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UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
Washington, D.C. 20549

Form 10-Q

(Mark One)

☒ **QUARTERLY REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934**

For the quarterly period ended March 31, 2019

OR

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

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)	**(I.R.S. Employer Identification No.)**

One First Avenue, Parris Building 34, Navy Yard Plaza
Boston, Massachusetts 02129
(617) 259-1970
(Address, including zip code, and telephone number, including area code, of registrant's principal executive offices)

Indicate by check mark whether the registrant (1) has filed all reports required to be filed by Section 13 or 15(d) of the Securities Exchange Act of 1934 during the preceding 12 months (or for such shorter period that the registrant was required to file such reports), and (2) has been subject to such filing requirements for the past 90 days. Yes: ☒ No: ☐

Indicate by check mark whether the registrant has submitted electronically 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, smaller reporting company, or an emerging growth company. See the definitions of "large accelerated filer," "accelerated filer," "smaller reporting company," and "emerging growth company" in Rule 12b–2 of the Exchange Act.

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 Exchange Act). Yes: ☐ No: ☒

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

Title of each class	Trading Symbol(s)	Name of each exchange on which registered
Common	**ZIOP**	**NASDAQ Capital Market**

The number of shares of the registrant's common stock, $0.001 par value, outstanding as of April 30, 2019, was 162,394,494 shares.

ZIOPHARM Oncology, Inc.

NOTE REGARDING FORWARD-LOOKING STATEMENTS

This Quarterly Report on Form 10-Q contains forward-looking statements that are based on our current beliefs and expectations. These forward-looking statements may be accompanied by such words as "anticipate," "believe," "estimate," "expect," "forecast," "intend," "may," "plan," "project," "target," "will" and other words and terms of similar meaning. Reference is made in particular to forward-looking statements regarding:

- our ability to raise substantial additional capital to fund our planned operations in the near term and to continue as a going concern;
- our estimates regarding expenses, use of cash, timing of future cash needs and capital requirements;
- the development of our product candidates, including statements regarding the timing of initiation, completion and the outcome of clinical studies or trials and related preparatory work and the period during which the results of the trials will become available;
- our ability to advance our product candidates through various stages of development, especially through pivotal safety and efficacy trials;
- the risk that final trial data may not support interim analysis of the viability of our product candidates;
- our expectation regarding the safety and efficacy of our product candidates, the progress and timing of our research and development programs;
- the timing, scope or likelihood of regulatory filings and approvals from the U.S. Food and Drug Administration or equivalent foreign regulatory agencies for our product candidates and for which indications;
- our ability to license additional intellectual property relating to our product candidates from third parties and to comply with our existing license 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".

These forward-looking statements involve risks and uncertainties, including those that are described in the "*Risk Factors*" section of this report and elsewhere within this report that could cause actual results to differ materially from those reflected in such statements. You should not place undue reliance on these statements. Forward-looking statements speak only as of the date of this report. We do not undertake any obligation to publicly update any forward-looking statements.

NOTE REGARDING COMPANY REFERENCES

Throughout this Quarterly Report on Form 10-Q, "Ziopharm," the "Company," "we," "us" and "our" refer to ZIOPHARM Oncology, Inc. and its subsidiaries.

NOTE REGARDING TRADEMARKS

All trademarks, trade names and service marks appearing in this Quarterly Report on Form 10-Q are the property of their respective owners.

ZIOPHARM Oncology, Inc.

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Part I - Financial Information

Item 1. Financial Statements

ZIOPHARM Oncology, Inc.

BALANCE SHEETS
(unaudited)

(in thousands, except share and per share data)

	March 31, 2019	December 31, 2018
ASSETS		
Current assets:		
Cash and cash equivalents	$ 51,487	$ 61,729
Receivables	854	1,864
Prepaid expenses and other current assets	21,752	20,692
Total current assets	74,093	84,285
Property and equipment, net	967	1,097
Operating lease right of use assets	1,589	—
Deposits	130	128
Other non-current assets	6,724	9,541
Total assets	$ 83,503	$ 95,051
LIABILITIES, PREFERRED STOCK AND STOCKHOLDERS' EQUITY (DEFICIT)		
Current liabilities:		
Accounts payable	$ 859	$ 707
Accrued expenses	6,836	8,763
Lease liability - current portion	644	—
Deferred rent - current portion	—	13
Total current liabilities	8,339	9,483
Lease liability - noncurrent portion	948	—
Deferred rent - noncurrent portion	—	4
Total liabilities	9,287	9,487
Commitments and contingencies (Note 6)		
Stockholders' deficit:		
Common stock, $0.001 par value; 250,000,000 shares authorized; 162,287,161 and 161,066,136 shares issued and outstanding at March 31, 2019 and December 31, 2018, respectively	162	161
Additional paid-in capital	653,817	651,732
Accumulated deficit	(579,763)	(566,329)
Total stockholders' equity	74,216	85,564
Total liabilities and stockholders' equity	$ 83,503	$ 95,051

The accompanying notes are an integral part of the unaudited interim financial statements.

ZIOPHARM Oncology, Inc.

STATEMENTS OF OPERATIONS
(unaudited)

(in thousands, except share and per share data)

	For the Three Months Ended March 31,	
	2019	2018
Collaboration revenue	$ —	$ 146
Operating expenses:		
Research and development	9,476	10,183
General and administrative	4,145	6,159
Total operating expenses	13,621	16,342
Loss from operations	(13,621)	(16,196)
Other income, net	187	148
Change in fair value of derivative liabilities	—	28
Net loss	$ (13,434)	$ (16,020)
Preferred stock dividends	$ —	$ (5,120)
Net loss applicable to common stockholders	$ (13,434)	$ (21,140)
Basic and diluted net loss per share	$ (0.08)	$ (0.15)
Weighted average common shares outstanding used to compute basic and diluted net loss per share	160,640,859	140,853,120

The accompanying notes are an integral part of the unaudited interim financial statements.

ZIOPHARM Oncology, Inc.

STATEMENTS OF CHANGES IN PREFERRED STOCK AND STOCKHOLDERS' Equity (DEFICIT)
For the Three months Ended March 31, 2018 and 2019
(unaudited)

(in thousands, except share and per share data)

	Series 1 Preferred Stock - Mezzanine		Common Stock		Additional Paid In Capital Common Stock	Accumulated Deficit	Total Stockholders' Deficit
	Shares	Amount	Shares	Amount			
Balance at December 31, 2017	119,644	$143,992	142,658,037	$ 143	$ 615,493	$ (712,442)	$ (96,806)
Adjustment for implementation of ASU No. 2014-09, Revenue from Contracts with Customers	—	—	—	—	—	(8,131)	(8,131)
Stock-based compensation	—	—	—	—	3,659	—	3,659
Cancelled restricted common stock	—	—	(70,867)	—	—	—	—
Forfeiture of restricted common stock	—	—	(188,234)	(1)	(730)	—	(731)
Preferred stock dividends	3,624	5,047	—	—	(5,120)	—	(5,120)
Net loss	—	—	—	—	—	(16,020)	(16,020)
Balance at March 31, 2018	123,268	$149,039	142,398,936	$ 142	$ 613,302	$ (736,593)	$ (123,149)

	Common Stock		Additional Paid In Capital	Accumulated Deficit	Total Stockholders' Equity
	Shares	Amount			
Balance at December 31, 2018	$161,066,136	$ 161	$ 651,732	$ (566,329)	$ 85,564
Stock-based compensation	—	—	1,456	—	1,456
Issuance of restricted common stock	1,393,536	1	999	—	1,000
Cancelled restricted common stock	(7,333)	—	—	—	—
Repurchase of restricted common stock	(165,178)	—	(370)	—	(370)
Net loss	—	—	—	(13,434)	(13,434)
Balance at March 31, 2019	162,287,161	$ 162	$ 653,817	$ (579,763)	$ 74,216

The accompanying notes are an integral part of the unaudited interim financial statements.

ZIOPHARM Oncology, Inc.

STATEMENTS OF CASH FLOWS
(unaudited)

(in thousands)

	For the Three Months Ended March 31,	
	2019	2018
Cash flows from operating activities:		
Net loss	$(13,434)	$(16,020)
Adjustments to reconcile net loss to net cash used in operating activities:		
Depreciation	140	117
Stock-based compensation	1,456	3,659
Bonus paid in common stock, net	630	—
Change in fair value of derivative liabilities	—	(28)
Change in operating assets and liabilities:		
(Increase) decrease in:		
Receivables	1,009	1
Prepaid expenses and other current assets	(1,058)	(1,172)
Other noncurrent assets	2,817	(490)
Deposits	(2)	—
Increase (decrease) in:		
Accounts payable	152	(3,811)
Accrued expenses	(1,929)	(1,030)
Deferred revenue	—	(146)
Deferred rent	17	(37)
Other liabilities	(30)	—
Net cash used in operating activities	(10,232)	(18,957)
Cash flows from investing activities:		
Purchases of property and equipment	(10)	(150)
Net cash used in investing activities	(10)	(150)
Cash flows from financing activities:		
Repurchase of common stock	—	(731)
Net cash provided by (used in) financing activities	—	(731)
Net decrease in cash and cash equivalents, and restricted cash	(10,242)	(19,838)
Cash and cash equivalents, and restricted cash, beginning of period	61,729	71,335
Cash and cash equivalents, and restricted cash, end of period	$ 51,487	$ 51,497
Supplementary disclosure of cash flow information:		
Bonus paid in common stock, gross	$ 1,000	$ —
Supplementary disclosure of noncash investing and financing activities:		
Payment of Series 1 preferred stock dividends in preferred stock	$ —	$ 5,120

The accompanying notes are an integral part of the unaudited interim financial statements.

