered into an agreement dated as of October 15, 2019 regarding the establishment of research and development capabilities at facility(ies) within or immediately proximate to the

UTMDACC campus in Houston, Texas (such facility(ies) the "**LEASED FACILITY**" and such agreement, the "**LEASE AGREEMENT**"). For the purposes hereof, LEASED FACILITY shall also include any GMP manufacturing facilities subsequently leased by ZIOPHARM from UTMDACC as well as any GMP manufacturing facilities subsequently leased by ZIOPHARM from any third party in the greater Houston, Texas area. Any costs and expenses incurred by ZIOPHARM in connection with the build out, improvement and maintenance of such LEASED FACILITY (including any purchase of equipment, apparatus, and other materials in connection therewith that will be owned by ZIOPHARM) and any rent paid by ZIOPHARM for such LEASED FACILITY shall be deemed DEVELOPMENT COSTS and funded by ZIOPHARM in accordance with Section 4. Unless otherwise agreed by the parties in the LEASE AGREEMENT, ZIOPHARM shall have the sole discretion to determine the layout of the LEASED FACILITY, including its floor plan(s), intended use(s), any special facility(ies), and occupants (which may include VISITING SCIENTISTS permitted by UTMDACC pursuant to Section 3.2), to the extent in compliance with APPLICABLE LAWS, including any applicable zoning requirements and any structural limitations and architectural restrictions. For the purpose of determining inventorship, ownership and rights to data, results and inventions (including STUDY DATA and INVENTIONS), activities conducted within the LEASED FACILITY shall be deemed activities conducted in a ZIOPHARM facility, despite its possible location on UTMDACC campus.

3.2 VISITING SCIENTIST AND STAFF STATUS. In furtherance of the parties collaboration on the TCR-T PROGRAM, UTMDACC will use its reasonable best efforts to allow ZIOPHARM's designated personnel to work on-site at UTMDACC (the "**VISITING SCIENTIST**") with badge and computer access to UTMDACC as well as access to UTMDACC resources to facilitate and enable (i) laboratory activities, (ii) pre-clinical research including animal studies, (iii) manufacturing of clinical-grade products; and (iv) implementation and completion of the CLINICAL TRIALS, all conducted in collaboration with and at UTMDACC. **[***]** currently have VISITING SCIENTIST status with UTMDACC and shall have VISITING SCIENTIST status or a form substantially similar for access to UTMDACC facilities. Additionally, **[***]** shall have VISITING SCIENTIST status or a form substantially similar for access to UTMDACC facilities subject to UTMDACC policy.

3.3 PERSONNEL. The parties acknowledge that current UTMDACC personnel related to the TCR-T PROGRAM, including the "**PROGRAM FACILITATOR**", are an integral part of the TCR-T PROGRAM and such personnel's continuing active dedication to the TCR-T PROGRAM is integral to the success of the conduct of the TCR-T PROGRAM. Accordingly, and in furtherance of the objectives and activities set forth under this AGREEMENT, UTMDACC hereby consents to ZIOPHARM's solicitation of the employment of the employees of UTMDACC working on the TCR-T PROGRAM. As of the EFFECTIVE DATE, UTMDACC shall ensure that all personnel in the laboratory of each PRINCIPAL INVESTIGATOR participating in the TCR-T PROGRAM understand and agree to be bound by the terms and condition of this AGREEMENT as applicable to such personnel's area of expertise or function. After the EFFECTIVE DATE, in the event any such personnel become an employee of ZIOPHARM while still engaged in the conduct of any of the TCR-T PROGRAM,

UTMDACC agrees that, in conjunction with the conduct of the TCR-T PROGRAM at UTMDACC subject to the VISITING SCIENTIST provisions attached hereto as EXHIBIT A, it will use its reasonable best efforts to arrange for such personnel to obtain a VISITING SCIENTIST or similar appointment at UTMDACC and have reasonable and mutually agreed upon access to facilities, intranet, equipment, databases, records, samples, patients, support staff, information, services and other infrastructures utilized or generated in, or necessary or reasonably useful for the conduct of, the TCR-T PROGRAM.

3.4 APPLICABLE LAWS. The lease as well as access to and use of UTMDACC's facilities and resources will be subject to APPLICABLE LAWS and the visiting scientist provisions attached hereto as EXHIBIT A and may not, as reasonably determined by UT system tax counsel, result in private business use and/or adverse tax consequences with respect to any of the tax-exempt bonds issued by UT System or covering any of UTMDACC's facilities.

4. FUNDING OF TCR-T PROGRAM.

4.1 FUNDING BY ZIOPHARM. Pursuant to the 2015 R&D AGREEMENT and subject to the terms and conditions of this AGREEMENT, during the TERM, ZIOPHARM agrees to fund the DEVELOPMENT COSTS up to the amount and in the manner established in accordance with this Section 4, and will reimburse UTMDACC for the DEVELOPMENT COSTS actually incurred by UTMDACC in accordance with this Section 4. ZIOPHARM may set off against amounts committed for funding under this AGREEMENT those expenditures incurred and actually paid by ZIOPHARM in support of the TCR-T PROGRAM, including any amounts paid to third party contractors and/or landlords and/or any build-out costs for the LEASED FACILITY. ZIOPHARM shall provide UTMDACC with all documentation substantiating all such expenditures as reasonably requested by UTMDACC.

4.2 ZIOPHARM FUNDING COMMITMENT; DEVELOPMENT MILESTONES; ROYALTY; WARRANTS.

(a) From the EFFECTIVE DATE until December 31, 2020, the total funding commitment for the DEVELOPMENT COSTS shall be funded under the 2015 R&D AGREEMENT, as amended from time to time, unless such funds are not sufficient, in which case such reimbursement shall be from the NEW FUNDING COMMITMENT.

(b) During the three (3) consecutive twelve (12) month periods after January 1, 2021 (each such twelve (12)-month period, a "**CONTRACT YEAR**"), ZIOPHARM shall reimburse DEVELOPMENT COSTS incurred under this AGREEMENT from any amounts available under the 2015 R&D AGREEMENT and, following the depletion of such funds, in an additional amount of twenty million dollars ($20,000,000) (the "**NEW FUNDING COMMITMENT**"). For each such CONTRACT YEAR, ZIOPHARM shall not be required to provide more than eight million dollars ($8,000,000). While ZIOPHARM has no obligation to fund more than twenty million dollars ($20,000,000) total and eight million dollars ($8,000,000) for each such CONTRACT YEAR, UTMDACC also has no obligation to undertake any activity at its

expense or cost or incur any cost or expense that will not be reimbursed by ZIOPHARM. With respect to DEVELOPMENT COSTS: (i) all expenses or costs associated with the possible preparation, filing, and maintenance of institutional and federal regulatory documents, including any supporting research thereto, including, but not limited to travel, salaries, laboratory work, supplies, animal work, equipment and maintenance, facility costs, bioprocessing, manufacturing, and correlative studies, shall be considered "clinical costs", and (ii) all expenses and costs associated with basic or fundamental research that has no current or future clinical impact shall be considered non-clinical costs.

(c) Unless this AGREEMENT has been terminated for UTMDACC's breach pursuant to Section 9.2 and subject to the terms and conditions of this AGREEMENT, ZIOPHARM shall pay to UTMDACC:

(i) **[***]**

For clarity, the foregoing milestones due to UTMDACC from ZIOPHARM shall be due once regardless of whether repeated with the same or any other TCR-T PRODUCT. For all purposes under this AGREEMENT: (1) [***]; (2) "**REGULATORY APPROVAL**" shall mean means (a) in the United States, a New Drug Application or an Abbreviated New Drug Application for a TCR-T PRODUCT, and (b) outside the United States, an equivalent application for regulatory approval required before commercial sale or use of a TCR-T PRODUCT in a regulatory jurisdiction; (3) "**TCR-T PRODUCT**" shall mean any T-cell therapy product of ZIOPHARM for the treatment and prevention of cancer in humans consisting of an isolated human, murine or human-murine hybrid T cell receptor restricted by any major histocompatibility complex class molecule, such as with specificity to a NEOANTIGEN or GERMLINE ANTIGEN or VIRAL ANTIGEN, whether such T-cell therapy product results from research and development efforts of UTMDACC and/or ZIOPHARM; (4) "**NEOANTIGENS**" are **[***]** ("**TCRs**"); (5) "**GERMLINE ANTIGENS**" shall mean **[***]**; and (6) "**VIRAL ANTIGENS**" shall mean **[***]**.

(d) The parties agree that the amounts set forth in any budget will be inclusive as to: (i) all overhead cost, salaries of laboratory technicians, students, postdocs and other researchers working on the TCR-T PROGRAM; (ii) all costs incurred in connection with the pre-clinical studies and clinical trials conducted as part of such TCR-T PROGRAM; (iii) the costs of all manufacturing process development and manufacturing activities in connection with the conduct of the TCR-T PROGRAM; (iv) the costs for any regulatory activities conducted in connection with the TCR-T PROGRAM; and (v) the costs of all laboratory facilities, supplies and equipment and other UTMDACC resources, including any leasehold improvements and/or payments related to the LEASE AGREEMENT to UTMDACC. In determining the applicable rate for any overhead costs, UTMDACC shall ensure a fair and equitable characterization of the applicable activities, either as "clinical" or "non-clinical" activities. Further, any facility-related costs (such as leasehold improvements and/or payments related to the LEASE AGREEMENT), as well as out-of-pocket costs paid to a third party vendor, contractor and/or collaborator, shall not be subject to any overhead payment to UTMDACC.

(e) UTMDACC shall maintain complete and accurate records, at its own cost and expense, in sufficient detail to permit ZIOPHARM to confirm the accuracy of the financial reports submitted pursuant to Section 6.2 and the amount of DEVELOPMENT COSTS incurred by UTMDACC and/or reimbursed by ZIOPHARM. Upon **[*******]** administrative business days advance written notice, UTMDACC shall allow ZIOPHARM (or its designee) to inspect, review and make copies of such records in order to verify the accuracy of the financial reports submitted by UTMDACC. In addition, upon ZIOPHARM's written request, UTMDACC shall make its accountant or other financial professional who is familiar with such records available to ZIOPHARM to assist ZIOPHARM with such review and answer ZIOPHARM's questions relating thereto.

(f) ZIOPHARM shall pay UTMDACC a royalty on NET SALES on all its TCR-T PRODUCTS (other than sales to UTMDACC) in accordance with the following schedules:

Royalty Tier	Cumulative NET SALES of TCR-T PRODUCTS in the United States	Royalty Rate
1	For the first $**[*******]** in cumulative NET SALES of all TCR-T PRODUCTS in the United States	**[*****]%
2	For all cumulative NET SALES of TCR-T PRODUCTS in the United States greater than $[***].	**[*****]%

Royalty Tier	Cumulative NET SALES of TCR-T PRODUCTS outside the United States	Royalty Rate
1	For the first $**[*******]** in cumulative NET SALES of all TCR-T PRODUCTS outside the United States	[***]%
2	For all cumulative NET SALES of TCR-T PRODUCTS outside the United States greater than $[***].	[***]%

For the purposes of this AGREEMENT, "**NET SALES**" shall have the meaning set forth in **Exhibit B**.

(g) Royalties under Section 4.2(f) will be payable on a country-by-country and TCR-T PRODUCT-by-TCR-T PRODUCT basis during the period commencing on the first commercial sale of a TCR-T PRODUCT in a particular country and ending **[*******]** years following the first commercial sale of such TCR-T PRODUCT in such country.

(h) The foregoing royalty rates and development milestone payments are based upon UTMDACC's active support of the TCR-T PROGRAM and shall be subject to reduction as follows:

(i) If, at the time ZIOPHARM's first TCR-T PRODUCT is approved in the United States, [***], then the foregoing royalty rates and milestone payments shall be reduced by [***]. As used herein, [***] ZIOPHARM in good faith

shall create and maintain a schedule of [***] owned, controlled or licensed by ZIOPHARM that are [***], as provided by ZIOPHARM to UTMDACC every **[***]** calendar months during the term of this AGREEMENT.

(ii) If at any time prior to the **[***]** anniversary of this AGREEMENT's EFFECTIVE DATE, UTMDACC enters into a non-viral TCR-T collaboration with a third party, then the foregoing royalty rates and milestone payments shall be reduced by **[***]**.

