

ZIOPHARM ONCOLOGY INC  
Form 10-Q  
May 10, 2018  
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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, 2018**

**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)**

<b>Delaware</b> <b>(State or other jurisdiction of</b>	<b>84-1475642</b> <b>(I.R.S. Employer</b>
<b>incorporation or organization)</b>	<b>Identification No.)</b>
<b>One First Avenue, Parris Building 34, Navy Yard Plaza</b>	

**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:

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Indicate by check mark whether the registrant has submitted electronically and posted on its corporate Web site, if any, every Interactive Data File required to be submitted and posted pursuant to Rule 405 of Regulation S-T during the preceding 12 months (or for such shorter period that the registrant was required to submit and post such files).

Yes:        No:

Indicate by check mark 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                    (Do not check if a smaller reporting company)

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:

The number of shares of the registrant's common stock, \$0.001 par value, outstanding as of April 24, 2018, was 142,398,936 shares.

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**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. I made in particular to forward-looking statements regarding:

our ability to raise substantial additional capital to fund our planned operations and to continue as a going concern;

our estimates regarding expenses, use of cash, timing of future cash needs and capital requirements;

the development of our product candidates, including statements regarding the timing of initiation, completion and the outcome of clinical studies or trials and related preparatory work and the period during which the results of the trials will become available;

our ability to advance our product candidates through various stages of development, especially through pivotal safety and efficacy trials;

the risk that final trial data may not support interim analysis of the viability of our product candidates;

our expectation regarding the safety and efficacy of our product candidates, the progress and timing of our research and development programs;

the timing, scope or likelihood of regulatory filings and approvals from the U.S. Food and Drug Administration or equivalent foreign regulatory agencies for our product candidates and for which indications;

our ability to license additional intellectual property relating to our product candidates from third parties and to comply with our existing license agreements;

our ability to achieve the results contemplated by our collaboration agreements and the benefits to be derived from relationships with collaborators;

developments and projections relating to competition from other pharmaceutical and biotechnology companies or our industry;

our estimates regarding the potential market opportunity for our product candidates;

the anticipated rate and degree of market acceptance of our product candidates for any indication if approved;

the anticipated amount, timing and accounting of 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; and

the impact of government laws and regulations in the United States and foreign countries.

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.

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**ZIOPHARM Oncology, Inc.**

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**Table of Contents****Part I - Financial Information****Item 1. Financial Statements****ZIOPHARM Oncology, Inc.****BALANCE SHEETS****(unaudited)****(in thousands, except share and per share data)**

	<b>March 31, 2018</b>	<b>December 31, 2017</b>
<b>ASSETS</b>		
Current assets:		
Cash and cash equivalents	\$ 51,108	\$ 70,946
Receivables	18	19
Prepaid expenses and other current assets	20,989	19,818
Total current assets	72,115	90,783
Property and equipment, net	1,244	1,211
Deposits	128	128
Other non-current assets	13,974	13,484
Total assets	\$ 87,461	\$ 105,606
<b>LIABILITIES, PREFERRED STOCK AND STOCKHOLDERS DEFICIT</b>		
Current liabilities:		
Accounts payable	\$ 606	\$ 4,417
Accrued expenses	8,878	9,909
Contract liability - current portion	476	6,389
Deferred rent - current portion	102	141
Total current liabilities	10,062	20,856
Contract liability, net of current portion	49,037	35,139
Deferred rent, net of current portion	3	1
Derivative liabilities	2,469	2,424
Total liabilities	61,571	58,420
Commitments and contingencies (Note 5)		
Preferred stock, \$0.001 par value, 30,000,000 shares authorized		
Series 1 preferred stock, \$1,200 stated value; 250,000 designated; 123,268 and 119,644 shares issued and outstanding at March 31, 2018 and December 31, 2017, respectively; liquidation value of \$147.9 million and \$143.6 million at March 31,	149,039	143,992

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2018 and December 31, 2017, respectively

Stockholders' deficit:

Common stock, \$0.001 par value; 250,000,000 shares authorized; 142,398,936 and 142,658,037 shares issued and outstanding at March 31, 2018 and December 31, 2017, respectively