ZIOPHARM Oncology, Inc.

NOTES TO FINANCIAL STATEMENTS
(unaudited)

1. Business

Overview

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 March 31, 2019, the Company had approximately $51.5 million of cash and cash equivalents and the Company's accumulated deficit was approximately $579.8 million. Given its current development plans, the Company anticipates cash resources will be sufficient to fund operations into the second quarter of 2020. 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 its product candidates, management may need to curtail its development efforts and planned operations to conserve cash.

Basis of Presentation

The accompanying unaudited interim financial statements have been prepared in accordance with the instructions to Form 10-Q pursuant to the rules and regulations of the Securities and Exchange Commission, or the SEC. Certain information and note disclosures required by generally accepted accounting principles in the United States have been condensed or omitted pursuant to such rules and regulations.

It is management's opinion that the accompanying unaudited interim financial statements reflect all adjustments (which are normal and recurring) that are necessary for a fair statement of the results for the interim periods. The unaudited interim financial statements should be read in conjunction with the audited financial statements and the notes thereto for the year ended December 31, 2018, included in the Company's Annual Report on Form 10-K for the fiscal year ended December 31, 2018 filed with the SEC on March 5, 2019, or the Form 10-K.

The year-end balance sheet data was derived from the audited financial statements but does not include all disclosures required by generally accepted accounting principles in the United States.

The results disclosed in the statements of operations for the three months ended March 31, 2019 are not necessarily indicative of the results to be expected for the full fiscal year.

ZIOPHARM Oncology, Inc.

NOTES TO FINANCIAL STATEMENTS (unaudited)

1. Business – (continued)

Use of Estimates

The preparation of financial statements in conformity with accounting principles generally accepted in the United States 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 its financial statements are:

- Clinical trial expenses;
- Collaboration agreements and revenue recognition;
- Fair value measurements of stock based compensation and Series 1 preferred stock; 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.

On December 18, 2018, Ziopharm and TriArm Therapeutics, Ltd. ("TriArm") announced that the companies plan to launch Eden BioCell, Ltd. ("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. TriArm is a cell therapy company with operations in Germany, China and the United States.

For the territory of China, Taiwan and Korea, Ziopharm will license the rights to Eden BioCell for third-generation *Sleeping Beauty*-generated CAR-T therapies targeting the CD19 antigen. Eden BioCell will be jointly-owned by Ziopharm and TriArm. TriArm has committed up to $35.0 million to this joint venture. Under the terms of the agreement, Eden BioCell has rights in the region to CAR-T cells very rapidly manufactured in two days or less using the *Sleeping Beauty* platform to express a CD19-specific CAR and membrane-bound interleukin 15, or mbIL15, along with a kill switch. Each party will share decision-making authority. TriArm will manage all clinical development to execute trials in China for Eden BioCell. On January 3, 2019 Eden BioCell was incorporated in Hong Kong. The definitive agreements are expected to be executed in the first half of 2019.

ZIOPHARM Oncology, Inc.

NOTES TO FINANCIAL STATEMENTS (unaudited)

2. Summary of Significant Accounting Policies

The Company's significant accounting policies were identified in the Company's Form 10-K. There have been no material changes in those policies since the filing of its Form 10-K except as noted below with respect to the Company's revenue recognition.

Leases

In February 2016, the FASB issued ASU 2016-02, Leases (Topic 842), to increase transparency and comparability among organizations by requiring the recognition of a right-of-use assets and lease liabilities for most lease arrangements on the balance sheet. Under the standard, disclosures are required to meet the objective of enabling users of financial statements to assess the amount, timing, and uncertainty of cash flows arising from leases. The new standard is effective for fiscal years beginning after December 15, 2018, and the Company adopted the standard on January 1, 2019.

The standard permits two transition methods, (1) to apply the new lease requirements at the beginning of the earliest period presented, or (2) to apply the new lease requirements at the effective date. Under both transition methods there is a cumulative effect adjustment. The Company adopted Topic 842 as of 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 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. The adoption did not have a material impact on the Company's statements of operations or accumulated deficit. The Company has implemented changes to related processes, controls and disclosures in connection with the adoption of Topic 842 (Note 8).

ZIOPHARM Oncology, Inc.

NOTES TO FINANCIAL STATEMENTS (unaudited)

2. Summary of Significant Accounting Policies (continued)

New Accounting Pronouncements

In November 2016, the FASB issued ASU 2016-18, *Statement of Cash Flows: Restricted Cash* or ASU 2016-18. The amendments in this update require that amounts generally described as restricted cash and restricted cash equivalents be included within cash and cash equivalents when reconciling the beginning-of-period and end-of-period total amounts shown on the statement of cash flows. ASU 2016-18 was effective January 1, 2018. As a result of adopting ASU 2016-18, the Company includes its restricted cash balance in the cash and cash equivalents reconciliation of operating, investing and financing activities. The following 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.

	March 31,	
	2019	2018
	(in thousands)	
Cash and cash equivalents	$51,487	$51,108
Restricted cash included in prepaid expenses and other current assets	—	389
Total cash, cash equivalents, and restricted cash shown in the statement of cash flows	$51,487	$51,497

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 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.

ZIOPHARM Oncology, Inc.

NOTES TO FINANCIAL STATEMENTS (unaudited)

3. Fair Value Measurements

The Company accounts for its financial assets and liabilities using fair value measurements. The authoritative accounting guidance defines fair value, establishes a framework for measuring fair value under generally accepted accounting principles and enhances 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 fair value hierarchy is 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 as follows:

- 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 March 31, 2019 and December 31, 2018 were as follows:

($ in thousands)

		Fair Value Measurements at Reporting Date Using		
Description	Balance as of March 31, 2019	Quoted Prices in Active Markets for Identical Assets/Liabilities (Level 1)	Significant Other Observable Inputs (Level 2)	Significant Unobservable Inputs (Level 3)
Assets:				
Cash equivalents	$ 24,568	$ 24,568	$ —	$ —

ZIOPHARM Oncology, Inc.

NOTES TO FINANCIAL STATEMENTS (unaudited)

3. Fair Value Measurements - (continued)

($ in thousands)

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

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

ZIOPHARM Oncology, Inc.

NOTES TO FINANCIAL STATEMENTS (unaudited)

4. Net Loss per Share

Basic net loss per share is computed by dividing net loss by the weighted average number of shares of common stock outstanding for the period. The Company's potentially dilutive shares, which include outstanding common stock options, unvested restricted stock and preferred stock, have not been included in the computation of diluted net loss per share for any of the periods presented as the result would be anti-dilutive. Such potentially dilutive shares of common stock at March 31, 2019 and 2018 consisted of the following:

	March 31,	
	2019	2018
Stock options	5,416,085	3,822,968
Unvested restricted stock	1,621,845	1,532,201
Warrants	18,939,394	—
Preferred stock	—	35,152,089
	25,977,324	40,507,258

During the year ended December 31, 2018, the Company and Precigen, Inc., or Precigen, a wholly owned subsidiary of Intrexon Corporation, or Intrexon, entered into a License Agreement to replace all existing agreements between the companies that will provide the Company with certain exclusive and non-exclusive rights to technology controlled by Precigen. The License Agreement was dated October 5, 2018. In consideration of the Company entering into the License Agreement, Intrexon agreed to forfeit and return to the Company all shares of the Company's Series 1 Preferred Stock held by or payable to Intrexon as of the date of the License Agreement (Note 6).

5. Revenue Recognition

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 License and Collaboration Agreement with Ares Trading S.A., a subsidiary of Merck KGaA, or the 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 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.

ZIOPHARM Oncology, Inc.

NOTES TO FINANCIAL STATEMENTS (unaudited)

5. Revenue Recognition (continued)

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 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.

ZIOPHARM Oncology, Inc.

NOTES TO FINANCIAL STATEMENTS (unaudited)

5. Revenue Recognition (continued)

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.

As it relates to the Ares Trading Agreement (Note 6), the Company recognized the upfront payment associated with its one 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 are classified in current liabilities. Amounts not expected to be recognized as revenue within the twelve months following the balance sheet date are 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 (see Note 6).

There are multiple distinct performance obligations, including material rights; thus, the Company allocates the transaction price to each distinct performance obligation based on its relative standalone selling price. The standalone selling price is generally determined based on the prices charged to customers or using expected cost-plus margin. Revenue is recognized by measuring the progress toward complete satisfaction of the performance obligations using an input measure. 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 does 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 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.