(i) For the avoidance of doubt, in the event of any acquisition of ZIOPHARM by a third party, merger of ZIOPHARM with a third party or sale of all or substantially all of ZIOPHARM's assets or stock to a third party ("**SALE EVENT**"), the royalties and milestone payments hereunder shall only be payable with respect to TCR-T PRODUCTS developed by ZIOPHARM prior to the SALE EVENT. Such obligation to pay royalties and milestones will continue after the SALE EVENT but not with respect to any pre-existing or independently developed TCR program of the third party. In addition, in the event of any acquisition by ZIOPHARM of a third party, whether by merger or acquisition of all or substantially all of a third party's assets or stock, the royalties and milestone payments hereunder shall not be payable upon any pre-existing or independently developed TCR program of the third party, unless such TCR program is then further developed under this AGREEMENT.

4.3 PAYMENT. ZIOPHARM will pay the amount due to UTMDACC pursuant to Section 4 either by wire transfer to:

JPMorgan Chase Bank, N.A.
707 Travis
Houston, Texas 77002
SWIFT: **[***]** (used for international wires)
ABA ROUTING NO: **[***]** (used for domestic wires)
ABA ROUTING NO: **[***]** (used for domestic ACH)
ACCOUNT NAME: The Univ. of Texas M. D. Anderson Cancer Center
Tech Commercialization
ACCOUNT NO.: **[***]**
REFERENCE: Ziopharm TCR-T Program Research & Development Agreement

or by checks made payable to UTMDACC and sent to:

The University of Texas
M. D. Anderson Cancer Center
P.O. Box 4390
Houston, Texas 77210-4390
Reference: Ziopharm TCR-T Program Research & Development Agreement

Each wire or check payment must reference the TCR-T PROGRAM project title and the name of the PRINCIPAL INVESTIGATOR.

4.4 WARRANTS. On the Effective Date, ZIOPHARM shall issue UTMDACC a warrant representing the right to purchase 3,333,333 shares of ZIOPHARM common stock (with an exercise price of $0.001 per share) in the form attached hereto as EXHIBIT C.

4.5 EXPENDABLES AND EQUIPMENT. To the extent paid for by ZIOPHARM, ZIOPHARM will own all expendables and equipment purchased or fabricated in the performance of the TCR-T PROGRAM in accordance with the TCR-T PROGRAM DEVELOPMENT PLAN and the budget contained therein. UTMDACC will store such expendables (if located at UTMDACC) under suitable storage conditions and use such expendables for the purpose of conducting the TCR-T PROGRAM only. UTMDACC will tag and maintain such equipment (if located at UTMDACC) in good working order and will use such equipment for the purpose of conducting the TCR-T PROGRAM, giving the highest priority to such use.

5. INTELLECTUAL PROPERTY; INVENTIONS.

5.1 OWNERSHIP OF INVENTIONS. All discoveries and inventions, whether or not patentable, that are conceived or reduced to practice in the performance of any of the TCR-T PROGRAM DEVELOPMENT PLAN under this AGREEMENT, together with all intellectual property rights therein, shall be deemed "**INVENTIONS**." ZIOPHARM shall solely own all INVENTIONS. Notwithstanding anything to the contrary in this Agreement, ZIOPHARM shall at all times retain all rights and interest in the ZIOPHARM MATERIALS.

5.2 EXCLUSIVE LICENSE. ZIOPHARM hereby grants to UTMDACC an exclusive (with the right to sublicense), fully paid, royalty-free, perpetual and irrevocable license in the EXCLUSIVE FIELD to make, have made, use, sell, offer for sale and import any products incorporating or based upon INVENTIONS. "**EXCLUSIVE FIELD**" means the research, development, manufacture and commercialization of (i) autologous TCR-T PRODUCTS engineered by viral gene transfer technologies to express TCRs for the treatment of human solid and liquid tumors, and (ii) any products or services for the treatment and prevention of any condition other than cancer, including without limitation any autologous and allogeneic cell therapy products engineered by viral gene transfer technologies to express TCRs.

5.3 NON-EXCLUSIVE LICENSE. ZIOPHARM hereby grants to UTMDACC a non-exclusive (with the right to sublicense), fully paid, royalty-free, perpetual and irrevocable license in the NON-EXCLUSIVE FIELD to make, have made, use, sell, offer for sale and import any products incorporating or based upon INVENTIONS. "**NON-EXCLUSIVE FIELD**" shall mean the research, development, manufacture and commercialization of allogeneic cell therapy products or services engineered by viral gene transfer technologies to express TCRs for the treatment of human solid and liquid tumors.

5.4 PATENT PROTECTION. As between the parties, ZIOPHARM shall have the sole right to prepare, file, prosecute, maintain, enforce and defend all U.S. and foreign patents, registrations and other forms of intellectual property in INVENTIONS but nothing herein will obligate ZIOPHARM to take any such actions. ZIOPHARM shall keep UTMDACC reasonably informed of all such preparations, filings, prosecution, maintenance, enforcement and defense. MDACC shall reasonably cooperate with ZIOPHARM with respect to matters concerning such INVENTIONS to the extent reasonably necessary for filing, prosecuting, maintaining, defending or enforcing any such patents, registrations and other forms of intellectual property protection.

5.5 COMMERCIALIZATION IN TEXAS. [***]

5.6 PREFERENTIAL PRICING. Following REGULATORY APPROVAL in the United States of any TCR-T PRODUCT developed pursuant to this AGREEMENT, ZIOPHARM shall offer to sell such TCR-T PRODUCT developed pursuant to this AGREEMENT to UTMDACC at [***] ZIOPHARM [***] such TCR-T PRODUCT developed pursuant to this AGREEMENT to [***]

5.7 UNIVERSITY PERSONNEL. All UNIVERSITY PERSONNEL who conduct any activities with respect to the TCR-T PROGRAM shall be obligated to assign to the BOARD OF REGENTS of THE UNIVERSITY OF TEXAS SYSTEM all inventions and intellectual property rights arising from their work in the TCR-T PROGRAM in a manner that enables the BOARD and UTMDACC to grant to ZIOPHARM all rights UTMDACC purports to grant under this AGREEMENT. "**UNIVERSITY PERSONNEL**" shall mean employees, other agents and consultants of UTMDACC.

6. GOVERNMENTAL COMMUNICATIONS; RECORDS AND REPORTS.

6.1 GOVERNMENTAL COMMUNICATIONS.

(a) ZIOPHARM will take the initiative in arranging discussions with any governmental authority involving data from or the conduct of any TCR-T PROGRAM or CLINICAL TRIAL. Formal meetings with governmental authorities concerning the design or data from a TCR-T PROGRAM or CLINICAL TRIAL will be discussed with the JSC. With the prior written consent of ZIOPHARM, UTMDACC will have the right to participate in all formal meetings with governmental authorities relating to a TCR-T PROGRAM or CLINICAL TRIAL unless legally precluded from doing so. Additionally, UTMDACC will, at the request of ZIOPHARM, cooperate with ZIOPHARM regarding any discussions with any governmental authority involving data from or the conduct of any TCR-T PROGRAM or CLINICAL TRIAL.

(b) In addition to all documents otherwise required to be provided to the other party by this AGREEMENT, the applicable TCR-T PROGRAM, applicable CLINICAL TRIAL and APPLICABLE LAWS, to the extent permitted by APPLICABLE LAWS each party agrees to promptly provide the other party with a copy of all documents

and other written or electronic communications related to any TCR-T PROGRAM or CLINICAL TRIAL which such party has submitted to any governmental authority including protocol amendments, information amendments, safety reports, annual reports, investigator reports, reports of unanticipated problems involving risks to subjects or others, reports of serious or continuing noncompliance with APPLICABLE LAWS and regulations or the requirements of an Institutional Biosafety Committee (IBC), institutional review board/ethics committee ("**IBC/IRB/EC**") or reports of the suspension or termination of IBC/IRB/EC approval of human subjects research related to a TCR-T PROGRAM or CLINICAL TRIAL. Information provided will be deemed CONFIDENTIAL INFORMATION (as defined in Section 14) of the party providing it as long as it otherwise qualifies as CONFIDENTIAL INFORMATION.

(c) To the extent permitted by APPLICABLE LAWS, each party will promptly notify the JSC of any of the following of which it becomes aware: (i) any correspondence from any governmental authorities related to a TCR-T PROGRAM or CLINICAL TRIAL that is received by that party, or its agents or affiliates, or by participating sites funded by that party; (ii) investigations or site visits by any governmental authorities related to a TCR-T PROGRAM or CLINICAL TRIAL whether announced or unannounced; (iii) enforcement actions by any governmental authorities related to a TCR-T PROGRAM or CLINICAL TRIAL; or (iv) any action taken by any governmental authority regarding manufacturing of a product used in a TCR-T PROGRAM or CLINICAL TRIAL. Each party will consult and cooperate with the other party and the JSC in responding to any such event, including providing documents, information and access as properly requested. Information provided will be deemed CONFIDENTIAL INFORMATION of the party providing it qualifies as CONFIDENTIAL INFORMATION as defined in Section 14.

6.2 RECORDS; REPORTS. UTMDACC shall keep accurate financial and scientific records relating to the TCR-T PROGRAM and will make such records available to ZIOPHARM (for review and/or copying) throughout the TERM and for three (3) years thereafter during normal administrative business hours. Each PRINCIPAL INVESTIGATOR will submit monthly oral reports and quarterly written reports to ZIOPHARM detailing TCR-T PROGRAM activities and results thereof, including all data and conclusions. The PRINCIPAL INVESTIGATOR shall submit to ZIOPHARM a comprehensive final report to ZIOPHARM within (90) days after this AGREEMENT expires or terminates summarizing the TCR-T PROGRAM accomplishments and significant findings, all INVENTIONS developed in the course of the TCR-T PROGRAM. Subject to Section 14, ZIOPHARM may utilize all information submitted to it pursuant to this Section 6 in any manner.

7. INTENTIONALLY OMITTED.

8. PUBLICATION; PUBLICITY.

8.1 PUBLICATION.

(a) UTMDACC has the right to publish, present or otherwise publicly disclose (to persons not bound by a confidentiality agreement) the STUDY DATA generated solely by UTMDACC PERSONNEL ("**DISCLOSURE**"), subject to the requirements set forth below. UTMDACC agrees to provide ZIOPHARM a copy of any proposed DISCLOSURE at least **[***]** days prior to the earlier of submission or publication, for the ZIOPHARM to ascertain whether ZIOPHARM's CONFIDENTIAL INFORMATION would be disclosed by the DISCLOSURE and/or whether the DISCLOSURE contains a potentially patentable INVENTION so that appropriate steps may be taken to protect such INVENTION. ZIOPHARM will provide comments on any proposed DISCLOSURE, if any, within **[***]** days of its receipt. If a patentable INVENTION is disclosed in an abstract, presentation, or manuscript and ZIOPHARM has not filed any patent applications on such INVENTION prior to the date ZIOPHARM receives such manuscript, ZIOPHARM will promptly advise UTMDACC whether it desires to file or to have filed a patent application thereon in accordance with Section 5.4. If necessary, UTMDACC shall delay submission or publication of the proposed DISCLOSURE to any third party for up to an additional **[***]** days for the purpose of preparing and filing a patent application claiming any INVENTION disclosed therein. Additionally, UTMDACC shall delete from the proposed DISCLOSURE any CONFIDENTIAL INFORMATION of ZIOPHARM (excluding STUDY DATA and INVENTIONS generated by UTMDACC PERSONNEL, either solely or jointly with ZIOPHARM) that ZIOPHARM reasonably requests UTMDACC to delete. UTMDACC hereby grants ZIOPHARM the option of receiving an acknowledgment in any DISCLOSURE it submits that relates to the TCR-T PROGRAM. ZIOPHARM shall exercise such option by written notice to UTMDACC within **[***]** days after receiving a proposed DISCLOSURE for review under this Section 8. The JSC shall assign responsibility for developing additional written procedures to facilitate efficient review of scientific communications, such as abstracts, presentations and other publications.