	142	143
Additional paid-in capital	613,302	615,493
Accumulated deficit	(736,593)	(712,442)
<b>Total stockholders' deficit</b>	<b>(123,149)</b>	<b>(96,806)</b>
<b>Total liabilities and stockholders' deficit</b>	<b>\$ 87,461</b>	<b>\$ 105,606</b>

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

Table of Contents**ZIOPHARM Oncology, Inc.****STATEMENTS OF OPERATIONS****(unaudited)****(in thousands, except share and per share data)**

	<b>For the Three Months Ended March 31,</b>	
	<b>2018</b>	<b>2017</b>
Collaboration revenue	\$ 146	\$ 1,597
Operating expenses:		
Research and development	10,183	11,967
General and administrative	6,159	3,595
Total operating expenses	16,342	15,562
Loss from operations	(16,196)	(13,965)
Other income (expense), net	148	38
Change in fair value of derivative liabilities	28	(1,560)
Net loss	\$ (16,020)	\$ (15,487)
Preferred stock dividends	\$ (5,120)	\$ (4,171)
Net loss applicable to common stockholders	\$ (21,140)	\$ (19,658)
Basic and diluted net loss per share	\$ (0.15)	\$ (0.15)
Weighted average common shares outstanding used to compute basic and diluted net loss per share	140,853,120	130,696,400

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



Table of Contents**ZIOPHARM Oncology, Inc.****STATEMENTS OF CHANGES IN PREFERRED STOCK AND STOCKHOLDERS' DEFICIT****For the Three Months Ended March 31, 2018****(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)				
Repurchase 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)

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

Table of Contents**ZIOPHARM Oncology, Inc.****STATEMENTS OF CASH FLOWS****(unaudited)****(in thousands)**

	<b>For the Three Months Ended March 31,</b>	
	<b>2018</b>	<b>2017</b>
Cash flows from operating activities:		
Net loss	\$ (16,020)	\$ (15,487)
Adjustments to reconcile net loss to net cash used in operating activities:		
Depreciation and amortization	117	79
Stock-based compensation	3,659	2,024
Change in fair value of derivative liabilities	(28)	1,560
(Increase) decrease in:		
Receivables	1	(46)
Prepaid expenses and other current assets	(1,172)	(2,426)
Other noncurrent assets	(490)	
Increase (decrease) in:		
Accounts payable	(3,811)	70
Accrued expenses	(1,030)	1,577
Contract liabilities	(146)	(1,597)
Deferred rent	(37)	(31)
Net cash used in operating activities	(18,957)	(14,277)
Cash flows from investing activities:		
Purchases of property and equipment	(150)	(358)
Net cash used in investing activities	(150)	(358)
Cash flows from financing activities:		
Proceeds from exercise of stock options		29
Repurchase of restricted common stock	(731)	
Net cash provided by (used in) financing activities	(731)	29
Net decrease in cash, cash equivalents, and restricted cash	(19,838)	(14,606)
Cash, cash equivalents, and restricted cash, beginning of period	71,335	81,441
Cash equivalents, and restricted cash, end of period	\$ 51,497	\$ 66,835

**Supplementary disclosure of cash flow information:**

Cash paid for interest	\$	\$
Cash paid for income taxes	\$	\$

**Supplementary disclosure of noncash investing and financing activities:**

Payment of Series 1 preferred stock dividends in preferred stock	\$ 5,120	\$ 4,171
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The accompanying notes are an integral part of the unaudited interim financial statements.

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**ZIOPHARM Oncology, Inc.**

**NOTES TO FINANCIAL STATEMENTS**

**(unaudited)**

**1. Business**

*Overview*

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

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

The Company has operated at a loss since its inception in 2003 and has minimal revenues. The Company anticipates that losses will continue for the foreseeable future. At March 31, 2018, the Company's accumulated deficit was approximately \$736.6 million. Given its current development plans, the Company anticipates cash resources will be sufficient to fund operations into the second quarter of 2019. The Company's ability to continue operations after its current cash resources are exhausted depends on its ability to obtain additional financing or to achieve profitable operations, as to which no assurances can be given. Cash requirements may vary materially from those now planned because of changes in the Company's focus and direction of its research and development programs, competitive and technical advances, patent developments, regulatory changes or other developments. Additional financing will be required to continue operations after the Company exhausts its current cash resources and to continue its long-term plans for clinical trials and new product development.