On October 5, 2018, the Company entered into the license agreement with Precigen. As between the Company and Precigen, the terms of the License Agreement replace the terms of: (a) the Channel Agreement previously entered into with Intrexon Corporation (the “Channel Agreement”), including all amendments to the Channel Agreement; (b) certain rights and obligations pursuant to the Ares Trading Agreement; (c) the MD Anderson License (Note 6); and (d) that certain Research and Development Agreement between the Company, Intrexon and The University of Texas MD Anderson Cancer Center, or MD Anderson, with an effective date of August 17, 2015 or the Research and Development Agreement, and any amendments or statements of work thereto.

In partial consideration of the Company entering into the License Agreement, Precigen is required to use diligent good faith efforts to transfer the Company’s rights and obligations under the Ares Trading Agreement to Intrexon (or it’s affiliate). As a result, the Company has very limited obligations under the Ares Trading Agreement.

ZIOPHARM Oncology, Inc.

NOTES TO FINANCIAL STATEMENTS (unaudited)

6. Commitments and Contingencies

License Agreements

Exclusive License Agreement with Precigen, Inc.

On October 5, 2018, the Company entered into an exclusive license agreement, or the License Agreement, with Precigen. As between the Company and Precigen, 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 Intrexon, 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 Intrexon to Precigen; (b) certain rights and obligations pursuant to that certain License and Collaboration Agreement effective March 27, 2015 between ZIOPHARM, Intrexon and ARES TRADING S.A., or Ares Trading, a subsidiary of Merck KGaA, or Merck, as assigned by Intrexon to Precigen, or the Ares Trading Agreement; (c) that certain License Agreement between the Company, Intrexon, and MD Anderson, with an effective date of January 13, 2015, or the MD Anderson License, which was subsequently assigned by Intrexon and assumed by Precigen effective as of January 1, 2018; and (d) that certain Research and Development Agreement between the Company, Intrexon 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, Precigen has granted the Company an exclusive, worldwide, royalty-bearing, sub-licensable license 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, 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. Precigen 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 will be 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.

Precigen 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 Precigen, the Company will pay Precigen an annual license fee of $0.1 million and has agreed to reimburse Precigen for certain historical costs of the licensed programs up to $1.0 million, payable quarterly.

The Company 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, the Company will pay Precigen 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 Precigen 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 Precigen 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 Precigen 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 Precigen responsible for the remaining 20% of the development costs and receiving 20% of the operating profits.

ZIOPHARM Oncology, Inc.

NOTES TO FINANCIAL STATEMENTS (unaudited)

6. Commitments and Contingencies (Continued)

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

In consideration of entering into the License Agreement, Intrexon has forfeited and returned to the Company all shares of Series 1 preferred stock held by or payable to Intrexon as of the date of the License Agreement (Note 7).

License Agreement—The University of Texas MD Anderson Cancer Center

On January 13, 2015, the Company, together with Intrexon, entered into the MD Anderson License with MD Anderson (which Intrexon subsequently assigned to Precigen). Pursuant to the MD Anderson License, the Company, together with Precigen, 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, Precigen 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.

ZIOPHARM Oncology, Inc.

NOTES TO FINANCIAL STATEMENTS (unaudited)

6. Commitments and Contingencies (Continued)

Pursuant to the Research and Development Agreement, the Company, Precigen and MD Anderson formed a joint steering committee to oversee and manage the new and ongoing research programs. Under the License Agreement with Precigen, the Company 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, 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. During the three months ended March 31, 2019, the Company expensed approximately $1.4 million for its research programs being conducted in Houston. The net balance of cash resources on hand at MD Anderson available to offset expenses and future costs is $26.4 million, of which $19.8 million is included in other current assets and the remaining $6.6 million is included in non-current assets at March 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 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 the Company and Precigen are not using commercially reasonable efforts to commercialize the licensed intellectual property on a case-by-case basis. After five years from the date of the MD Anderson License and subject to a 180-day cure period, MD Anderson will have the right to terminate the MD Anderson License with respect to specific technology(ies) funded by the government or subject to a third-party contract if the Company and Precigen are not meeting the diligence requirements in such funding agreement or contract, as applicable. MD Anderson may also terminate the agreement with written notice upon material breach by the Company 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 the Company and Precigen and may be terminated by the mutual written agreement of the Company, Precigen, and MD Anderson.

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

On January 10, 2017, the Company announced the signing of a Cooperative Research and Development Agreement, or CRADA, with the National Cancer Institute, or 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.

In February 2019, the Company extended the CRADA with the NCI for two years, committing an additional $5.0 million to this program through January 2022. The remaining obligation, as of March 31, 2019, to the NCI under the CRADA is $6.9 million over the next two years, payable in $625 thousand payments on a quarterly basis. The Company made one payment of $625 thousand, during the three months ended March 31, 2019 and 2018, respectively.

Exclusive Channel Partner Agreement with Precigen for the Cancer Programs

From 2011 to 2018, the Company was party to various arrangements with Intrexon (now Precigen) in which the Company used Precigen'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.

ZIOPHARM Oncology, Inc.

NOTES TO FINANCIAL STATEMENTS (unaudited)

6. Commitments and Contingencies (Continued)

Ares Trading License and Collaboration Agreement

On March 27, 2015, the Company, together with Intrexon (now Precigen), signed the Ares Trading Agreement, with Ares Trading, 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.

Precigen 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 three months ended March 31, 2018, the Company expensed $1.6 million under the Ares Trading Agreement. The Company did not incur any costs under the agreement for the three months ended March 31, 2019 as there are no continuing obligations to reimburse Precigen for expenses under the Ares Trading Agreement following the October 2018 license.

Ares Trading paid a non-refundable upfront fee of $115.0 million to Intrexon as consideration for entry into the Ares Trading Agreement. Pursuant to the Third Amendment to Exclusive Channel Partner Agreement, or the 2016 ECP Amendment, the Company was entitled to receive 50% of the upfront fee, or $57.5 million, which was received from Intrexon in July 2015.

Under the License Agreement, Precigen 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 (unaudited)

6. 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, the Company was granted an exclusive, worldwide license to rights (including rights to U.S. and foreign patent and patent applications and related improvements and know-how) for the manufacture and commercialization of two classes of organic arsenicals (water- and lipid-based) for human and animal use. The class of water-based organic arsenicals includes darinaparsin.

The Company issued options to purchase 50,222 shares outside of its stock option plans. The options vested upon completion of certain clinical milestones, all of which have occurred and the options are now fully vested. An expense of $87 thousand was charged to research and development expense for the final vesting event which occurred in March 2016 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. 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 $1.0 million milestone payment was subsequently made to MD Anderson and reported net. In addition, the Company may be required to make additional payments to the Licensors upon achievement of certain other milestones in varying amounts which, on a cumulative basis could total up to an additional $4.5 million. In addition, the Licensors are entitled to receive single digit percentage royalty payments on sales from a licensed product and will also be entitled to receive a portion of any fees that the Company may receive from a possible sublicense under certain circumstances.

Collaboration Agreement with Solasia Pharma K.K.

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

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

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

ZIOPHARM Oncology, Inc.

NOTES TO FINANCIAL STATEMENTS (unaudited)

6. Commitments and Contingencies (Continued)

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

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

7. Related Party Transactions

Collaborations with Intrexon/ Precigen

During the three months ended March 31, 2018, the Company issued an aggregate of 3,624 shares of Series 1 preferred stock to Intrexon, the holder of all of the outstanding shares of the Company's Series 1 preferred stock, as monthly dividend payments. At March 31, 2018, the Company recorded such shares of Series 1 preferred stock at a fair value of $5.1 million which is a component of temporary equity. During the three months ended March 31, 2018, the Company recorded a gain on the change of the derivative liabilities in the amount of $28 thousand.

During the three months ended March 31, 2019, and 2018, the Company expensed $1.2 million and $2.8 million, respectively, for services performed by Precigen. As of March 31, 2019, and 2018, the Company recorded $0.9 million and $2.8 million, respectively, in current liabilities on its balance sheet for amounts due to Precigen.

As discussed further in Note 1, on October 5, 2018, the Company entered into the License Agreement, the terms of which replaced the terms of the Channel Agreement.

ZIOPHARM Oncology, Inc.

NOTES TO FINANCIAL STATEMENTS (unaudited)

Collaboration with Precigen and MD Anderson

On January 13, 2015, the Company, together with Intrexon, entered into the MD Anderson License with MD Anderson (which Intrexon subsequently assigned to Precigen). Pursuant to the MD Anderson License, the Company, together with Precigen, hold an exclusive, worldwide license to certain technologies owned and licensed by MD Anderson including technologies relating to novel 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.

The Company has determined that the rights acquired in the MD Anderson License represent in-process research and development with no alternative future use. During the three months ending March 31, 2018, the Company made one quarterly payment totaling $2.7 million, bringing the total aggregate payments to $41.9 million under this arrangement. The net balance of cash resources on hand at MD Anderson available to offset expenses and future costs is $26.4 million, of which $19.8 million is included in other current assets and the remaining $6.6 million is included in non-current assets at March 31, 2019. 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.

Settlement of a Related Party Relationship

Exclusive License Agreement with Precigen

On October 5, 2018, the Company entered into the license agreement with Precigen. As between the Company and Precigen, the terms of the License Agreement replace the terms of: (a) the Channel Agreement, including all amendments to the Channel Agreement; (b) certain rights and obligations pursuant to the Ares Trading Agreement; (c) the MD Anderson License; and (d) the Research and Development Agreement, and any amendments or statements of work thereto.