(b) Notwithstanding anything to the contrary, with respect to any CLINICAL TRIAL DATA resulting from a multi-center CLINICAL TRIAL, UTMDACC shall have the right to publish such CLINICAL TRIAL DATA only after the publication of the first multi-center publication, *provided, however, that*, if such multicenter publication is not submitted within **[***]** after the completion, termination or abandonment of such CLINICAL TRIAL for all such sites, then UTMDACC shall have the right to publish its own CLINICAL TRIAL DATA resulting from the portion of the study conducted at UTMDACC, subject to this Section 8.1. UTMDACC and ZIOPHARM shall publish any CLINICAL TRIAL DATA resulting from a CLINICAL TRIAL in which UTMDACC is the sole clinical trial site jointly; *provided, however, that*, if such joint publication is not submitted within **[***]** after the completion, termination or abandonment of such CLINICAL TRIAL, then UTMDACC shall have the right to publish on its own the CLINICAL TRIAL DATA resulting from the study, subject to this Section 8.1; *provided, further, however, that*, ZIOPHARM shall have the right to issue a press release regarding top-line data from any such CLINICAL TRIAL prior to such joint publication. "**CLINICAL TRIAL DATA**" means all data and results generated by UTMDACC in a UTMDACC-INVOLVED CLINICAL TRIAL.

(c) UTMDACC acknowledges that ZIOPHARM is a public company

and as such, is subject to certain disclosure requirements and other rules and regulations promulgated by the SEC and/or any stock exchange. As a result, other than the right to publish STUDY DATA in accordance with this Section 8.1, UTMDACC agrees that it will not make any public statements regarding any STUDY DATA or any aspect of the TCR-T PROGRAM that may be construed as the disclosure of material non-public information, without first consulting with ZIOPHARM and obtaining ZIOPHARM's prior written approval to do so.

8.2 PUBLICITY. Except as required by APPLICABLE LAWS (including to comply with regulations promulgated by the SEC and/or any stock exchange), no party shall use the name, logos, trademarks or other identifier of the other parties or the name, likeness or image of any other party's employees or staff members (except in an acknowledgment of sponsorship) in publications, advertising, press releases or for any other commercial purpose without such other party's prior written consent, such consent not to be unreasonably withheld. ZIOPHARM shall not state or imply in any publication, advertisement or other medium that any product or service bearing any of ZIOPHARM's names or trademarks and/or manufactured, sold or distributed by ZIOPHARM has been tested, approved or endorsed by UTMDACC. Notwithstanding any other provision of this AGREEMENT, but subject to Section 8.1, each party and its researchers and employees will have the right, without any other party's approval, to acknowledge any other party and any other party's involvement with research hereunder in scientific or academic publications and communications describing the research or reporting the results of the research.

9. TERM; TERMINATION.

9.1 TERM OF THE AGREEMENT. The term of this AGREEMENT (the "**TERM**") shall commence on the EFFECTIVE DATE and expire on December 31, 2026, unless earlier terminated pursuant to this Section 9 or as otherwise provided in this AGREEMENT, or extended pursuant to mutual written agreement.

9.2 TERMINATION FOR MATERIAL BREACH. Either ZIOPHARM or UTMDACC may terminate this AGREEMENT for any material breach of this AGREEMENT by the other party, if such breach is not cured within sixty (60) days after the breaching party receives written notice of such breach by the non-breaching party.

9.3 EFFECT OF TERMINATION. Termination or expiration of this AGREEMENT shall not affect the rights and obligations of the parties that accrued prior to the EFFECTIVE DATE of such termination or expiration. After termination, UTMDACC will submit to ZIOPHARM a final report of all costs incurred and all funds received under this AGREEMENT as set forth in Section 4. The report will be accompanied by a check for any funds remaining which were paid to UTMDACC under Section 4, if any, after allowable costs and non-cancelable commitments have been paid.

9.4 SURVIVAL. The provisions of Sections 1 (last sentence), 2.2 (second and third sentence), 2.3(e), 2.3(f), 2.3(h), 2.4(c), 2.4(d)(i)(last sentence), 2.4(d)(iii), 2.4(d)(iv), 2.5 (excluding clause (f)), 2.6, 3.1 (last sentence), 4.2(c) through (i), 4.3, 4.4, 4.5, 5, 6.2, 8, 9.3, 9.4, 10, 11, 12 13.2, 13.3, 14, 15, and 16 and Exhibit B shall survive termination or expiration of this AGREEMENT.

10. NOTICE. Any notice given under this AGREEMENT must be in writing and must be delivered by mail, by personal delivery or delivery service, or by facsimile addressed to the parties as follows:

UTMDACC:
The University of Texas M. D. Anderson Cancer Center
Office of Technology Commercialization, Unit 1669
PO Box 301407
Houston, Texas 77230-1407
ATTENTION: Ferran Prat, J.D., Ph.D.
Fax No.: **[***]**

With a copy to with copies (which copies shall not constitute notice):

The University of Texas M. D. Anderson Cancer Center
Legal Services—Unit 1674
PO Box 301407
Houston, Texas 77230-1407
Attn: Chief Legal Officer
Fax No.: **[*****]

ZIOPHARM:
ZIOPHARM Oncology, Inc.
1 First Avenue
Parris Building, #34
Navy Yard Plaza
Boston, MA 02129
Attention: Rob Hadfield, General Counsel
Email: **[***]**
Fax No.: **[***]**

With a copy to with copies (which copies shall not constitute notice):
Cooley LLP
500 Boylston Street
Boston, MA 02116
Attention: Marc Recht
Email: **[***]**
Fax No.: **[***]**

All notices will be effective and will be deemed delivered (i) if by personal delivery or delivery service, on the date of delivery, (ii) if by electronic facsimile communication, on the date of transmission of the communication; and (iii) if by mail, three (3) days after

deposit in the mail. Any party from time to time may change its address, facsimile number or other information for the purpose of notices to that party by giving notice specifying such change to the other party hereto.

11. INDEMNIFICATION.

11.1 INDEMNIFICATION BY ZIOPHARM. ZIOPHARM hereby agrees to indemnify, hold harmless, and subject to the statutory duties of the Texas Attorney General, defend UTMDACC, SYSTEM, and BOARD, and their respective regents, officers, employees, agents and affiliates (collectively, the "**UTMDACC INDEMNITEES**") from any third party damage, loss, or expense (including reasonable attorneys' fees and expenses of litigation) (collectively "**LOSSES**") incurred by or imposed upon any of the UTMDACC INDEMNITEES in connection with any claims, suits, actions, demands, or judgments (collectively, "**CLAIMS**") arising out of or connected with (i) ZIOPHARM's activities under this AGREEMENT or the TCR-T PROGRAM performed by ZIOPHARM under this AGREEMENT, (ii) the personal injury (including death) or property damage arising out of or connected with a defect in the design or manufacture of the STUDY PRODUCTS by ZIOPHARM, including ZIOPHARM's failure to manufacture and provide the STUDY PRODUCTS in accordance with good manufacturing practices; (iii) the use by ZIOPHARM of any of the STUDY DATA or STUDY SPECIMENS; or (iv) the gross negligence or intentional misconduct or unlawful act or omission by ZIOPHARM or a ZIOPHARM representative, or the injury or death of any person and/or the damage to property that arises, directly or indirectly, from the intentional, wrongful, or negligent act or omission of a VISITING SCIENTIST. The foregoing indemnity obligation shall not apply to the extent that such LOSSES are due to the negligence, recklessness, willful misconduct or breach of this AGREEMENT by the UTMDACC INDEMNITEE.

11.2 INDEMNIFICATION BY UTMDACC. To the extent authorized by the constitution and laws of the State of Texas, UTMDACC hereby agrees to indemnify, hold harmless and defend ZIOPHARM and their respective directors, officers, employees, agents and affiliates (collectively, the "**ZIOPHARM INDEMNITEES**") from any third party LOSSES incurred by or imposed upon any of the ZIOPHARM INDEMNITEES in connection with any CLAIMS arising out of or connected with (i) UTMDACC's activities under this AGREEMENT or the TCR-T PROGRAM performed by UTMDACC under this AGREEMENT or (ii) the gross negligence or intentional misconduct or unlawful act or omission by UTMDACC or a UTMDACC representative. The foregoing indemnity obligation shall not apply to the extent that such LOSSES are due to the negligence, recklessness, willful misconduct or breach of this AGREEMENT by the ZIOPHARM INDEMNITEE.

11.3 TERMS OF INDEMNIFICATION. The indemnified party will promptly notify the indemnifying party of any CLAIM and will cooperate with the indemnifying party in the defense of the CLAIM; *provided, however, that* the indemnifying party will control such defense (subject in the case of the UTMDACC INDEMNITEES to the statutory duties of the Texas Attorney General). Any settlement agreed to by the indemnifying party may not require an indemnitee to contribute to the settlement, admit fault, or change operations or business practices. The indemnifying party agrees, at its own

expense, to provide attorneys reasonably acceptable to the indemnified party to defend against any CLAIM with respect to which the indemnifying party has agreed to provide indemnification hereunder. This indemnity shall not be deemed excess coverage to any insurance or self-insurance the indemnified party may have covering a CLAIM.

12. INSURANCE.

12.1 UNIVERSITY. UTMDACC will maintain worker's compensation insurance and/or other coverage, including but not limited to clinical trial insurance on all TCR-T PROGRAM and its employees as required by APPLICABLE LAWS, and will self-insure or maintain insurance covering its liability under this AGREEMENT.

12.2 ZIOPHARM. ZIOPHARM shall maintain comprehensive general liability insurance, including product liability insurance, with reputable and financially secure insurance carrier(s). Such insurance shall be maintained at levels sufficient to support ZIOPHARM's obligations, including indemnification obligations, under this AGREEMENT and at least provide minimum limits of liability of **[***]** as of the EFFECTIVE DATE, and of **[*******]** as of the commencement of human clinical trials of any products developed by ZIOPHARM. At UTMDACC's request, ZIOPHARM shall furnish a certificate of insurance evidencing such coverage and requiring **[*****] prior written notice of cancellation or material change to UTMDACC.

13. WARRANTIES; DISCLAIMER; LIMITATIONS OF LIABILITIES.

13.1 WARRANTY.

(a) UTMDACC hereby represents and warrants that it has the full right and power to grant to ZIOPHARM all rights it purports to grant under this AGREEMENT.

(b) WITH REGARD TO EACH CLINICAL TRIAL, ZIOPHARM REPRESENTS ON A CONTINUING BASIS THAT TO THE BEST OF THEIR KNOWLEDGE (1) THE STUDY PRODUCTS SUPPLIED BY ZIOPHARM HAVE BEEN MANUFACTURED IN ACCORDANCE WITH GOOD MANUFACTURING PRACTICES, AND (2) EXCEPT AS HAS BEEN DISCLOSED TO UTMDACC, WHICH DISCLOSURE SHALL BE MADE PROMPTLY BY ZIOPHARM UPON ANY KNOWLEDGE THEREOF, THERE ARE NO KNOWN DEFECTS IN, OR HAZARDOUS OR ADVERSE AFFECTS FROM, THE STUDY PRODUCTS SUPPLIED BY ZIOPHARM, AND ZIOPHARM IS NOT AWARE OF ANY CLAIM THAT THE USE OF THE STUDY PRODUCT BY UTMDACC IN ACCORDANCE WITH THE TCR-T PROGRAM DEVELOPMENT PLAN INFRINGES OR VIOLATES ANY PATENT OR OTHER PROPRIETARY RIGHTS OF ANY THIRD PARTY.

(c) UTMDACC REPRESENTS ON A CONTINUING BASIS THAT TO THE BEST OF ITS KNOWLEDGE (1) THE HCT STUDY PRODUCTS PRODUCED BY UTMDACC HAVE BEEN MANUFACTURED IN ACCORDANCE WITH GOOD MANUFACTURING PRACTICES, AND (2) EXCEPT AS HAS BEEN DISCLOSED TO ZIOPHARM IN WRITING THERE ARE NO KNOWN DEFECTS IN, OR HAZARDOUS OR ADVERSE AFFECTS FROM, THE HCT STUDY PRODUCTS PRODUCED BY UTMDACC.

13.2 DISCLAIMER. EXCEPT AS PROVIDED HEREIN, NO PARTY MAKES ANY WARRANTIES, EXPRESS OR IMPLIED, AS TO ANY MATTER WHATSOEVER, INCLUDING, WITHOUT LIMITATION, THE RESULTS OF THE RESEARCH OR ANY INVENTION, MATERIAL, PROCESS OR PRODUCT, WHETHER TANGIBLE OR INTANGIBLE, CONCEIVED, DISCOVERED, OR DEVELOPED UNDER THIS AGREEMENT; OR THE MERCHANTABILITY, OR FITNESS FOR A PARTICULAR PURPOSE, OF THE RESEARCH OR ANY SUCH INVENTION, MATERIAL, PROCESS OR PRODUCT.