As of March 31, 2018, the Company had approximately \$51.1 million of cash and cash equivalents. Given its development plans, the Company anticipates cash resources will be sufficient to fund its operations into the second quarter of 2019 and the Company has no committed sources of additional capital. The forecast of cash resources is forward-looking information that involves risks and uncertainties, and the actual amount of the Company's expenses could vary materially and adversely as a result of a number of factors. The Company has based its estimates on assumptions that may prove to be wrong, and the Company's expenses could prove to be significantly higher than currently anticipated. Management does not know whether additional financing will be available on terms favorable or acceptable to the Company when needed, if at all. If adequate additional funds are not available when required, or if the Company is unsuccessful in entering into partnership agreements for further development of its products, management may need to curtail development efforts. Based on the forecast, management determined that there is substantial doubt regarding our ability to continue as a going concern.

*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.

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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, 2017, included in the Company's Annual Report on Form 10-K for the fiscal year ended December 31, 2017 filed with the SEC on March 1, 2018, 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, 2018 are not necessarily indicative of the results to be expected for the full fiscal year.

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**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. During this period, the Company did not have any material subsequent events that impacted its financial statements or disclosures.

**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.

***Revenue Recognition***

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

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**Table of Contents****ZIOPHARM Oncology, Inc.****NOTES TO FINANCIAL STATEMENTS (unaudited)****2. Summary of Significant Accounting Policies (continued)**

ASC 606 clarifies the principles for recognizing revenue and develops a common revenue standard for U.S. GAAP providing a more robust framework for addressing revenue issues, improves comparability of revenue recognition practices across entities, industries, jurisdictions, and capital markets, provides more useful information to users of financial statements through improved disclosure requirements, and simplifies the preparation of financial statements by reducing the number of requirements to which an entity must refer. This update is effective for annual periods beginning after December 15, 2017, including interim periods within that reporting period. The Company adopted this standard using the modified retrospective approach on January 1, 2018. The Company has 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 is related to the Company's Ares Trading License and Collaboration Agreement (Note 6), which is the Company's sole contract outstanding at January 1, 2018 (Note 5). The Company has a full valuation allowance so there will be no effect on incomes taxes as a result of this adoption.

***New Accounting Pronouncements***

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

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



Table of Contents**ZIOPHARM Oncology, Inc.****NOTES TO FINANCIAL STATEMENTS (unaudited)****2. Summary of Significant Accounting Policies (continued)**

In November 2016, the FASB issued ASU 2016-18, *Statement of Cash Flows: Restricted Cash ( 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.

<i>in thousands</i>	March 31,	
	2018	2017
Cash and cash equivalents	\$ 51,108	\$ 66,447
Restricted cash included in prepaid expenses and other current assets	389	
Restricted cash included in other non-current assets		388
Total cash, cash equivalents, and restricted cash shown in the statement of cash flows	\$ 51,497	\$ 66,835

Table of Contents**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, 2018 and December 31, 2017 were as follows:

*(\$ in thousands)*

Description	Balance as of March 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)
<b>Assets:</b>				
Cash equivalents	\$ 47,325	\$ 47,325	\$	\$
<b>Liabilities:</b>				
Derivative liabilities	\$ (2,469)	\$	\$	\$ (2,469)



Table of Contents**ZIOPHARM Oncology, Inc.****NOTES TO FINANCIAL STATEMENTS (unaudited)****3. Fair Value Measurements (continued)**

(\$ in thousands)

Description	Balance as of December 31, 2017	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)
<b>Assets:</b>				
Cash equivalents	\$ 66,156	\$ 66,156	\$	\$
<b>Liabilities:</b>				
Derivative liabilities	\$ (2,424)	\$	\$	\$ (2,424)