Pursuant to the terms of the License Agreement, Precigen has granted the Company an exclusive, worldwide, royalty-bearing, sub-licensable license 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, subject to the rights of Ares Trading (now Intrexon) to pursue such target under the Ares Trading Agreement, and (iii) TCR Products designed for neoantigens for the treatment of cancer. Precigen 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.

ZIOPHARM Oncology, Inc.

NOTES TO FINANCIAL STATEMENTS (unaudited)

7. Related Party Transactions (continued)

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. Precigen has also granted the Company an exclusive, worldwide, royalty-bearing, sub-licensable license to research, develop and commercialize Gorilla IL-12 Products.

Ziopharm agreed to reimburse Precigen 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 and it has been included in accrued expense 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 Precigen 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 Precigen 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 Precigen 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 Precigen 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 Precigen responsible for the remaining 20% of the development costs and receiving 20% of the operating profits.

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

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

The Company determined that this transaction represented a capital transaction between related parties. The Company calculated the fair value of 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 Company'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 8). 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 (Note 3).

ZIOPHARM Oncology, Inc.

NOTES TO FINANCIAL STATEMENTS (unaudited)

8. Leases

The Company adopted 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. The adoption did not have a material impact on the Company's statements of operations or accumulated deficit. The Company has implemented changes to related processes, controls and disclosures in connection with the adoption of Topic 842. 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 headquarters in Boston office, which was originally set to expire in August 2016. On December 21, 2015 and April 15, 2016, the Company renewed the sublease for the Company's corporate headquarters, through August 31, 2021. As of March 31, 2019 and 2018, a total security deposit of $128 thousand is included in deposits on the balance sheet.

On January 30, 2018, the Company entered into a lease agreement for office space in Houston at MD Anderson. Under the terms of the Houston lease agreement, the Company leases approximately two hundred and ten square feet and are required to make rental payments at an average monthly rate of approximately $1 thousand through April 2021. 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 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 thousand through April 2021. As of March 31, 2019, a total security deposit of $2 thousand is included in deposits on the balance sheet.

The components of lease expense were as follows:

(in thousands)	Three Months Ended March 31, 2019
Operating lease cost	$ 178
Total lease cost	$ 178
Weighted-average remaining lease term (years)	2.40
Weighted-average discount rate	8.00%

Cash paid for amounts included in the measurement of the lease liabilities were $178 thousand for the quarter ended March 31, 2019.

ZIOPHARM Oncology, Inc.

NOTES TO FINANCIAL STATEMENTS (unaudited)

8. Leases (continued)

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

Maturity of Lease Liabilities	Operating Leases
2019 (excluding the three months ended March 31, 2019)	557
2020	755
2021	491
Total lease payments	1,803
Less: Imputed Interest	211
Present value of lease payments	$ 1,592

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 for the three months ended March 31, 2018 was approximately $178 thousand.

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

ZIOPHARM Oncology, Inc.

NOTES TO FINANCIAL STATEMENTS (unaudited)

9. Stock-Based Compensation

The Company recognized stock-based compensation expense on all employee and non-employee awards as follows:

(in thousands)	For the three months ended March 31, 2019	2018
Research and development	$ 433	$ 603
General and administrative	1,023	3,056
Stock-based compensation expense	$ 1,456	$ 3,659

The Company granted an aggregate of 1,496,333 stock options during the three months ended March 31, 2019 with a weighted-average grant date fair value of $1.62 per share. The Company granted an aggregate of 7,500 stock options during the three months ended March 31, 2018 with a weighted-average grant date fair value of $3.00 per share.

The Company recognizes forfeitures as they occur.

For the three months ended March 31, 2019 and 2018, the fair value of stock options was estimated on the date of grant using a Black-Scholes option valuation model with the following assumptions:

	For the three months ended March 31, 2019	2018
Risk-free interest rate	2.28 - 2.53%	2.56 - 2.74%
Expected life in years	6 - 6.25	6
Expected volatility	78.87 - 85.00%	80.75 - 81.10%
Expected dividend yield	0	0

ZIOPHARM Oncology, Inc.

NOTES TO FINANCIAL STATEMENTS (unaudited)

9. Stock-Based Compensation – (continued)

Stock option activity under the Company's stock option plan for the three months ended March 31, 2019 is 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, 2018	5,277,085	$ 4.24		
Granted	1,496,333	2.24		
Exercised	—	—		
Cancelled	(1,357,333)	4.33		
Outstanding, March 31, 2019	5,416,085	$ 3.66	7.82	$ 5,494
Options exercisable, March 31, 2019	2,213,008	$ 5.14	5.33	$ 1,025
Options exercisable, December 31, 2018	3,099,935	$ 5.15	4.93	$ 88
Options available for future grant	3,996,638			

At March 31, 2019, total unrecognized compensation costs related to unvested stock options outstanding amounted to $6.2 million. The cost is expected to be recognized over a weighted-average period of 1.61 years.

A summary of the status of unvested restricted stock for the three months ended March 31, 2019 is as follows:

	Number of Shares	Weighted-Average Grant Date Fair Value
Non-vested, December 31, 2018	682,070	$ 3.47
Granted	1,393,536	2.24
Vested	(446,428)	2.24
Cancelled	(7,333)	4.14
Non-vested, March 31, 2019	1,621,845	$ 2.92

At March 31, 2019, total unrecognized compensation costs related to unvested restricted stock outstanding amounted to $4.1 million. The cost is expected to be recognized over a weighted-average period of 1.59 years.

ZIOPHARM Oncology, Inc.

NOTES TO FINANCIAL STATEMENTS (unaudited)

10. Preferred Stock

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

On June 29, 2016, the Company entered into the 2016 ECP Amendment and Amendment to Exclusive Channel Collaboration Agreement, or the 2016 GvHD Amendment, with Intrexon (now Precigen) (Note 6). In consideration for the execution and delivery of the 2016 ECP Amendment and the 2016 GvHD Amendment, the Company issued to Intrexon 100,000 shares of its newly designated Series 1 preferred stock. Each share of the Company's Series 1 preferred stock 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 Precigen 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 Precigen. In consideration of the Company entering into the License Agreement, Intrexon forfeited and returned to the Company all shares of the Company's Series 1 preferred stock held by or payable to Intrexon as of the date of the License Agreement (Notes 6 and 7).

11. 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 Precigen. In partial consideration for the termination of the former agreements, the companies agreed that Intrexon would forfeit all outstanding shares of the Series 1 preferred stock held by Intrexon, including any accrued dividends (Note 10).

12. Warrants

The Company assesses whether an equity classified financial instrument is indexed to an entity's own stock for purposes of determining whether a financial instrument should be treated as a derivative.

In connection with the Company's November 2018 private placement, the Company issued warrants to purchase an aggregate of 18,939,394 shares of common stock which are 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.

The Company assessed whether the warrants 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.

Item 2. Management's Discussion and Analysis of Financial Condition and Results of Operations

Forward Looking Statements

This Quarterly Report on Form 10-Q contains "forward-looking statements" within the meaning of Section 27A of the Securities Act of 1933, as amended, and Section 21E of the Securities Exchange Act of 1934, as amended. These statements relate to our future plans, objectives, expectations and intentions and may be identified by words such as "may," "will," "should," "expects," "plans," "anticipates," "intends," "targets," "projects," "contemplates," "believes," "seeks," "goals," "estimates," "predicts," "potential" and "continue" or similar words. In particular, statements contained in this Quarterly Report, including but not limited to, statements regarding our ability to raise substantial additional capital to fund our planned operations; the costs and timing of our clinical trials and of the development and commercialization of our pipeline products; the sufficiency of our cash and cash flows from operations and our expected uses of cash; our ability to finance our operations and business initiatives and obtain funding for such activities; our future results of operations and financial position, business strategy and plan prospects, projected revenue or costs and objectives of management for future research, development or operations, are forward-looking statements. Readers are cautioned that these forward-looking statements are only predictions and are subject to risks, uncertainties, and assumptions that are difficult to predict, including those discussed in Part II, Item 1A. "Risk Factors" section of this Quarterly Report. Therefore, actual results may differ materially and adversely from those expressed in any forward-looking statements. Except as required by law, we undertake no obligation to revise or update any forward-looking statements after the date of this Quarterly Report.

Overview

We are a biopharmaceutical company focused on discovering, acquiring, developing and commercializing next generation immunotherapy platforms that leverage cell- and gene-based therapies to treat patients with cancer. We are developing two immuno-oncology platform technologies that utilize the patient's immune system by employing novel, controlled gene expression and innovative cell engineering technologies designed to deliver safe, effective, and scalable cell- and viral-based 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 to stably reprogram T cells outside of the body for subsequent infusion. Our second platform is termed Controlled IL-12, which 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 believe these two platforms will provide unique and powerful solutions to address the issues associated with (1) treating solid tumors with heterogeneous and unknown antigens, and (2) providing cost-effective scalable manufacturing solutions for T-cell receptor T-cell, or TCR$^+$ T, and chimeric antigen receptor, or CAR T-cell, or CAR$^+$ T, therapies for solid tumors and hematologic malignancies. We expect programs from our two platform technologies to be in the clinic in 2019.