13.3 LIMITATIONS OF LIABILITIES. EXCEPT FOR BREACH OF CONFIDENTIALITY OBLIGATIONS UNDER SECTION 14 OR THE INDEMNIFICATION OBLIGATIONS UNDER SECTION 11, NO PARTY SHALL BE LIABLE TO ANOTHER PARTY FOR ANY CONSEQUENTIAL OR INDIRECT DAMAGES, INCLUDING, BUT NOT LIMITED TO, ANY SUCH DAMAGES ARISING FROM THE LOSS OF DATA OR DELAY OR TERMINATION OF THE RESEARCH, OR FROM THE USE OF THE RESULTS OF THE RESEARCH, OR ANY INVENTION, PROCESS OR PRODUCT. THE PROVISIONS OF THIS CLAUSE SHALL SURVIVE TERMINATION OF THIS AGREEMENT.

14. CONFIDENTIALITY.

14.1 CONFIDENTIAL INFORMATION. UTMDACC (including the PRINCIPAL INVESTIGATOR) and ZIOPHARM may reveal to each other in the course of the TCR-T PROGRAM certain confidential information. UTMDACC and ZIOPHARM agree to hold in confidence, not use, and not disclose to any third party, any confidential information which one party (the "**RECEIVING PARTY**") obtains from the other party (the "**DISCLOSING PARTY**") during the course of the TCR-T PROGRAM (collectively, "**CONFIDENTIAL INFORMATION**"), except as permitted by this AGREEMENT (including the performance of its obligations and the exercise of its rights hereunder) or otherwise with the express written consent of the DISCLOSING PARTY. The obligations of confidentiality, non-use and non-disclosure under this Section 14 shall remain in force for a period of **[*****]** following the disclosure of the CONFIDENTIAL INFORMATION. All INVENTIONS shall be deemed CONFIDENTIAL INFORMATION of ZIOPHARM, and ZIOPHARM shall be deemed a DISCLOSING PARTY and UTMDACC shall be deemed the RECEIVING PARTY to such CONFIDENTIAL INFORMATION, subject, however, to the right of UTMDACC to publish in accordance with Section 8.1.

14.2 PERMITTED DISCLOSURE. The RECEIVING PARTY may disclose CONFIDENTIAL INFORMATION:

(a) to its employees, other agents or consultants (including public members of its scientific or institutional review boards) on a need-to-know basis, *provided, however, that* such employees, other agents or consultants are bound by obligations of non-use and nondisclosure with respect to such CONFIDENTIAL INFORMATION at least as

stringent as those provided in this AGREEMENT. In addition, ZIOPHARM shall have the right to disclose CONFIDENTIAL INFORMATION of UTMDACC to its affiliates and actual or potential licensees, sublicensees, consultants, agents, contractors, acquirers and/or investors, in connection with its exercise of the rights and fulfillment of the obligations under this AGREEMENT or the LICENSE AGREEMENT. Each party shall ensure that all employees, agents, or consultants of such party engaged in the performance of the TCR-T PROGRAM (in the case of UTMDACC, including the PRINCIPAL INVESTIGATOR), shall be subject to obligations of confidentiality and non-use consistent with the obligations of confidentiality and non-use contained herein;

(b) to the extent necessary in order to obtain informed consent from patients or subjects who may wish to enroll in a CLINICAL TRIAL, *provided, however, that* the information will be disclosed only to the extent necessary and will not be provided in answer to unsolicited inquiries by telephone or to individuals who are not eligible study candidates;

(c) to study subjects for the safety or well-being of the study subject; and

(d) if required to be disclosed by law or regulation, *provided, however, that* to the extent reasonably practicable the RECEIVING PARTY provides advance notice of the legally required disclosure to the DISCLOSING PARTY so that the DISCLOSING PARTY may seek to obtain confidential treatment of such information to the extent available under such law or regulation.

14.3 EXCEPTIONS. CONFIDENTIAL INFORMATION will not include and the obligations of confidentiality and non-use contained in this Section 14.3 will not apply to information that the RECEIVING PARTY can demonstrate by competent written evidence:

(a) Is in the public domain as of the EFFECTIVE DATE or comes into the public domain during the TERM through no wrongful act of the RECEIVING PARTY;

(b) Is known by the RECEIVING PARTY prior to the execution of this AGREEMENT or prior to the disclosure of the CONFIDENTIAL INFORMATION to the RECEIVING PARTY, as evidenced by the RECEIVING PARTY's pre-existing written records;

(c) Is rightfully received by the RECEIVING PARTY after disclosure under this AGREEMENT from a third party without a binding obligation of confidentiality to the DISCLOSING PARTY with respect to such information; or

(d) Is independently invented by an employee of the RECEIVING PARTY who did not have use of or have actual access to the information provided to the RECEIVING PARTY hereunder, as evidenced by its contemporaneously-maintained written records.

For purposes of this Section 14.3, no combination of elements within the CONFIDENTIAL INFORMATION shall be deemed to be part of the public domain merely because the individual elements of such combination are part of the public domain, unless the entire combination itself, or the entire principle of use or operation of such combination (if any), is part of the public domain. In addition, no element within the CONFIDENTIAL INFORMATION shall be deemed to be a part of the public domain merely because it is embraced by more general information or data that is part of the public domain.

14.4 PROTECTED HEALTH INFORMATION. If ZIOPHARM comes into knowledge or possession of any "**PROTECTED HEALTH INFORMATION**" (as such term is defined under HIPAA) by or through UTMDACC or any information that could be used to identify any of UTMDACC's patients or research subjects, then in accordance with APPLICABLE LAWS as applicable to UTMDACC, ZIOPHARM shall maintain in strict confidence and not disclose any such PROTECTED HEALTH INFORMATION or other legally private information; shall use any such PROTECTED HEALTH INFORMATION or other legally private information solely as permitted by APPLICABLE LAWS and the informed consent/authorization of the patient/research subject, and shall not use or disclose any such PROTECTED HEALTH INFORMATION or other legally private information in any manner that would constitute a violation of any APPLICABLE LAWS if such use or disclosure was made by UTMDACC.

15. FORCE MAJEURE. Neither party will be liable for any failure to perform as required by this AGREEMENT, if the failure to perform is caused by circumstances beyond such party's reasonable control, such as labor disturbances or labor disputes of any kind, accidents, failure of either party to obtain any governmental approval required for full performance, civil disorders or commotions, acts of aggression, acts of God, energy or other conservation measures, explosions, failure of utilities, mechanical breakdowns, material shortages, disease, thefts, or other such occurrences; *provided, however, that* such affected party shall use reasonable efforts to overcome such circumstances.

16. MISCELLANEOUS.

16.1 ASSIGNMENT. No party may assign this AGREEMENT without the prior written consent of the other parties, such consent not to be unreasonably withheld or delayed; *provided, however, that* ZIOPHARM may assign the AGREEMENT in connection with a merger, consolidation or sale of all or substantially all of ZIOPHARM's stock or assets to which this AGREEMENT relates.

16.2 SEVERABILITY. If any provision of this AGREEMENT becomes or is declared illegal, invalid, or unenforceable, such provision will be separable from this AGREEMENT and the remaining provisions shall continue in full force and effect. If such separation substantially alters the basis of this AGREEMENT, the parties will negotiate in good faith to amend the provisions of this AGREEMENT to give effect to the original intent of the parties.

16.3 INDEPENDENT CONTRACTORS. The activities contemplated by this AGREEMENT do not constitute a partnership, joint venture, or separate legal entity, but a contractual relationship. Unless otherwise agreed in writing, each party will act as an independent contractor with respect to the other parties and no party will have authority to act on behalf of or bind the other party without the written agreement of the party to be bound.

16.4 GOVERNING LAW. This AGREEMENT will be construed and enforced in accordance with the laws of the United States of America and of the State of Texas, without regard to its conflict of law provisions. The Texas State Courts of Harris County, Texas (or, if there is exclusive federal jurisdiction, the United States District Court for the Southern District of Texas) shall have exclusive jurisdiction and venue over any dispute arising out of this AGREEMENT, and ZIOPHARM consents to the jurisdiction and venue of such courts and hereby explicitly waives the rights to any other venue to which it might be entitled by cause of action, domicile or otherwise. Nothing in this AGREEMENT shall be deemed as a waiver by BOARD, SYSTEM or UTMDACC of its sovereign immunity. Notwithstanding the foregoing, to the extent that Chapter 2260, Texas Government Code, as it may be amended from time to time ("**CHAPTER 2260**"), is applicable to this AGREEMENT, ZIOPHARM acknowledges and agrees that the dispute resolution process provided for in CHAPTER 2260 shall be ZIOPHARM's sole and exclusive process for seeking a remedy for any and all alleged breaches of the AGREEMENT by BOARD and/or UTMDACC or the State of Texas.

16.5 TEXAS STATE AGENCY. UTMDACC, as an agency of the State of Texas and a member institution of The University of Texas System, is subject to the constitution and laws of the State of Texas and, under the constitution and laws of the State of Texas, possesses certain rights and privileges, is subject to certain limitations and restrictions, and only has such authority as is granted under the constitution and laws of the State of Texas. Notwithstanding any other provision to the contrary, nothing in this AGREEMENT is intended to be, nor shall it be construed to be, a waiver of the sovereign immunity of the State of Texas or a prospective waiver or restriction of any of the rights, remedies, claims, and privileges of the State of Texas. Moreover, notwithstanding the generality or specificity of any provision of this AGREEMENT, the provisions of this AGREEMENT as they pertain to UTMDACC are enforceable only to the extent authorized by the constitution and laws of the State of Texas. No party to this AGREEMENT will be required to perform any act or to refrain from any act that would violate any APPLICABLE LAWS, including the constitution and laws of the State of Texas.

16.6 ENTIRE AGREEMENT; CONFLICTS. This AGREEMENT, together with Exhibits and Schedules attached hereto, and the 2015 R&D AGREEMENT represent the entire agreement and understanding between the parties with respect to its subject matter and supersedes any prior and/or contemporaneous discussions, representations, or agreements, whether written or oral, of the parties regarding the subject matter hereof. In the event of any conflict between the terms of this AGREEMENT and the 2015 R&D AGREEMENT, the terms of this AGREEMENT shall govern.

16.7 AMENDMENTS. Amendments or changes to this AGREEMENT shall be valid and binding only if in writing and signed by duly authorized representatives of the parties. No provision of this AGREEMENT can be waived except by the express written consent of the party waiving compliance.

16.8 COUNTERPARTS. This AGREEMENT may be executed in one or more counterparts, which shall together constitute the same legal instrument.

IN WITNESS WHEREOF, these duly authorized representatives of the parties hereby execute this RESEARCH AND DEVELOPMENT AGREEMENT as of the EFFECTIVE DATE:

THE UNIVERSITY OF TEXAS M. D. ANDERSON CANCER CENTER

By: /s/ Ben Melson
Name: Ben Melson
Title: Senior Vice President and Chief Financial Officer

ZIOPHARM ONCOLOGY, INC.

By: /s/ Robert Hadfield
Name: Robert Hadfield
Title: General Counsel

LIST OF EXHIBITS

Exhibit A: **VISITING SCIENTIST PROVISIONS**

Exhibit B: **NET SALES**

Exhibit C: **FORM OF WARRANT**

EXHIBIT A
VISITING SCIENTIST PROVISIONS

1.0 ZIOPHARM may assign one or more scientists that are employee(s) of ZIOPHARM to work on the TCR-T PROGRAM on-site at UTMDACC's facilities (the "**VISITING SCIENTISTS"**). The number and identity of the VISITING SCIENTISTS may be proposed by PROGRAM FACILITATOR and are subject to the reasonable approval of UTMDACC.

2.0 The VISITING SCIENTISTS may use UTMDACC's facilities only for purposes of collaborating with UTMDACC in the TCR-T PROGRAM, unless otherwise agreed by UTMDACC.

3.0 The VISITING SCIENTIST(s) are ZIOPHARM employees and will report to a ZIOPHARM supervisor/manager, and ZIOPHARM is solely responsible for all salary, compensation, benefits and related costs associated with the VISITING SCIENTISTS. Accordingly, ZIOPHARM is responsible for issuing payroll checks to the VISITING SCIENTISTS; for making appropriate payroll deductions for the VISITING SCIENTISTS, as required by APPLICABLE LAWS and authorized by the VISITING SCIENTISTS; for paying the appropriate amount of all federal, state, and local taxes with respect to all compensation and benefits paid and provided to the VISITING SCIENTISTS; and for filing all appropriate and applicable forms for tax purposes. Moreover, either ZIOPHARM or the VISITING SCIENTISTS is responsible for the VISITING SCIENTISTS' relocation and travel to and from Houston, as well as for any and all housing, transportation, parking, meals, and/or other personal needs of the VISITING SCIENTISTS while working at UTMDACC. Because the VISITING SCIENTISTS are not employees of UTMDACC and are instead employees of ZIOPHARM working on behalf of ZIOPHARM, the VISITING SCIENTISTS will not receive any salary, compensation, financial remuneration, benefits, and/or fringe benefits from UTMDACC, and in particular, the VISITING SCIENTISTS will not assign their interest in any INVENTIONS to UTMDACC, and will not receive from UTMDACC any portion of any royalties or proceeds resulting from any INVENTIONS made by the VISITING SCIENTISTS while working as VISITING SCIENTISTS at UTMDACC.

4.0 Subject to availability and UTMDACC's space needs, UTMDACC will provide, at ZIOPHARM's expense, a separate office for the VISITING SCIENTISTS at UTMDACC. Each such office will have a separate telephone line (either ZIOPHARM or the VISITING SCIENTIST is responsible for long distance phone charges), intranet and high-speed internet access, as well as appropriate keys, badges, and parking privileges (subject to the VISITING SCIENTISTS paying any existing parking rates) that will allow the VISITING SCIENTISTS to work under substantially the same conditions as UTMDACC employees with whom the VISITING SCIENTISTS work. UTMDACC may re-allocate, substitute, replace, modify and/or terminate the resources and space made available to the VISITING SCIENTISTS while working at UTMDACC as UTMDACC may reasonably determine from time to time.

5.0 The VISITING SCIENTISTS will be subject to and must abide by all UTMDACC written guidelines, policies, procedures, rules, and regulations, including all premises rules applicable to UTMDACC facilities. UTMDACC may:

i) arrange for emergency health care for a VISITING SCIENTIST, if needed, while the VISITING SCIENTIST is on-site at UTMDACC, but UTMDACC is not responsible for costs, follow-up care, or hospitalization associated with such emergency care; and

ii) immediately dismiss a VISITING SCIENTIST from UTMDACC if UTMDACC reasonably determines that:

(a) the presence of the VISITING SCIENTIST has a detrimental or disruptive effect upon UTMDACC' facilities, patients, or personnel;

(b) the VISITING SCIENTIST compromises UTMDACC standards of care or performance; and/or

(c) the VISITING SCIENTIST does not abide by UTMDACC guidelines, policies, procedures, rules, or regulations.

If UTMDACC dismisses a VISITING SCIENTIST, UTMDACC will promptly provide to ZIOPHARM notice of such dismissal which will specify the reasons for such dismissal. Upon request from ZIOPHARM, UTMDACC will promptly meet with ZIOPHARM and discuss such situation with ZIOPHARM, and the PARTIES will work together in good faith to determine if, when and under what circumstances and conditions the VISITING SCIENTIST may return to work at UTMDACC.

6.0 Before beginning work at UTMDACC, the VISITING SCIENTISTS will be subject to a criminal background check and will, if requested by UTMDACC, provide proof of a history of vaccinations sufficient to meet UTMDACC's Department of Employee Health Services guidelines, including proof of a negative tuberculosis screening test within thirty (30) days prior to beginning work at UTMDACC. If the VISITING SCIENTISTS cannot provide proof of a negative tuberculosis screening test within thirty (30) days prior to beginning work at UTMDACC, then the VISITING SCIENTISTS must successfully undergo tuberculosis screening through UTMDACC's Department of Employee Health Services prior to beginning work at UTMDACC. UTMDACC may dismiss the VISITING SCIENTISTS if the VISITING SCIENTISTS do not meet UTMDACC's health criteria.

7.0 Because of the VISITING SCIENTIST presence at UTMDACC, the VISITING SCIENTISTS may be exposed to research and/or other activities at UTMDACC that are independently undertaken by UTMDACC separate and apart from the TCR-T PROGRAM under this AGREEMENT, and/or which may be sponsored by, and/or undertaken with, or for, third parties, including third party research collaborators and/or sponsors, such as other academic institutions, other government agencies, and/or commercial organizations ("**NON-ZIOPHARM ACTIVITIES"**).

8.0 Such NON-ZIOPHARM ACTIVITIES may impose confidentiality obligations upon UTMDACC with respect to such activities and/or grant third parties rights in intellectual property and inventions arising from such research or activities. With respect to the

VISITING SCIENTISTS, and notwithstanding any other provisions of this AGREEMENT, "**OTHER CONFIDENTIAL INFORMATION**" means any and all information that the VISITING SCIENTISTS obtain as a result of the presence of the VISITING SCIENTISTS at UTMDACC and that pertains to NON-ZIOPHARM ACTIVITIES and VISITING SCIENTISTS have not obtained such information as part of the collaborative activities being conducted at UTMDACC with respect to the TCR-T PROGRAM. Notwithstanding any other provision of the AGREEMENT, but subject to the exceptions that may exist with respect to OTHER CONFIDENTIAL INFORMATION in the agreements governing the OTHER CONFIDENTIAL INFORMATION, the VISITING SCIENTISTS (and ZIOPHARM, to the extent ZIOPHARM learns such information) will keep confidential, and may not disclose to any individual or entity, including to ZIOPHARM, any OTHER CONFIDENTIAL INFORMATION that relates to or regards the NON-ZIOPHARM ACTIVITIES. The VISITING SCIENTISTS (and ZIOPHARM, to the extent ZIOPHARM learns such information) may also not use OTHER CONFIDENTIAL INFORMATION that relates to or regards the NON-ZIOPHARM ACTIVITIES in a manner that is adverse to or competes with UTMDACC, the principal investigator of such research, or any third party participant, collaborator, supporter, or sponsor of such research or activity, and the VISITING SCIENTISTS and ZIOPHARM may not assert any rights to, or any ownership of, other interest in any intellectual property and inventions arising from the NON-ZIOPHARM ACTIVITIES if the assertion of such rights to, ownership of, or other interest would conflict with, or diminish, any rights, ownership, or other interests either held by UTMDACC or granted by UTMDACC to a third party with respect to such OTHER CONFIDENTIAL INFORMATION. The VISITING SCIENTIST (and ZIOPHARM, to the extent ZIOPHARM learns such information) will not publicly disclose or publish any articles or make any presentations regarding such NON-ZIOPHARM ACTIVITIES without prior, written consent from UTMDACC, which consent is in the sole discretion of UTMDACC.

9.0 ZIOPHARM will take reasonable steps to protect the confidentiality of any patient's health and medical information that it or the VISITING SCIENTISTS have access to as a result of the presence of the VISITING SCIENTISTS at UTMDACC. Moreover, ZIOPHARM will maintain, and will ensure that the VISITING SCIENTISTS maintain, the security and confidentiality of individually identifiable patient health information that either ZIOPHARM or the VISITING SCIENTIST obtain as a result of the presence of the VISITING SCIENTISTS at UTMDACC, and ZIOPHARM will comply, and will ensure that the VISITING SCIENTISTS comply, with all applicable federal and state health information confidentiality laws and regulations (including, as applicable, the Standards for Privacy of Individually Identifiable Health Information, published at Title 45 of the United States Code of Federal Regulations Parts 160 and 164), as well as any applicable national or state privacy and security laws and regulations. If the VISITING SCIENTISTS (and ZIOPHARM, to the extent ZIOPHARM learns such information) obtains any health or medical information of any patient of UTMDACC, then, unless disclosure has been authorized by a patient, the VISITING SCIENTISTS (and ZIOPHARM, to the extent ZIOPHARM learns such information) will hold in confidence the identity of the patient and the health/medical information of such patient and the VISITING SCIENTISTS (and ZIOPHARM, to the extent ZIOPHARM learns such information) must comply with

APPLICABLE LAWS and UTMDACC policies regarding confidentiality of such information. UTMDACC will undertake reasonable efforts to shield NON-ZIOPHARM ACTIVITIES and OTHER CONFIDENTIAL INFORMATION from the VISITING SCIENTISTS and advise the VISITING SCIENTISTS if they are exposed to, or become involved, in NON-ZIOPHARM ACTIVITIES or OTHER CONFIDENTIAL INFORMATION, *provided, however, that*, any failure in these regards does not abrogate the other terms and provisions of this Article 9.0. The obligations set forth in this Article 9.0 survive the termination and expiration of the AGREEMENT.

10.0 The activities of the VISITING SCIENTISTS at UTMDACC are limited to the following activities, all of which are subject to and must be in accordance with APPLICABLE LAWS and UTMDACC'S written policies, and as mutually agreed upon by the parties: (i) current and future research activities under the TCR-T PROGRAM and VISITING SCIENTISTS may work on the TCR-T PROGRAM at UTMDACC, (ii) participating in the manufacture and release of products for human application, (iii) applying to, receiving and maintaining grants from federal, state, local, private, institutional and other funding sources, including maintaining any and all funding granted to VISITING SCIENTISTS prior to and after the Effective Date, (iv) benefiting from, attending and participating in activities related to philanthropy and fund raising activities, (v) supervising and at times directing trainees, post-docs, staff and faculty at UTMDACC. The VISITING SCIENTISTS will not perform the following activities in the capacity of the attending physician, unless otherwise expressly agreed to in writing by UTMDACC: i) diagnosing disease or other conditions in humans; or ii) the cure, mitigation, therapy, treatment, treatment planning, or prevention of disease in humans, or to affect the structure or function thereof, regardless of whether the VISITING SCIENTISTS are certified or qualified for the foregoing. UTMDACC will allow the VISITING SCIENTISTS to observe patients, provided that UTMDACC i) has obtained any necessary consent and/or authorization from the patient, ii) has otherwise complied with all APPLICABLE LAWS related thereto, and iii) directly supervises such observations.

11.0 ZIOPHARM is responsible for any acts and omissions of the VISITING SCIENTISTS and ZIOPHARM shall ensure that the VISITING SCIENTISTS are informed of these provisions and are obligated to abide by them.

EXHIBIT B
NET SALES

[***]

EXHIBIT C
FORM OF WARRANT

THIS WARRANT AND THE SECURITIES ISSUABLE UPON EXERCISE OF THIS WARRANT HAVE NOT BEEN REGISTERED UNDER THE SECURITIES ACT OF 1933, AS AMENDED (THE "SECURITIES ACT"), OR THE SECURITIES LAWS OF ANY STATE OR OTHER JURISDICTION. THIS WARRANT AND THE SECURITIES ISSUABLE UPON EXERCISE OF THIS WARRANT MAY NOT BE SOLD OR OFFERED FOR SALE, PLEDGED OR HYPOTHECATED EXCEPT PURSUANT TO AN EFFECTIVE REGISTRATION STATEMENT UNDER THE SECURITIES ACT OR PURSUANT TO AN EXEMPTION FROM REGISTRATION THEREUNDER, IN EACH CASE IN ACCORDANCE WITH ALL APPLICABLE SECURITIES LAWS OF THE STATES OR OTHER JURISDICTIONS, AND IN THE CASE OF A TRANSACTION EXEMPT FROM REGISTRATION, SUCH WARRANTS AND THE SECURITIES ISSUABLE UPON EXERCISE OF SUCH WARRANTS MAY ONLY BE TRANSFERRED IF THE TRANSFER AGENT FOR SUCH WARRANTS AND THE SECURITIES ISSUABLE UPON EXERCISE OF SUCH WARRANTS HAS RECEIVED DOCUMENTATION SATISFACTORY TO IT THAT SUCH TRANSACTION DOES NOT REQUIRE REGISTRATION UNDER THE SECURITIES ACT.

ZIOPHARM ONCOLOGY, INC.

WARRANT TO PURCHASE COMMON STOCK

No. [CSW]-[●] **[●], 2019 ("Issuance Date")**

Void After the Expiration Date

THIS CERTIFIES THAT, for value received, The Board of Regents of The University of Texas System (the "***Holder***"), on behalf of The University of Texas M.D. Anderson Cancer Center ("***MD Anderson***"), or its permitted assigns, is entitled to subscribe for and purchase at the Exercise Price from Ziopharm Oncology, Inc. (the "***Company***") up to three million three hundred thirty-three thousand three hundred thirty-three (3,333,333) shares of common stock, $0.001 par value per share, of the Company (the "***Common Stock***"), all subject to the terms, conditions and adjustments set forth below in this Warrant.