Using our *Sleeping Beauty* platform, we are developing TCR$^+$ T therapies initially to target solid tumors. Our T cell receptor, or TCR, program designs and manufactures T cells that target antigens unique to each patient, thereby delivering truly 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 (addressing inter-tumor heterogeneity) and to express more than one TCR for each patient (addressing intra-tumor heterogeneity). We believe the scalability of our approach provides a competitive advantage to alternative viral-based approaches to T-cell manufacturing. Under our Cooperative Research and Development Agreement, or CRADA, the National Cancer Institute, or the NCI, intends to initiate a Phase 1 clinical trial in patients with a variety of solid tumors using the *Sleeping Beauty* platform to genetically modify T-cells to target patient-specific neoantigens in mid-2019. The clinical trial will be under the direction of Steven A. Rosenberg, M.D., Ph.D., Chief of the Surgery Branch at the NCI.

We are also developing CAR+ T therapies using our *Sleeping Beauty* platform. This CAR+ T program seeks to solve the complex and costly manufacturing limitations of existing CAR+ T therapies that we believe will continue limiting their commercial potential. We believe using DNA plasmids in the *Sleeping Beauty* system to express CAR and our proprietary membrane-bound interleukin 15, or mbIL15, in resting T cells obtained from peripheral blood will enable infused T cells to propagate within the patient to target leukemia and lymphoma, thus avoiding the need to numerically expand T cells for weeks in bioreactors before patient administration. We expect the lower cost of DNA plasmids compared with the virus used by other CAR+ T programs, together with the avoidance of lengthy *ex vivo* manufacturing, will reduce the cost and complexity of manufacturing CAR+ T cells. These technologies should enable T cells to be infused within two days of gene transfer in a process we refer to as rapid personalized manufacture, or RPM. We are advancing our CAR+ T therapies in the United States in collaboration with The University of Texas MD Anderson Cancer Center, or MD Anderson, to target CD19 on malignant B cells. In 2019, we expect to initiate a Phase 1 clinical trial in the United States of our third-generation *Sleeping Beauty* modified CAR+ T cells, co-expressing CAR and mbIL15, manufactured and reinfused into the patient in less than two days from gene transfer. In addition, in a joint venture with TriArm Therapeutics, Ltd., or TriArm, we are forming Eden BioCell, Ltd., or Eden BioCell, to lead clinical development and commercialization of *Sleeping Beauty*-generated CD19-specific CAR-T therapies in the People's Republic of China, Taiwan and Korea. Eden BioCell will be owned equally by us and TriArm and the parties will 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. We expect our joint venture with TriArm to close in the first half of 2019 and we may evaluate additional programs to pursue in this joint venture.

Our Controlled IL-12 platform uses virotherapy based on an engineered replication-incompetent adenovirus (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, including brain cancer. Our Controlled IL-12 platform allows us to deliver IL-12 in a tunable dose, which is critical for this potent cytokine. In a Phase 1 clinical trial of patients with recurrent glioblastoma multiforme, or rGBM, a subset of patients (n=6) who received low-dose steroids along with 20 mg of veledimex plus Ad-RTS-hIL-12, achieved 17.8 months median overall survival, or OS, compared with five to eight months OS established in historical controls. Thirty-six additional patients with rGBM have been recruited into a sub study 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. In June 2018, we began enrolling patients with rGBM to receive Ad-RTS-hIL-12 plus veledimex in combination with OPDIVO® (nivolumab) in a Phase 1 dose-escalation trial. In November 2018, we announced a clinical supply agreement with Regeneron Pharmaceuticals, Inc., or Regeneron, to evaluate Ad-RTS-hIL-12 plus veledimex in combination with Regeneron's PD-1 antibody Libtayo® (cemiplimab-rwlc) for the treatment of patients with rGBM. We currently expect to initiate a Phase 2 clinical trial in the first half of 2019 in approximately 30 patients with rGBM to measure preliminary safety and efficacy of Ad-RTS-hIL-12 plus veledimex in combination with Libtayo.

As of March 31, 2019, we had cash and cash equivalents of approximately $51.5 million. We expect that our existing cash and cash equivalents will be sufficient to fund our current operations into the second quarter of 2020, 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 not generated significant revenue and have incurred significant net losses in each year since our inception. For the three months ended March 31, 2019, we had a net loss of $13.4 million, and, as of March 31, 2019, we have incurred approximately $579.8 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.

Recent Developments

Clinical and Regulatory Developments

- On April 1, 2019, we announced that the U.S. Food and Drug Administration, or FDA, has granted Fast Track Designation for our Controlled IL-12 program which consists of Ad-RTS-hIL-12 plus veledimex, for the treatment of recurrent or progressive glioblastoma multiforme in adults. The FDA's Fast Track program is designed to facilitate the development and expedite the review of drugs to treat serious conditions and fill an unmet medical need.
- On February 11, 2019, we announced enrollment had been completed in our substudy to expand a Phase 1 clinical trial evaluating our Controlled IL-12 platform as a monotherapy for the treatment of rGBM. A total of 36 patients were enrolled in the substudy in less than six months. The substudy includes patients who have not received bevacizumab for their disease and are not receiving steroids for the four weeks prior to therapy initiation.
- Enrollment continues in our Phase 1 clinical trial to evaluate Ad-RTS-hIL-12 plus veledimex in combination with OPDIVO® (nivolumab). The Data and Safety Monitoring Board for the clinical trial has authorized escalation to the second dosing cohort for this clinical trial.
- Under our CRADA, the NCI is planning a Phase 1 clinical trial of *Sleeping Beauty*-modified TCRs to treat solid tumors, with enrollment expected to begin in mid-2019. NCI is developing autologous peripheral blood lymphocytes genetically modified with the *Sleeping Beauty* system to express TCRs that recognize specific neoantigens expressed within patients' solid tumors.
- We expect to respond to the request for more information by the FDA in the second half of 2019 for our third-generation Phase 1 trial to evaluate CD19-specific CAR-T therapies under our technology referred to as rapid personalized manufacture (previously referred to as point-of-care).
- Enrollment continues in the Phase 1 investigator-led trial at MD Anderson to infuse CD19-specific CAR-T cells based on genetic modification with the *Sleeping Beauty* system for patients with B-cell leukemias and lymphomas. This second-generation trial explores T-cell dosing and time to manufacture.

Financial Overview

Overview of Results of Operations

Three Months Ended March 31, 2019 Compared to Three Months Ended March 31, 2018

Revenue. Revenue during the three months ended March 31, 2019 and 2018 was as follows:

($ in thousands)	Three months ended March 31, 2019	2018	Change	
Collaboration revenue	$ —	$ 146	$(146)	-100%

We recognized previously deferred revenue from our License and Collaboration Agreement among us, Precigen and Ares Trading S.A., or the Ares Trading Agreement, amounting to $146 thousand for the three months ended March 31, 2018 under ASC 605 (Note 3). During the three months ended March 31, 2019, we did not recognize any revenue as we did not have any outstanding contract liability under ASC 606 (Note 3).

Research and development expenses. Research and development expenses during the three months ended March 31, 2019 and 2018 were as follows:

($ in thousands)	Three months ended March 31, 2019	2018	Change	
Research and development	$9,476	$10,183	$(707)	-7%

Research and development expenses for the three months ended March 31, 2019 decreased by $0.7 million when compared to the three months ended March 31, 2018. During the three months ended March 31, 2019, our clinical trial and development costs decreased by $2.3 million as a result of our entry into the October 2018 exclusive license agreement with Precigen, Inc., or the License Agreement, pursuant to which we transferred all activities and rights related to our CD33-specific CAR$^+$ therapy under the Ares Trading Agreement to Precigen. This decrease was offset by an increase of approximately $1.4 million related to our ongoing gene therapy trials and $0.2 million in employee related and contracted outside service expenses during the three months ended March 31, 2019.

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 three months ended March 31, 2019, our clinical stage projects included a Phase 1 clinical trial with Ad-RTS-IL-12 plus veledimex in progressive glioblastoma; a Phase 1b/2 clinical trial with Ad-RTS-IL-12 plus veledimex in metastatic breast cancer; an investigator-led Phase 1 clinical trial infusing our 2nd generation CD19-specific CAR+ T cells in patients with advanced lymphoid malignancies; 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 $0.9 million for the three months ended March 31, 2019, and $7.7 million from the project's inception in June 2015 through March 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 $0.5 million for the three months ended March 31, 2019 and $5.2 million from the project's inception in December 2015 through March 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 $0.3 million for the three months ended March 31, 2019 and $1.8 million from the projects inception in October 2017 through March 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 to focus our resources on more promising products or indications. Completion of clinical trials may take several years or more, and the length of time generally varies substantially according to the type, complexity, novelty and intended use of a product. It is not unusual for preclinical and clinical development of each of these types of products to require the expenditure of substantial resources.

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

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

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

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

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

General and administrative expenses. General and administrative expenses during the three months ended March 31, 2019 and 2018 were as follows:

	Three months ended March 31,		Change	
($ in thousands)	**2019**	**2018**		
General and administrative	$ 4,145	$ 6,159	$(2,014)	-33%

General and administrative expenses for the three months ended March 31, 2019 decreased by $2.0 million as compared to three months ended March 31, 2018. The decrease for the three months ended March 31, 2019 was primarily due to a decrease of $2.2 million incurred during the three months ended March 31, 2018 relating to stock option modifications for a departing officer and director. The $2.2 million increase in stock compensation and employee related expenses was offset by a decrease of $0.2 million related to contracted outside services and facility expenses incurred during the three months ended March 31, 2019.

Other income (expense). Other income (expense) for the three months ended March 31, 2019 and 2018 were as follows:

	Three months ended March 31,		Change	
($ in thousands)	**2019**	**2018**		
Other income (expense), net	$ 187	$ 148	$ 39	26%
Change in derivative value	—	28	(28)	(100%)
Total	$ 187	$ 176		

During the three months ended March 31, 2019, we recorded $187 thousand in other income compared to $148 thousand earned during the three months ended March 31, 2018. The increase is due to interest earned on our cash accounts which was higher during the three months ended March 31, 2019. During the three months ended March 31, 2018, we recorded a gain on the change in fair value of the derivative liabilities of $28 thousand relating to our Series 1 preferred stock that was outstanding at the time. The Series 1 preferred stock was forfeited and returned to us in October 2018 and is no longer outstanding.

Liquidity and Capital Resources

As of March 31, 2019, we have approximately $51.5 million of cash and cash equivalents. Given our development plans, we anticipate our cash resources will be sufficient to fund our operations into the second quarter of 2020 and we currently have no committed sources of additional capital. The forecast of cash resources is forward-looking information that involves risks and uncertainties, and the actual amount of our expenses could vary materially and adversely as a result of a number of factors. We have based our estimates on assumptions that may prove to be wrong, and our expenses could prove to be significantly higher than we currently anticipate. Management does not know whether additional financing will be on terms favorable or acceptable to us when needed, if at all. If adequate additional funds are not available when required, or if we are unsuccessful in entering into partnership agreements for further development of our products, management may need to curtail development efforts.

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 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.

The following table summarizes our net decrease in cash, cash equivalents, and restricted cash for the three months ended March 31, 2019 and 2018:

($ in thousands)	Three months ended March 31, 2019	2018
Net cash provided by (used in):		
Operating activities	$(10,232)	$(18,957)
Investing activities	(10)	(150)
Financing activities	—	(731)
Net increase (decrease) in cash, cash equivalents, and restricted cash	$(10,242)	$(19,838)

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

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

Net cash used in operating activities for the three months ended March 31, 2019 was $10.2 million, as compared to net cash used in operating activities of $19.0 million for the three months ended March 31, 2018. The net cash used in operating activities for the three months ended March 31, 2019 was primarily due to our net loss of $13.2 million, offset by the change in prepaid and other expenses of $2.5 million, and change in accrued expenses and other liabilities of $1.9 million. The net cash used in operating activities for the three months ended March 31, 2018 was primarily due to our net loss of $16.0 million, offset by the change in prepaid expenses of $1.2 million, and change in accrued expenses and other liabilities of $3.1 million.

Net cash used in investing activities was $10 thousand for the three months ended March 31, 2019 compared to $150 thousand for the three months ended March 31, 2018. The change was due to a decrease during the three months ended March 31, 2019 in expenses related to the purchase of offsite equipment to support our programs at MD Anderson.

Net cash used in financing activities for the three months ended March 31, 2018 was $731 thousand and we did not use any cash in financing activities for the three months ended March 31, 2019. The $731 thousand used in financing activities is primarily attributable to restricted stock to cover taxes on stock exercises during the three months ended March 31, 2018.

Operating capital and capital expenditure requirements

We anticipate that losses will continue for the foreseeable future. At March 31, 2019, our accumulated deficit was approximately $579.6 million. Our actual cash requirements may vary materially from those planned because of a number of factors, including:

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

Working capital as of March 31, 2019 was $65.8 million, consisting of $74.1 million in current assets and $8.3 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 March 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	$ 1,803	$ 745	$ 1,058	$ —	$ —
CRADA	$ 6,875	2,500	4,375	—	—
Royalty and license fees	$ 2,000	100	200	200	1,500
Total	$10,678	$ 3,345	$ 3,758	$ 2,075	$ 1,500

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

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 for two years, committing an additional $5.0 million to this program. Our respective obligations for the CRADA is reflected above with $2.5 million in the column “Less than 1 Year”, and $4.4 million in the column “2-3 Years.”

On October 5, 2018, we entered into an exclusive license agreement with Precigen. Under the license agreement, we are obligated to pay Precigen an annual licensing fees of $100 thousand, which we expect to be paid through the term of the agreement.

Off-balance sheet arrangements

During the three months ended March 31, 2019 and 2018, we did not engage in any off-balance sheet arrangements.

Critical Accounting Policies and Estimates

In our Annual Report on Form 10-K for the fiscal year ended December 31, 2018, our most critical accounting policies and estimates upon which our financial status depends were identified as those relating to clinical trial expenses; collaboration agreements; fair value measurements for stock-based compensation; and income taxes. We reviewed our policies and determined that those policies remain our most critical accounting policies for the three months ended March 31, 2019. See Note 5, Summary of Significant Accounting Policies for a discussion of our adoption of ASC 606 relating to revenue recognition and Note 8 relating to our adoption of ASC 842, Leases.

Item 3. Quantitative and Qualitative Disclosures about Market Risk

Our exposure to market risk is limited to our cash. The goals of our investment policy are preservation of capital, fulfillment of liquidity needs and fiduciary control of cash. We also seek to maximize income from our investments without assuming significant risk. To achieve our goals, we maintain our cash in interest-bearing bank accounts in global banks, United States treasuries and other government-backed investments, which are subject to minimal interest rate risk.

Effect of Currency Exchange Rates and Exchange Rate Risk Management

We currently have no studies outside of the United States. Therefore, any currency fluctuations will not have a material impact on our financial position, results of operations or cash flows.

Item 4. Controls and Procedures

Our management, with the participation of our principal executive officer and principal financial officer, has evaluated the effectiveness of our disclosure controls and procedures (as defined in Rules 13a-15(e) or 15d-15(e) under the Securities Exchange Act of 1934, as amended, or the Exchange Act) as of the end of the period covered by this report. Based on such evaluation, our principal executive officer and principal financial officer have concluded that, as of the end of such period, our disclosure controls and procedures were effective in ensuring that information required to be disclosed by us in the reports that we file or submit under the Exchange Act is recorded, processed, summarized and reported, on a timely basis, and is accumulated and communicated to our management, including our principal executive officer and principal financial officer, as appropriate, to allow timely decisions regarding required disclosure.

There were no changes in our internal control over financial reporting during the quarter ended March 31, 2019 that have materially affected, or are reasonably likely to materially affect, our internal control over financial reporting. We implemented internal controls to ensure we adequately evaluated and accounted for our lease recognition under the new accounting standard. There were no significant changes to our internal control over financial reporting due to the adoption of the new standard.

Part II - Other Information

Item 1. 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 from time to time. 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 attention and resources and other factors.

As of March 31, 2019, based on information readily available, there are no matters that, in the opinion of management, are likely to result in a material adverse effect on our financial position, results of operations or cash flows.

Item 1A. Risk Factors

The following important factors could cause our actual business and financial results to differ materially from those contained in forward-looking statements made in this Quarterly Report on Form 10-Q or elsewhere by management from time to time. The risk factors in this Quarterly Report have been revised to incorporate changes to our risk factors from those included in our Annual Report on Form 10-K for the fiscal year ended December 31, 2018. The risk factors set forth below with an asterisk (*) next to the title are new risk factors or risk factors containing changes, which may be material, from the risk factors previously disclosed in Item 1A of our Annual Report on Form 10-K for the fiscal year ended December 31, 2018, as filed with the Securities and Exchange Commission.

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 three months ended March 31, 2019, we had a net loss of $13.4 million, and, as of March 31, 2019, we have incurred approximately $579.8 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.

We continue to seek additional financial resources to fund the further development of our product candidates. If we are unable to obtain sufficient additional capital, one or more of these programs could be placed on hold.

As of March 31, 2019, we have approximately $51.5 million of cash and cash equivalents. Given our current development plans, we anticipate cash resources will be sufficient to fund our operations into the second quarter of 2020, 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 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 may finance our cash needs through a combination of equity offerings, debt financings and license and collaboration agreements. As of March 31, 2019, we have incurred approximately $579.8 million of accumulated deficit and had approximately $51.5 million of cash and cash equivalents. Given our current development plans, we anticipate that our current cash resources will be sufficient to fund our operations into the second quarter of 2020. However, changes may occur that would consume our existing capital prior to then, including expansion of the scope of, and/or slower than expected progress of, our research and development efforts and changes in governmental regulation. Actual costs may ultimately vary from our current expectations, which could materially impact our use of capital and our forecast of the period of time through which our financial resources will be adequate to support our operations.