This Warrant is being issued pursuant to the terms of the 2019 Research and Development Agreement, dated as of [●], 2019, by and between the Company and the Holder (the "***R&D Agreement***"). If any term or provision of this Warrant conflicts with any term or provision of the R&D Agreement, the terms and provisions of this Warrant shall control.

1. DEFINITIONS. As used herein, the following terms shall have the following respective meanings:

(a) "***Business Day***" means any day other than Saturday, Sunday, a federal holiday or other day on which commercial banks in Boston, Massachusetts are closed to the public.

(b) "***Commission***" means the United States Securities and Exchange Commission.

(c) "***Effectiveness Date***" means the date the Registration Statement has been declared effective by the Commission.

(d) "***Effectiveness Period***" has the meaning set forth in Section 18.1 hereof.

(e) "***Exercise Period***" shall mean the period commencing at 12:00:01 a.m., Boston, Massachusetts time, on the Issuance Date and ending at 11:59:59 p.m., Boston, Massachusetts time, on the Expiration Date, unless sooner terminated as provided herein.

(f) "***Exercise Price***" shall mean $0.001 per share of Common Stock, subject to adjustment pursuant to Section 6 below.

(g) "***Exercise Shares***" shall mean the shares of Common Stock issuable upon exercise of this Warrant, subject to adjustment pursuant to the terms herein, including but not limited to, adjustment pursuant to Section 6 below.

(h) "***Exchange Act***" has the meaning set forth in Section 4.4 hereof.

(i) "***Expiration Date***" means 11:59:59 p.m., Boston, Massachusetts time, on December 31, 2026.

(j) "***Filing Date***" means the sixtieth (60th) Business Day following a written request from Holder; *provided*, *that* any such request shall only occur after this Warrant has been exercised in full or in part in accordance with Section 3.2 and payment of the Exercise Price was made; *provided*, *however*, that if the Filing Date falls on a day that is not a Business Day, then the Filing Date shall be extended to the next Business Day.

(k) "***Prospectus***" means any prospectus included in a Registration Statement (including, without limitation, a prospectus that includes any information previously omitted from a prospectus filed as part of an effective registration statement in reliance upon Rule 430A promulgated under the Securities Act), as amended or supplemented by any prospectus supplement, with respect to the terms of the offering of any portion of the Registrable Securities covered by a Registration Statement, and all other amendments and supplements to any such Prospectus, including post-effective amendments, and all material incorporated by reference in such Prospectus.

(l) "***Registrable Securities***" means shares of Common Stock issued or issuable to the Holder upon exercise of the Warrants; *provided*, *however*, that the applicable Holder has completed and delivered to the Company a questionnaire in the form as may reasonably be requested by the Company from time to time; *provided*, *further*, that such securities shall no longer be deemed Registrable Securities if (i) such securities have been sold pursuant to a Registration Statement, (ii) such securities have been sold in compliance with Rule 144, or (ii) all such securities may be sold without limitation or restriction pursuant to Rule 144.

(m) "***Registration Statement***" means the registration statements and any additional registration statements contemplated by this Agreement, including (in each case) the related Prospectus, amendments and supplements to such registration statement or Prospectus, including pre- and post-effective amendments, all exhibits thereto, and all material incorporated by reference in such registration statement. "Registration Statement" shall include the Company's existing automatic Registration Statement on Form S-3 filed on June 21, 2019 (File no. 333-232283) if the Company elects to file a post-effective amendment or a prospectus supplement pursuant to such Registration Statement that would be deemed to be part of such existing automatic Registration Statement in accordance with Rule 430B under the Securities Act and would permit the sale and distribution of all the Registrable Securities (an "***ASR Pro Supp***").

(n) "***Rule 144***" means Rule 144 promulgated by the Commission pursuant to the Securities Act, as such Rule may be amended from time to time, or any similar rule or regulation hereafter adopted by the Commission having substantially the same effect as such Rule.

(o) "***Rule 415***" means Rule 415 promulgated by the Commission pursuant to the Securities Act, as such Rule may be amended from time to time, or any similar rule or regulation hereafter adopted by the Commission having substantially the same effect as such Rule.

(p) "***Securities Act***" means the Securities Act of 1933, as amended, and related regulations and guidance promulgated by the Commission.

2. DURATION OF WARRANT. The rights represented by this Warrant may be exercised in whole or in part at any time or times during the Exercise Period, subject to the vesting schedule set forth in Section 3.1. If not exercised at or before the Expiration Date, this Warrant shall become void, and all rights of the Holder under this Warrant shall cease.

3. VESTING SCHEDULE; EXERCISE.

3.1 Vesting Schedule. The Exercise Shares shall vest and become exercisable as set forth below, provided that on each vesting date, the R&D Agreement has not been earlier terminated in accordance with its terms. Upon termination of the R&D Agreement, vesting of the Exercise Shares shall cease and this Warrant shall thereafter remain exercisable during the Exercise Period for up to that number of Exercise Shares as were vested as of the effective time of such termination.

(a) [***]

3.2 Exercise. The rights represented by this Warrant may be exercised in whole or in part at any time, subject to the terms of Section 2 and as further specified herein, during the Exercise Period, so long as the Exercise Shares for which this Warrant is being exercised are then vested and exercisable hereunder in accordance with Section 3.1, by delivery by the Holder of the following to the Company at its address set forth above (or at such other address as it may designate by notice in writing to the Holder):

(a) An executed Notice of Exercise in the form attached hereto as Exhibit A;

(b) Payment of the Exercise Price either in cash or by wire transfer of immediately available funds; provided, however, that, for so long as the R&D Agreement is in effect, the Holder may, at its option in writing in the Notice of Exercise, elect to offset the Exercise Price against any amounts then owed to the Holder from the Company; and

(c) This Warrant.

For the avoidance of doubt, this Warrant may not be exercised for any Exercise Shares that have not vested in accordance with Section 3.1. Upon the exercise of the rights represented by this Warrant, a book-entry statement for the Exercise Shares so purchased, registered in the name of the Holder or persons affiliated with the Holder, if the Holder so designates, shall be delivered to the Holder within a reasonable time after the rights represented by this Warrant shall have been so exercised.

The person in whose name any book-entry statements for Exercise Shares are to be delivered upon exercise of this Warrant shall be deemed to have become the holder of record of such shares of Common Stock purchased on the date on which this Warrant was surrendered and payment of the Exercise Price was made, irrespective of the date of delivery of such book-entry statement, except that, if the date of such surrender and payment is a date when the stock transfer books of the Company are closed, such person shall be deemed to have become the holder of such shares at the close of business on the next succeeding date on which the stock transfer books are open.

4. COVENANTS OF THE COMPANY.

4.1 Covenants as to Exercise Shares. The Company covenants and agrees that all Exercise Shares that may be issued upon the exercise of the rights represented by this Warrant will, upon issuance, be validly issued and outstanding, fully paid and nonassessable, and free from all taxes, liens and charges with respect to the issuance thereof. The Company further covenants and agrees that the Company will at all times during the Exercise Period, have authorized and reserved, free from preemptive rights, a sufficient number of shares of its Common Stock to provide for the exercise of the rights represented by this Warrant. If at any time during the Exercise Period the number of authorized but unissued shares of Common Stock shall not be sufficient to permit exercise of this Warrant, the Company will take such corporate action as may, in the opinion of its counsel, be necessary to increase its authorized but unissued shares of Common Stock to such number of shares as shall be sufficient for such purposes.

4.2 Delivery of New Warrant. Unless the purchase rights represented by this Warrant shall have expired or shall have been fully exercised, the Holder shall, at the time of delivery of the Exercise Shares being issued in accordance with Section 3.2, surrender this Warrant to the Company pursuant to Section 3.2(c) and promptly after such surrender, the Company shall deliver to the Holder a new Warrant evidencing the rights of the Holder to purchase the unexpired and unexercised Exercise Shares called for by this Warrant. Such new Warrant shall in all other respects be identical to this Warrant.

4.3 Notices of Record Date. In the event of any taking by the Company of a record of the holders of any class of securities for the purpose of determining the holders thereof

who are entitled to receive any dividend (other than a cash dividend which is the same as cash dividends paid in previous quarters) or other distribution, the Company shall mail to the Holder, at least ten (10) days prior to the date specified herein, a notice specifying the date on which any such record is to be taken for the purpose of such dividend or distribution.

4.4 Rule 144. As long as any Holder owns any Registrable Securities, the Company covenants to use its commercially reasonable efforts to timely file (or obtain extensions in respect thereof and file within the applicable grace period) all reports required to be filed by the Company after the date hereof pursuant to Section 13(a) or 15(d) of the Securities Exchange Act of 1934, as amended (the "***Exchange Act***"). The Company further covenants that it will take such further action as any Holder may reasonably request, all to the extent required from time to time to enable such person to sell the Registrable Securities without registration under the Securities Act within the limitation of the exemptions provided by Rule 144 promulgated under the Securities Act, including providing any legal opinions relating to such sale pursuant to Rule 144. Upon the request of any Holder, the Company shall deliver to such Holder a written certification of a duly authorized officer as to whether it has complied with such requirements.

5. REPRESENTATIONS OF HOLDER.

5.1 Acquisition of Warrant for Personal Account. The Holder represents and warrants that it is acquiring the Warrant and the Exercise Shares solely for its account for investment and not with a view to or for sale or distribution of said Warrant or Exercise Shares or any part thereof. The Holder also represents that the entire legal and beneficial interests of the Warrant and Exercise Shares the Holder is acquiring is being acquired for, and will be held for, its account only.

5.2 Information and Sophistication. The Holder hereby: (i) acknowledges that it has received all the information it has requested from the Company and it considers necessary or appropriate for deciding whether to acquire this Warrant and the Exercise Shares, (ii) represents that it has had an opportunity to ask questions and receive answers from the Company regarding the financial condition of the Company and the risks associated with the acquisition of this Warrant and the Exercise Shares and (iii) further represents that it has such knowledge and experience in financial and business matters that it is capable of evaluating the merits and risk of this investment.

5.3 Ability to Bear Economic Risk. The Holder acknowledges that investment in the securities of the Company involves a high degree of risk, and represents that it is able, without materially impairing its financial condition, to hold the Exercise Shares for an indefinite period of time and to suffer a complete loss of its investment.

5.4 Securities Are Not Registered.

(a) The Holder understands that the Warrant and the Exercise Shares have not been registered under the Securities Act of 1933, as amended (the "***Act***") on the basis that no distribution or public offering of the stock of the Company is to be effected. The Holder realizes that the basis for the exemption may not be present if, notwithstanding its representations, the Holder has a present intention of acquiring the securities for a fixed or determinable period in the future, selling (in connection with a distribution or otherwise), granting any participation in, or otherwise distributing the securities. The Holder has no such present intention.

(b) The Holder recognizes that the Warrant and the Exercise Shares must be held indefinitely unless they are subsequently registered on a Registration Statement or an exemption from such registration is available. The Holder recognizes that the Company has no obligation to comply with any exemption from such registration.

(c) The Holder is aware that neither the Warrant nor the Exercise Shares may be sold pursuant to Rule 144 adopted under the Securities Act unless certain conditions are met, which may include, among other things, the existence of a public market for the shares, the availability of certain current public information about the Company and the resale following the required holding period under Rule 144. The Holder is aware that the conditions for resale set forth in Rule 144 may not occur in the foreseeable future.

5.5 Disposition of Warrant and Exercise Shares.

(a) The Holder further agrees not to make any disposition of all or any part of the Warrant or Exercise Shares in any event unless and until:

(i) The Company shall have received a letter secured by the Holder from the Commission stating that no action will be recommended to the Commission with respect to the proposed disposition;

(ii) There is then in effect a Registration Statement covering such proposed disposition and such disposition is made in accordance with said registration statement; or

(iii) The Holder shall have notified the Company of the proposed disposition and shall have furnished the Company with a detailed statement of the circumstances surrounding the proposed disposition, and if reasonably requested by the Company, the Holder shall have furnished the Company with an opinion of counsel, reasonably satisfactory to the Company, for the Holder to the effect that such disposition will not require registration of such Warrant or Exercise Shares under the Securities Act or any applicable state securities laws.