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

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

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

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 Precigen, 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;
- 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 Precigen 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, 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 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 biopharmaceutical industry, and the rapidly evolving market for developing genetically engineered T-cells in particular, is characterized by intense competition and rapid innovation. The business of genetically engineering T-cells faces 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 products include Juno Therapeutics Inc./Celgene Corporation, 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. 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 also compete with our product candidates.

Our TCR program faces competition from companies targeting shared antigens, including from Adaptimmune Therapeutics plc in collaboration with GlaxoSmithKline plc, Kite Pharma Inc./Gilead Sciences, Inc., Tmunity Therapeutics Inc, Medigene AG, Tactiva Therapeutics, LLC, Takara Bio, Inc., TC Biopharm Ltd., TCR2 Therapeutics Inc. and Zelluna Immunotherapy AS and others. Several companies, including Advaxis Inc./Amgen Inc., BioNTech AG, Neon Therapeutics Inc. and Gritstone Oncology, Inc., are pursuing vaccine platforms to target neoantigens for solid tumors.

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.

Several companies have product candidates in Phase 3 development for the treatment of glioblastoma, including Tocagen Inc., Vascular Biogenics Ltd., and DelMar Pharmaceuticals, Inc. Several companies and institutions have product candidates currently in Phase 2 clinical trials, including Abbvie Inc., Duke University and MedImmune LLC/AstraZeneca plc.

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

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

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

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

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

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

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

In addition, under our License Agreement, Precigen is obligated to provide certain transition services and transfer certain know-how to us. There is no guarantee that Precigen will perform these activities to our satisfaction, if at all. If Precigen 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 and Precigen, on acceptable terms, we may be unable to successfully develop and commercialize the affected potential products. We are generally also subject to all of the same risks with respect to protection of intellectual property that we license as we are for intellectual property that we own. If we or our licensors fail to adequately protect this intellectual property, our ability to commercialize potential products under our applicable licenses could suffer. There is a substantial amount of litigation involving patents and other intellectual property rights in the biotechnology and pharmaceutical industries, as well as administrative proceedings for challenging patents, including interference, derivation, and reexamination proceedings before the United States Patent and Trademark Office, or USPTO, or oppositions and other comparable proceedings in foreign jurisdictions. Recently, due to changes in U.S. law referred to as patent reform, new procedures including inter partes review and post-grant review have been implemented, which adds uncertainty to the possibility of challenge to our or our licensors' patents in the future.

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

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

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

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

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 will incur additional expenses in connection with our License Agreement with Precigen.

We expect our overall research and development expenses will continue to increase as we move forward with our research and development efforts under the License Agreement with Precigen. Although all human clinical trials are expensive and difficult to design and implement, we believe that due to complexity, costs associated with clinical trials for immuno-oncology products are greater than the corresponding costs associated with clinical trials for small-molecule candidates. We now control many of the activities previously performed by Precigen on our behalf, including the manufacturing of our products in development. As a result, we expect to add increased headcount to support these efforts, among other expenses, which would add to our research and development expenses going forward.

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

We may incur additional expenses in connection with our License Agreement with MD Anderson.

Pursuant to the MD Anderson License with MD Anderson, we, together with Precigen, obtained an exclusive, worldwide license to certain technologies owned and licensed by MD Anderson including technologies relating to novel CAR+ T cell and TCR cell therapies arising from the laboratory of Laurence Cooper, M.D., Ph.D., who was then at MD Anderson, as well as either co-exclusive or non-exclusive licenses under certain related technologies. Pursuant to the MD Anderson License, we, together with Precigen, entered into a research and development agreement with MD Anderson pursuant to which we agreed to provide funding for certain research and development activities of MD Anderson for a period of three years from the date of the MD Anderson License, in an amount between $15.0 and $20.0 million per year. We made the final payment in January 2018.

Although our forecasts for expenses and the sufficiency of our capital resources takes into account the funds available at MD Anderson, our actual cash requirements may vary materially from our current expectations for a number of other factors that may include, but are not limited to, changes in the focus and direction of our development programs, competitive and technical advances, costs associated with the development of our product candidates and costs of filing, prosecuting, defending and enforcing our intellectual property rights. If we exhaust the funds available at MD Anderson more quickly than anticipated, regardless of the reason, and we are unable to obtain additional financing on terms acceptable to us or at all, we will be unable to proceed with development of some or all of our product candidates on expected timelines and will be forced to prioritize among them.

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

Under the MD Anderson License, we, together with Precigen, received an exclusive, worldwide license to certain technologies owned and licensed by MD Anderson including technologies relating to novel CAR+ T cell and TCR cell therapies arising from the laboratory of Laurence Cooper, M.D., Ph.D., who was then at MD Anderson, as well as either co-exclusive or non-exclusive licenses under certain related technologies. When combined with Precigen's technology suite and Ziopharm's clinically tested RTS® interleukin 12 modules, the resulting proprietary methods and technologies may help realize the promise of genetically modified CAR+ T 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 Precigen shall then have a fully-paid up, royalty free, perpetual, irrevocable and sublicensable license to use the licensed intellectual property thereunder.

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

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

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

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

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

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

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. Any future growth will place a significant strain on our management and on our administrative, operational, and financial resources. Therefore, our future financial performance and our ability to commercialize our product candidates and to compete effectively will depend, in part, on our ability to manage any future growth effectively. To manage this growth, we must expand our facilities, augment our operational, financial and management systems, and hire and train additional qualified personnel. If we are unable to manage our growth effectively, our business may be harmed.

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

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

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

We are highly dependent on Dr. Laurence J.N. Cooper, our Chief Executive Officer; Dr. David Mauney, our President; and our principal scientific, regulatory, and medical advisors. Each of Drs. Cooper and 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 Drs. Cooper or Mauney, or any of our other key personnel, could result in delays in product development, loss of customers and sales, and diversion of management resources, which could adversely affect our operating results. We do not carry "key person" life insurance policies on any of our officers or key employees.

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

We will need to hire additional qualified personnel with expertise in preclinical and clinical research and testing, government regulation, formulation and manufacturing, and eventually, sales and marketing. 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. 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.

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

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

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

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

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

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

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

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

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

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

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

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

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

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

Furthermore, there have been and continue to be a number of initiatives at the federal and state level that seek to reduce healthcare costs. Most significantly, in March 2010, President Obama signed into law the Patient Protection and Affordable 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 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; 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.

Some of the provisions of the ACA have yet to be implemented, and there have been legal and political challenges to certain aspects of the ACA. Since January 2017, President Trump has signed two executive orders and other directives designed to delay, circumvent, or loosen certain requirements mandated by the ACA. Concurrently, Congress has considered legislation that would repeal or repeal and replace all or part of the ACA. While Congress has not passed repeal legislation, two bills affecting the implementation of certain taxes under the ACA have been signed into law. 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. On January 22, 2018, President Trump signed a continuing resolution on appropriations for fiscal year 2018 that delayed the implementation of certain ACA-mandated fees, including the so-called "Cadillac" tax on certain high cost employer-sponsored insurance plans and the annual fee imposed on certain health insurance providers based on market share. 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 July 2018, CMS published a 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 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. While the Texas U.S. District Court Judge, as well as the Trump administration and CMS, have stated that the ruling will have no immediate effect pending appeal of the decision, it is unclear how this decision, 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 legislation 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 2027 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 2019 contains further drug price control measures that could be enacted during the 2019 budget process or in other future legislation, including, for example, measures to permit Medicare Part D plans to negotiate the price of certain drugs under Medicare Part B, to allow some states to negotiate drug prices under Medicaid, and to eliminate cost sharing for generic drugs for low-income patients. Further, the Trump administration 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 already started the process of soliciting feedback on some of these measures and, at the same, is immediately implementing others under its existing authority. For example, in September 2018, CMS announced that it will allow Medicare Advantage plans the option to use step therapy for Part B drugs beginning January 1, 2019, and in October 2018, CMS proposed a new rule that would require direct-to-consumer television advertisements of prescription drugs and biological products, for which payment is available through or under Medicare or Medicaid, to include in the advertisement the Wholesale Acquisition Cost, or list price, of that drug or biological product. On January 31, 2019, the U.S. Department of Health and Human Services, Office of Inspector General, proposed modifications to the federal Anti-Kickback Statute discount safe harbor for the purpose of reducing the cost of drug products to consumers which, among other things, if finalized, will affect discounts paid by manufacturers to Medicare Part D plans, Medicaid managed care organizations and pharmacy benefit managers working with these organizations. While some of these, and other proposed, measures may require additional 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. 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 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.

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 our trade secrets, to prevent third parties from infringing on our proprietary rights, and to operate without infringing the proprietary rights of third parties.