(b) The Holder understands and agrees that all certificates and/or book entry-statements evidencing the shares to be issued to the Holder may bear the following legend:

> THESE SECURITIES HAVE NOT BEEN REGISTERED UNDER THE SECURITIES ACT OF 1933, AS AMENDED (THE “SECURITIES ACT”), OR THE SECURITIES LAWS OF ANY STATE OR OTHER JURISDICTION. THESE SECURITIES MAY NOT BE SOLD OR OFFERED FOR SALE, PLEDGED OR HYPOTHECATED EXCEPT PURSUANT TO AN EFFECTIVE REGISTRATION STATEMENT UNDER THE SECURITIES ACT OR PURSUANT TO AN EXEMPTION FROM REGISTRATION THEREUNDER, IN EACH CASE IN ACCORDANCE WITH ALL APPLICABLE SECURITIES LAWS OF THE STATES OR OTHER JURISDICTIONS, AND IN THE CASE

OF A TRANSACTION EXEMPT FROM REGISTRATION, SUCH SECURITIES MAY ONLY BE TRANSFERRED IF THE TRANSFER AGENT FOR SUCH WARRANTS AND THE SECURITIES ISSUABLE UPON EXERCISE OF SUCH WARRANTS HAS RECEIVED DOCUMENTATION SATISFACTORY TO IT THAT SUCH TRANSACTION DOES NOT REQUIRE REGISTRATION UNDER THE SECURITIES ACT.

5.6 Accredited Investor Status. The Holder is an "accredited investor" as defined in Regulation D promulgated under the Securities Act.

5.7 Brokers and Finders. No person will have, as a result of the issuance of this Warrant, any valid right, interest or claim against or upon the Company or the Holder for any commission, fee or other compensation pursuant to any agreement, arrangement or understanding entered into by or on behalf of the Holder.

6. ADJUSTMENT OF EXERCISE PRICE AND NUMBER OF EXERCISE SHARES. In the event of changes in the outstanding Common Stock of the Company by reason of stock dividends, split-ups, recapitalizations, reclassifications, combinations or exchanges of shares, separations, reorganizations, liquidations, or the like, the number and class of shares available under the Warrant in the aggregate and the Exercise Price shall be correspondingly adjusted to give the Holder of the Warrant, on exercise for the same aggregate Exercise Price, the total number, class, and kind of shares as the Holder would have owned had the Warrant been exercised prior to the event and had the Holder continued to hold such shares until after the event requiring adjustment; *provided*, *however*, that such adjustment shall not be made with respect to, and this Warrant shall terminate if not exercised prior to, the events set forth in Section 8 below. The form of this Warrant need not be changed because of any adjustment in the number of Exercise Shares subject to this Warrant.

7. FRACTIONAL SHARES. No fractional shares shall be issued upon the exercise of this Warrant as a consequence of any adjustment pursuant hereto. All Exercise Shares (including fractions) issuable upon exercise of this Warrant may be aggregated for purposes of determining whether the exercise would result in the issuance of any fractional share. If, after aggregation, the exercise would result in the issuance of a fractional share, the Company shall, in lieu of issuance of any fractional share, pay the Holder otherwise entitled to such fraction a sum in cash equal to the product resulting from multiplying the then current fair market value of an Exercise Share by such fraction.

8. EARLY TERMINATION. In the event of, at any time during the Exercise Period, any capital reorganization, or any reclassification of the capital stock of the Company (other than a change in par value or from par value to no par value or no par value to par value or as a result of a stock dividend or subdivision, split-up or combination of shares), or the consolidation or merger of the Company with or into another corporation (other than a merger solely to effect a reincorporation of the Company into another state), or the sale or other disposition of all or substantially all the properties and assets of the Company in its entirety to any other person, the Company shall provide to the Holder twenty (20) days advance written notice of such reorganization, reclassification, consolidation, merger or sale or other disposition of the Company's assets, and this Warrant shall terminate unless exercised prior to the occurrence of such reorganization, reclassification, consolidation, merger or sale or other disposition of the Company's assets.

9. NO STOCKHOLDER RIGHTS. Except as otherwise specifically provided herein, the Holder, solely in such person's capacity as a Holder of this Warrant, shall not be entitled to vote or receive dividends or be deemed the holder of capital stock of the Company for any purpose, nor shall anything contained in this Warrant be construed to confer upon the Holder, solely in such person's capacity as the Holder of this Warrant, any of the rights of a stockholder of the Company or any right to vote, give or withhold consent to any corporate action (whether any reorganization, issue of stock, reclassification of stock, consolidation, merger, conveyance or otherwise), receive notice of meetings, receive dividends or subscription, or otherwise, prior to the issuance to the Holder of the Warrant Shares which such person is then entitled to receive upon the due exercise of this Warrant. In addition, nothing contained in this Warrant shall be construed as imposing any liabilities on the Holder to purchase any securities (upon exercise of this Warrant or otherwise) or as a stockholder of the Company, whether such liabilities are asserted by the Company or by creditors of the Company.

10. TRANSFER AND ASSIGNMENT OF WARRANT. During such time as any of the Exercise Shares remain unvested, this Warrant shall not be assigned or transferred by Holder, whether by operation of law or otherwise. Following such time as all of the Exercise Shares have vested and become exercisable in accordance with Section 3.1 above, and subject to applicable laws, the restriction on transfer set forth in this Warrant (including the foregoing sentence), and any restrictions applicable to the transfer of shares set forth in the Company's charter or bylaws or in the R&D Agreement, as each may be amended from time to time, this Warrant and all rights hereunder (including registration rights pursuant to Section 18) shall be freely transferable, by the Holder in person or by duly authorized attorney, upon: (i) delivery of this Warrant and an executed version of the form of assignment attached hereto as Exhibit B to any transferee designated by the Holder within ten (10) days of the date of such transfer or assignment; and (ii) execution and delivery of an investment letter in the form and substance satisfactory to the Company pursuant to which the transferee or assignee, among other things, shall agree with the Company to be bound by all of the provisions of this Warrant. The rights to transfers and assignment shall apply to the Holders (and to subsequent) successors and assigns. This Warrant and the rights evidenced hereby shall be binding upon and shall inure to the benefit of the parties hereto and the successors of the Company and the successors and permitted assigns of the Holder. Such successors and/or permitted assigns of the Holder shall be deemed to be a Holder for all purposes hereunder.

11. NO THIRD-PARTY BENEFICIARIES. This Warrant is for the sole benefit of the Company and the Holder and their respective successors and, in the case of the Holder, permitted assigns and nothing herein, express or implied, is intended to or shall confer upon any other person any legal or equitable right, benefit or remedy of any nature whatsoever, under or by reason of this Warrant.

12. LOST, STOLEN, MUTILATED OR DESTROYED WARRANT. If this Warrant is lost, stolen, mutilated or destroyed, the Company may, on such terms as to indemnity or otherwise as it may reasonably impose (which shall, in the case of a mutilated Warrant, include the surrender thereof), issue a new Warrant of like denomination and tenor as the Warrant so lost, stolen, mutilated or destroyed. Any such new Warrant shall constitute an original contractual obligation of the Company, whether or not the allegedly lost, stolen, mutilated or destroyed Warrant shall be at any time enforceable by anyone.

13. WAIVERS. No waiver by either party of any default with respect to any provision, condition or requirement of this Warrant shall be deemed to be a continuing waiver in the future or a waiver of any other provision, condition or requirement hereof, nor shall any delay or omission of any party to exercise any right hereunder in any manner impair the exercise of any such right accruing to it thereafter.

14. AMENDMENT. This Warrant and any term hereof may be changed, waived, discharged or terminated only by an instrument in writing signed by the Company and the Holder.

15. NOTICES, ETC. All notices required or permitted hereunder shall be in writing and shall be deemed effectively given: (a) upon personal delivery to the party to be notified, (b) when sent by confirmed telex or facsimile if sent during normal business hours of the recipient, if not, then on the next business day, (c) five (5) days after having been sent by registered or certified mail, return receipt requested, postage prepaid, (d) one (1) day after deposit with a nationally recognized overnight courier, specifying next day delivery, with written verification of receipt, or (e) when sent by email upon receipt of an acknowledgment by return email by the recipient as to receipt, which acknowledgment shall not be unreasonably delayed or withheld by the recipient. All communications shall be sent to the Company at the physical address or email listed on the signature page and to the Holder at M. D. Anderson Cancer Center, Strategic Industry Ventures, 7007 Bertner Avenue, 1MC9.2216, Houston, Texas 77030-3907, Attention: Larry Hope, Director, New Ventures and Business Development, or [***] or at such other physical address or email address as the Company or the Holder may designate by ten (10) days advance written notice to the other parties hereto.

16. ACCEPTANCE. Receipt of this Warrant by the Holder shall constitute acceptance of and agreement to all of the terms and conditions contained herein.

17. GOVERNING LAW. This Warrant and all rights, obligations and liabilities hereunder shall be governed by the laws of the State of Delaware.

18. REGISTRATION RIGHTS.

18.1 Registration Obligations; Filing Date Registration. The Company shall use reasonable best efforts to prepare and file with the Commission on or prior to the Filing Date a Registration Statement covering the resale of the Registrable Securities as would permit the sale and distribution of all the Registrable Securities from time to time pursuant to Rule 415 in the manner reasonably requested by the Holder. The Registration Statement shall be on Form S-3 (except if the Company is not then eligible to register for resale the Registrable Securities on Form S-3, in which case the Company shall undertake to register the Registrable Securities on Form S-3 as soon as practicable following the availability of such form). The Registration Statement shall contain the "Plan of Distribution" section in the form reasonably acceptable to the Company and the Holder. The Company shall use reasonable best efforts to cause the Registration Statement filed by it to be declared effective under the Securities Act as promptly as practicable after the filing thereof but in any event on or prior to the Effectiveness Date, and to keep such Registration

Statement continuously effective under the Securities Act until the earlier of (i) such date as all Registrable Securities covered by such Registration Statement have ceased to be Registrable Securities or (ii) the date that is two (2) years following the Effectiveness Date (the "***Effectiveness Period***"). If an ASR Pro Supp is not used to comply with this Section 18.1, then by 4:00 p.m., New York City time, on the Business Day following the Effectiveness Date, the Company shall file with the Commission in accordance with Rule 424 under the Securities Act the final prospectus to be used in connection with sales pursuant to such Registration Statement. For the avoidance of doubt, the Company may elect, in its sole discretion, to satisfy its obligations pursuant to this Warrant by filing an ASR Pro Supp on or prior to the Filing Date in lieu of a new Registration Statement, in which case the Company shall have satisfied its obligations pursuant to this Section 18.1 in full, and such ASR Pro Supp shall constitute a "Registration Statement" for all purposes hereof, with such necessary changes in the details of the provisions hereof as are necessitated by the context, including, without limitation, to take into account that the ASR Pro Supp is a Prospectus filed after the effectiveness of a Registration Statement and not a newly filed Registration Statement.

18.2 Registration Expenses. All reasonable fees and expenses incident to the performance of or compliance with this Section 18 by the Company (excluding underwriters' discounts and commissions and all fees and expenses of legal counsel, accountants and other advisors for the Holder except as specifically provided below), except as and to the extent specified in this Section 18.2, shall be borne by the Company whether or not a Registration Statement is filed by the Company or becomes effective and whether or not any Registrable Securities are sold pursuant to a Registration Statement. The fees and expenses referred to in the foregoing sentence shall include, without limitation, (i) all registration and filing fees (including, without limitation, fees and expenses (A) with respect to filings required to be made with the Nasdaq Stock Market, LLC and each other securities exchange or market on which Registrable Securities are required hereunder to be listed, (B) with respect to filings required to be made by the Company with the Financial Industry Regulatory Authority and (C) in compliance with state securities or Blue Sky laws by the Company or with respect to Registrable Securities); (ii) messenger, telephone and delivery expenses; (iii) fees and disbursements of counsel for the Company; (iv) Securities Act liability insurance, if the Company so desires such insurance; and (v) fees and expenses of all other persons retained by the Company in connection with the consummation of the transactions contemplated by this Warrant, including, without limitation, the Company's independent public accountants. In addition, the Company shall be responsible for all of its internal expenses incurred in connection with the consummation of the transactions contemplated by this Warrant (including, without limitation, all salaries and expenses of its officers and employees performing legal or accounting duties), the expense of any annual audit, the fees and expenses incurred in connection with the listing of the Registrable Securities on any securities exchange as required hereunder. In no event shall the Company be responsible for any underwriting, broker or similar fees or commissions of the Purchaser or, except to the extent provided for above or in the related transaction documents, any legal fees or other costs of the Holder.

18.3 Survival. Notwithstanding anything herein to the contrary, this Section 18 shall survive until the end of the Effectiveness Period; *provided*, *however*, that the terms set forth in Section 18.2 shall remain in effect in accordance with their terms.

(*Signature Page Follows*)

IN WITNESS WHEREOF, the Company has caused this Warrant to be executed by its duly authorized officer as of [●], 2019.

ZIOPHARM ONCOLOGY, INC.

By: _____
Name: _____
Title: _____

Address: One First Avenue
Parris Building #34
Navy Yard Plaza
Boston, MA 02129
Attn: [ ]
Email: [ ]

EXHIBIT A

NOTICE OF EXERCISE

TO: ZIOPHARM ONCOLOGY, INC.

(1) The undersigned hereby elects to purchase shares of common stock, par value $0.001 per share (the "Common Stock"), of Ziopharm Oncology, Inc. (the "Company") pursuant to the terms of the attached Warrant, and [tenders herewith payment of the exercise price in full, together with all applicable transfer taxes, if any/elects to offset payments owed to the undersigned pursuant to the R&D Agreement, as defined in the Warrant].

(2) Please issue a book-entry statement representing said shares of Common Stock of the Company in the name of the undersigned or in such other name as is specified below:

_____

(Name)

_____

_____

(Address)

(3) The undersigned represents that (i) the aforesaid shares of Common Stock are being acquired for the account of the undersigned for investment and not with a view to, or for resale in connection with, the distribution thereof and that the undersigned has no present intention of distributing or reselling such shares; (ii) the undersigned is aware of the Company's business affairs and financial condition and has acquired sufficient information about the Company to reach an informed and knowledgeable decision regarding its investment in the Company; (iii) the undersigned is experienced in making investments of this type and has such knowledge and background in financial and business matters that the undersigned is capable of evaluating the merits and risks of this investment and protecting the undersigned's own interests; (iv) the undersigned understands that the shares of Common Stock issuable upon exercise of this Warrant have not been registered under the Securities Act of 1933, as amended (the "***Securities Act***"), by reason of a specific exemption from the registration provisions of the Securities Act, which exemption depends upon, among other things, the bona fide nature of the investment intent as expressed herein, and, because such securities have not been registered under the Securities Act, they must be held indefinitely unless subsequently registered under the Securities Act or an exemption from such registration is available; (v) the undersigned is aware that the aforesaid shares of Common Stock may not be sold pursuant to Rule 144 adopted under the Securities Act unless certain conditions are met and until the undersigned has held the shares for the amount of time prescribed by Rule 144; and (vi) the undersigned agrees not to make any disposition of all or any part of the aforesaid shares of Common Stock unless and until there is then in effect a Registration Statement covering such proposed disposition and such disposition is made in accordance with said registration statement, or the undersigned has provided the Company with an opinion of counsel satisfactory to the Company, stating that such registration is not required.

(4) No Exercise Shares subject to the attached Warrant may be exercised prior to the vesting of such Exercise Shares in accordance with Section 3 of such Warrant.

(Date)

(Signature)

(Print name)

EXHIBIT B

ASSIGNMENT FORM

[To assign the foregoing Warrant, execute this form and supply required information. Do not use this form to purchase shares.]

FOR VALUE RECEIVED, the foregoing Warrant and all rights evidenced thereby are hereby assigned in full to:

Name: _____
(Please Print)

Address: _____
(Please Print)

Email Address: _____
(Please Print)

Date of Transfer/Assignment: _____, 20__

Date of this Form: _____, 20__

Holder's
Signature: _____

Holder's
Address: _____

NOTE: The signature to this Assignment Form must correspond with the name as it appears on the face of the Warrant, without alteration or enlargement or any change whatever. Officers of corporations and those acting in a fiduciary or other representative capacity should file proper evidence of authority to assign the foregoing Warrant.

Pursuant to the requirements of Section 10 of the Warrant, attached hereto is a copy of the Warrant so transferred or assigned to the person or entity first named above.

CERTAIN CONFIDENTIAL INFORMATION CONTAINED IN THIS DOCUMENT, MARKED BY [*****], HAS BEEN OMITTED BECAUSE ZIOPHARM ONCOLOGY, INC. HAS DETERMINED THE INFORMATION (I) IS NOT MATERIAL AND (II) WOULD LIKELY CAUSE COMPETITIVE HARM TO ZIOPHARM ONCOLOGY, INC. IF PUBLICLY DISCLOSED.

PUBLIC HEALTH SERVICE

Amendment

This **Agreement** is based on the model Amendment Agreement adopted by the U.S. Public Health Service ("**PHS**") Technology Transfer Policy Board for use by components of the National Institutes of Health ("**NIH**"), the Centers for Disease Control and Prevention ("**CDC**"), and the Food and Drug Administration ("**FDA**"), which are agencies of the **PHS** within the Department of Health and Human Services ("**HHS**").

This Cover Page identifies the Parties to this **Agreement:**

The U.S. Department of Health and Human Services, as represented by

National Cancer Institute

an Institute or Center (hereinafter referred to as the "**IC**") of the

NIH

and

Ziopharm Oncology, Inc.,

hereinafter referred to as the "**Licensee**",

having offices at One First Avenue, Parris Building #34, Navy Yard Plaza, Boston, MA 02129,

created and operating under the laws of Delaware.

Tax ID No.: 84-1475642

A-506-2019

FIRST AMENDMENT TO L-190-2019/0

This is the first amendment ("**First Amendment**") of the agreement by and between the **IC** and **Licensee** having an effective date of May 28, 2019 and having **IC** Reference Number L-190-2019/0 ("**Agreement**"). This **First Amendment**, having **IC** Reference Number L-190-2019/1 includes, in addition to the amendments made below, 1) a Signature Page, 2) Attachment 1 (Royalty Payment Information), and 3) Appendix A- Patent(s) or Patent Application(s).

WHEREAS, the **IC** and the **Licensee** desire that the **Agreement** be amended a first time as set forth below in order to bring additional patent rights within the scope of the **Agreement**.

NOW, THEREFORE, in consideration of the mutual covenants and promises contained herein, the **IC** and the **Licensee**, intending to be bound, hereby mutually agree to the following:

1) The cover page's "Serial Number(s) of Licensed Patent(s) or Patent Application(s)" section of the **Agreement** shall be amended to include the following patent applications:

    1. **[***]**

2) Appendix A - Patent(s) or Patent Application(s) of the **Agreement** shall be deleted and replaced with Appendix A- Patent(s) or Patent Application(s) of this **First Amendment**.

3) Within sixty (60) days of the execution of this **First Amendment**, the **Licensee** shall pay the **IC** an amendment issue royalty in the sum of six hundred thousand US Dollars ($600,000.00). Payment options may be found in Attachment 1. The parties agree that the foregoing payment obligation shall be in lieu of the non-creditable, non-refundable amendment issue royalty set forth in Paragraph VII of Appendix C of the **Agreement** for all Additional T Cell Receptors added pursuant to this **First Amendment**.

4) In the event any provision(s) of the **Agreement** is/are inconsistent with Attachment 1, such provision(s) is/are hereby amended to the extent required to avoid such inconsistency and to give effect to the payment information in such Attachment 1.

5) All terms and conditions of the **Agreement** not herein amended remain binding and in effect.

6) The terms and conditions of this **First Amendment** shall, at the **IC's** sole option, be considered by the **IC** to be withdrawn from the **Licensee's** consideration and the terms and conditions of this **First Amendment**, and the **First Amendment** itself, to be null and void, unless this **First Amendment** is executed by the **Licensee** and a fully executed original is received by the **IC** within sixty (60) days from the date of the **IC's** signature found at the Signature Page.

7) This **First Amendment** is effective upon execution by all parties.

SIGNATURES BEGIN ON NEXT PAGE

FIRST AMENDMENT TO L-190-2019/0

SIGNATURE PAGE

In Witness Whereof, the parties have executed this **First Amendment** on the dates set forth below. Any communication or notice to be given shall be forwarded to the respective addresses listed below.

For the **IC**:

Richard U. Rodriguez, MBA
Associate Director
Technology Transfer Center, National Cancer Institute

Date

National Institutes of Health Mailing Address or E-mail Address for **Agreement** notices and reports:

License Compliance and Administration
Monitoring & Enforcement
Office of Technology Transfer
National Institutes of Health
6011 Executive Boulevard, Suite 325
Rockville, Maryland 20852-3804 U.S.A.

E-mail: LicenseNotices_Reports@mail.nih.gov

For the **Licensee** (Upon information and belief, the undersigned expressly certifies or affirms that the contents of any statements of the **Licensee** made or referred to in this document are truthful and accurate.):

Signature of Authorized Official

Date

Name:
Title:

I. Official and Mailing Address for **Agreement** notices:

Rob Hadfield
Name

General Counsel
Title

Mailing Address:

One First Avenue, Parris Building #34
Navy Yard Plaza
Boston, MA 02129

Email Address: [***]

Phone: [***]

Fax: [***]

II. Official and Mailing Address for Financial notices (the **Licensee's** contact person for royalty payments):

Eshane Dupre
Name

Accounts Payable
Title

Mailing Address:

One First Avenue, Parris Building #34
Navy Yard Plaza
Boston, MA 02129

Email Address: [***]

Phone: [***]

Fax: [***]

Any false or misleading statements made, presented, or submitted to the **Government**, including any relevant omissions, under this **Agreement** and during the course of negotiation of this **Agreement** are subject to all applicable civil and criminal statutes including Federal statutes 31 U.S.C. §§3801-3812 (civil liability) and 18 U.S.C. §1001 (criminal liability including fine(s) or imprisonment).

A-506-2019

ATTACHMENT 1 – ROYALTY PAYMENT INFORMATION

New Payment Options Effective March 2018

The License Number MUST appear on payments, reports and correspondence.

[***]

A-506-2019

CONFIDENTIAL -NIH

APPENDIX A – PATENT(S) OR PATENT APPLICATION(S)

Patent(s) or Patent Application(s):

Group A

[***]

Group B

[***]

Group C

[***]

Group D

[***]

Group E

[***]

Group F

[***]

Subsidiaries of the Registrant.

ZIOPHARM Oncology, Ltd (United Kingdom)
ZIOPHARM Oncology, Ltd (Ireland)

Exhibit 23.1

CONSENT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

We consent to the incorporation by reference in the Registration Statements (Nos. 333-129884, 333-134280, 333-142701, 333-160496, 333-167925, 333-185433, 333-199304, 333-220804, and 333-228291) on Form S-8 and Registration Statements (Nos. 333-134279, 333-141014, 333-161453, 333-162160, 333-163517, 333-166444, 333-174292, 333-177793, 333-201826, 333-229555 and 333-232283) on Form S-3 of ZIOPHARM Oncology, Inc. of our report dated March 2, 2020 relating to the financial statements of ZIOPHARM Oncology, Inc. and subsidiaries (the Company) and our report relating to the effectiveness of the Company's internal control over financial reporting dated March 2, 2020, which report expresses an adverse opinion on the effectiveness of the Company's internal control over financial reporting because of a material weakness, appearing in this Annual Report on Form 10-K of ZIOPHARM Oncology, Inc. for the year ended December 31, 2019.

/s/ RSM US LLP

Boston, Massachusetts
March 2, 2020

CERTIFICATION OF PRINCIPAL EXECUTIVE OFFICER

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

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

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

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

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

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

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

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

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

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

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

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

Date: March 2, 2020

/s/ Laurence J.N. Cooper

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

CERTIFICATION OF PRINCIPAL FINANCIAL OFFICER

I, Satyavrat Shukla, certify that:

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

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

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

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

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

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

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

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

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

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

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

Date: March 2, 2020

/s/ Satyavrat Shukla

Satyavrat Shukla
Executive Vice President and Chief Financial Officer
(Principal Financial 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, 2019, as filed with the Securities and Exchange Commission on the date hereof (the "Report"), I, Laurence J.N. Cooper, Principal Executive Officer of the Company, certify, pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002, that:

(1) The Report fully complies with the requirements of Section 13(a) or 15(d) of the Securities Exchange Act of 1934; and

(2) The information contained in the Report fairly presents, in all material respects, the financial condition and result of operations of the Company.

/s/ Laurence J.N. Cooper
Laurence J.N. Cooper, M.D., Ph.D.
Chief Executive Officer
(Principal Executive Officer)
March 2, 2020

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, 2019, as filed with the Securities and Exchange Commission on the date hereof (the "Report"), I, Satyavrat Shukla, Principal Financial 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/ Satyavrat Shukla
Satyavrat Shukla
Executive Vice President and Chief Financial Officer
(Principal Financial Officer)
March 2, 2020