To date, we have exclusive rights in the field of cancer treatment to certain U.S. and foreign intellectual property with respect to the Precigen 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 Precigen, Precigen 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. Precigen 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 Precigen has agreed to consider in good faith and consult with us regarding any comments we may have regarding these patents and patent applications, we cannot guarantee that our comments will be solicited or followed. Under the MD Anderson License, future filings and applications require the agreement of each of MD Anderson, Precigen and us, and MD Anderson has the right to control the preparation and filing of additional patent applications unless the parties agree that we or Precigen may prosecute the application directly. Although under the agreement MD Anderson has agreed to review and incorporate any reasonable comments that we or Precigen may have regarding these patents and patent applications, we cannot guarantee that our comments will be solicited or followed. Without direct control of the in-licensed patents and patent applications, we are dependent on Precigen or MD Anderson, as applicable, to keep us advised of prosecution, particularly in foreign jurisdictions where prosecution information may not be publicly available. We anticipate that we, Precigen and MD Anderson will file additional patent applications both in the United States and in other countries. However, we cannot predict or guarantee:

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

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

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

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

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

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

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

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

Our success also depends upon the skills, knowledge, and experience of our scientific and technical personnel, our consultants and advisors, as well as our licensors and contractors. To help protect our proprietary know-how and our inventions for which patents may be unobtainable or difficult to obtain, and to maintain our competitive position, we rely on trade secret protection and confidentiality agreements. To this end, it is our general policy to require our employees, consultants, advisors, and contractors to enter into agreements that prohibit the disclosure of confidential information and, where applicable, require disclosure and assignment to us of the ideas, developments, discoveries, and inventions important to our business. These agreements may not provide adequate protection for our trade secrets, know-how or other proprietary information in the event of any unauthorized use or disclosure or the lawful development by others of such information. Moreover, we may not be able to obtain adequate remedies for any breaches of these agreements. Our trade secrets may also be obtained by third parties by other means, such as breaches of our physical or computer security systems. Enforcing a claim that a party illegally disclosed or misappropriated a trade secret is difficult, expensive and time-consuming, and the outcome is unpredictable. In addition, some courts inside and outside the United States are less willing or unwilling to protect trade secrets. If any of our trade secrets were to be lawfully obtained or independently developed by a competitor, we would have no right to prevent them, or those to whom they communicate it, from using that technology or information to compete with us. If any of our trade secrets, know-how or other proprietary information is disclosed, the value of our trade secrets, know-how and other proprietary rights would be significantly impaired and our business and competitive position would suffer.

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

In order to protect or enforce patent rights, we 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. In addition, there may be patents and patent applications in the field of which we are not aware. The technology we license from Precigen and MD Anderson 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 upon patent claims even if we do not believe such claims to be valid and enforceable.

If a claim for patent infringement is asserted, there can be no assurance that the resolution of the claim would permit us to continue marketing the relevant product on commercially reasonable terms, if at all. We may not have sufficient resources to bring these actions to a successful conclusion. If we do not successfully defend any infringement actions to which we become a party or are unable to have infringed patents declared invalid or unenforceable, we may have to pay substantial monetary damages, which can be tripled if the infringement is deemed willful or be required to discontinue or significantly delay commercialization and development of the affected products.

Any legal action against us or our collaborators claiming damages and seeking to enjoin developmental or marketing activities relating to affected products could, in addition to subjecting us to potential liability for damages, require us or our collaborators to obtain licenses to continue to develop, manufacture, or market the affected products. Such a license may not be available to us on commercially reasonable terms, if at all.

An adverse determination in a proceeding involving our owned or licensed intellectual property may allow entry of generic substitutes for our products.

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

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

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

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

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

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

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

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

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

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

OTHER RISKS RELATED TO OUR COMPANY

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

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

- Price and volume fluctuations in the overall stock market;
- Market conditions or trends in our industry or the economy as a whole;
- Laboratory or clinical trial results;
- Public concern as to the safety of drugs developed by us or others;
- Changes in operating results and performance and stock market valuations of other biopharmaceutical companies generally, or those that develop and commercialize cancer drugs in particular;
- The financial or operational projections we may provide to the public, any changes in these projections or our failure to meet these projections;
- Comments by securities analysts or changes in financial estimates or ratings by any securities analysts who follow our common stock, our failure to meet these estimates or failure of those analysts to initiate or maintain coverage of our common stock;
- The public's response to press releases or other public announcements by us or third parties, including our filings with the 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 our executive officers, directors and significant stockholders;
- Announcements of mergers or acquisition transactions;
- Our inclusion or deletion from certain stock indices;
- Developments in patent or other proprietary rights;
- Changes in reimbursement policies;
- Announcements of medical innovations or new products by our competitors;
- Announcements of changes in our senior management;
- Other events or factors, including those resulting from war, incidents of terrorism, natural disasters or responses to these events; and
- Changes in accounting principles.

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

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

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

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 March 31, 2019, our executive officers, directors and holders of five percent or more of our outstanding common stock, beneficially owned, in the aggregate, 30.2% of our outstanding common stock. These stockholders may have interests that conflict with our other stockholders and, if acting together, have the ability to influence the outcome of matters submitted to our stockholders for approval, including the election and removal of directors and any merger, consolidation or sale of all or substantially all of our assets. Accordingly, this concentration of ownership may harm the market price of our common stock by:

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

The 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 2. Unregistered Sale of Equity Securities and Use of Proceeds

Unregistered Sale of Equity Securities and Use of Proceeds

None.

Issuer Purchases of Equity Securities

The following table provides information about our purchases of common stock for the three months ended March 31, 2019:

Period	Total Number of Shares Purchased	Average Price Paid Per Share
January 1 to January 31, 2019	165,178 (1)	$ 2.24
February 1 to February 28, 2019	—	$ —
March 1 to March 31, 2019	—	$ —
Total	165,178	

(1) Represents the total number of shares of our common stock delivered to us by certain employees to satisfy the statutory tax withholding obligations owed in connection with stock awards granted to such employees under the Ziopharm Oncology, Inc. 2012 Equity Incentive Plan, as amended to date.

Item 3. Defaults upon Senior Securities

Not applicable.

Item 4. Mine Safety Disclosures

Not applicable.

Item 5. Other Information

None.

Item 6. Exhibits

The exhibits listed in the Exhibit Index immediately preceding such exhibits are filed as part of this report and such Exhibit Index is incorporated herein by reference.

Exhibit Number	Description
3.1	Amended and Restated Certificate of Incorporation of the Registrant, 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	Bylaws of the Registrant, as amended to date (incorporated by reference to Exhibit 3.3 to the Registrant's Current Report on Form 8-K, SEC File No. 000-32353, filed September 19, 2005).
3.3	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).
31.1*	Certification pursuant to Section 302 of the Sarbanes-Oxley Act of 2002
31.2*	Certification pursuant to Section 302 of the Sarbanes-Oxley Act of 2002
32.1**	Certifications pursuant to 18 U.S.C. Section 1350
101.INS*	XBRL Instance Document
101.SCH*	XBRL Taxonomy Extension Schema Document
101.CAL*	XBRL Taxonomy Extension Calculation Linkbase Document
101.DEF*	XBRL Taxonomy Definition Linkbase Document
101.LAB*	XBRL Taxonomy Extension Label Linkbase Document
101.PRE*	XBRL Taxonomy Extension Presentation Linkbase Document

* Filed herewith.

** This certification is deemed not filed for purposes of Section 18 of the Securities Exchange Act of 1934, as amended, or otherwise subject to the liability of that section, nor shall it be deemed incorporated by reference into any filing under the Securities Act of 1933, as amended, or the Securities Exchange Act of 1934, as amended.

SIGNATURES

Pursuant to the requirements 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.

By: /s/ Laurence J.N. Cooper
Laurence J.N. Cooper, M.D., Ph.D.
Chief Executive Officer
(Principal Executive Officer)
Dated: May 8, 2019

By: /s/ Kevin G. Lafond
Kevin G. Lafond
Senior Vice President Finance, Chief Accounting Officer and Treasurer
(Principal Financial Officer and Principal Accounting Officer))
Dated: May 8, 2019

EXHIBIT 31.1

CERTIFICATION

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

1. I have reviewed this quarterly report on Form 10-Q 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: May 8, 2019

/s/ Laurence J.N. Cooper

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

EXHIBIT 31.2

CERTIFICATION

I, Kevin G. Lafond, certify that:

1. I have reviewed this quarterly report on Form 10-Q 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: May 8, 2019

/s/ Kevin G. Lafond

Kevin G. Lafond
Senior Vice President Finance, Chief Accounting Officer and Treasurer
(Principal Financial Officer and Principal Accounting Officer)

EXHIBIT 32.1

CERTIFICATION

In connection with the Quarterly Report on Form 10-Q of ZIOPHARM Oncology, Inc. (the "Company") for the quarter ended March 31, 2019, as filed with the Securities and Exchange Commission on the date hereof (the "Report"), we Laurence J.N. Cooper, the Principal Executive Officer of the Company and Kevin G. Lafond, the Principal Financial and Accounting Officer of the Company, hereby certify, pursuant to 18 U.S.C. 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002, that, to our knowledge:

(1) the Report fully complies with the requirements of Section 13(a) or 15(d), as applicable, of the Securities Exchange Act of 1934, as amended, and

(2) the information in the Report fairly presents, in all material respects, the financial condition and results of operations of the Company.

Dated: May 8, 2019

/s/ Laurence J.N. Cooper

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

Dated: May 8, 2019

/s/ Kevin G. Lafond

Kevin G. Lafond
Senior Vice President Finance, Chief Accounting Officer and Treasurer
(Principal Financial Officer and Principal Accounting Officer)