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

As discussed further in Notes 5 and 8, the Company issued Intrexon Corporation, or Intrexon, 100,000 shares of the Company's Series 1 preferred stock, a class of preferred stock authorized by the Company's board of directors, in consideration of the parties entering into a Third Amendment to Exclusive Channel Partner Agreement, or the 2016 ECP Amendment, amending their existing Exclusive Channel Partner Agreement, effective January 6, 2011 and as amended to date, which the Company refers to as the Channel Agreement, and an Amendment to Exclusive Channel Collaboration Agreement, or the 2016 GvHD Amendment, amending their existing Exclusive Channel Collaboration Agreement, effective September 28, 2015, which the Company refers to as the GvHD Agreement.

**Table of Contents****ZIOPHARM Oncology, Inc.****NOTES TO FINANCIAL STATEMENTS (unaudited)****3. Fair Value Measurements (continued)**

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

The Company's Level 3 financial liabilities consist of a conversion option and a redemption feature associated with the Company's Series 1 preferred stock issued to Intrexon that has been bifurcated from the Series 1 preferred stock and are accounted for as derivative liabilities at fair value. The preferred stock derivative liabilities were valued using a probability-weighted approach and a Monte Carlo simulation model. The fair value of the embedded derivatives was estimated using the with and without method where the preferred stock was first valued with all of its features (with scenario) and then without derivatives subject to the valuation analysis (without scenario). The fair value of the derivatives was then estimated as the difference between the fair value of the preferred stock in the with scenario and the preferred stock in the without scenario. See Note 6 for additional disclosures on the 2016 ECP Amendment and 2016 GvHD Amendments and Note 9 for additional disclosure on the rights and preferences of the Series 1 preferred stock and valuation methodology.

**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, 2018 and 2017 consisted of the following:

	March 31,	
	2018	2017
Stock options	3,822,968	3,539,669
Unvested restricted stock	1,532,201	1,680,492
Preferred stock	35,152,089	20,507,501
	40,507,258	25,727,662

The Series 1 preferred stock automatically converts into shares of common stock upon the date the first approval in the United States of (i) a Ziopharm Product, as defined in and developed under the Exclusive Channel Partner Agreement dated as of January 6, 2011 and as amended from time to time, by and between the Company and Intrexon,

or (ii) a Product, as defined in and developed under the Exclusive Channel Collaboration Agreement dated September 28, 2015 and as amended from time to time, by and between the Company and Intrexon, or (iii) a Product as defined in and developed under the License and Collaboration Agreement dated March 27, 2015 and as amended from time to time, by and among Intrexon, Ares Trading, S.A. and the Company, is publicly announced. Assuming a conversion event date of March 31, 2018, the Series 1 preferred stock would convert into 35,152,089 shares of common stock using the greater of (i) the volume weighted average closing price of the Company's Common Stock as reported by the Nasdaq Stock Market, LLC over the previous 20 trading days ending on the conversion event date or (ii) \$1.00 per share. See Note 6 and Note 9 for additional disclosure regarding the 2016 ECP Amendment and 2016 GvHD Amendment, valuation methodology and significant assumptions.

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**ZIOPHARM Oncology, Inc.**

**NOTES TO FINANCIAL STATEMENTS (unaudited)**

**5. Revenue Recognition**

The Company adopted Accounting Standards Codification ( ASC ), Topic 606, *Revenue from Contracts with Customers* ( Topic 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 is related to the Company's Ares Trading License and Collaboration Agreement (Note 6), which is 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 recognizes revenue in accordance with ASC 606. The core principle of ASC 606 is that an entity should recognize revenue to depict the transfer of promised goods and/or services to customers in an amount that reflects the consideration to which the entity expects to be entitled in exchange for those goods and/or services. To determine the appropriate amount of revenue to be recognized for arrangements that the Company determines are within the scope of ASC 606, the Company performs the following steps: (i) Identify the contract(s) with the customer, (ii) Identify the performance obligations in the contract, (iii) Determine the transaction price, (iv) Allocate the transaction price to the performance obligations in the contract and (v) Recognize revenue when (or as) each performance obligation is satisfied.

The Company will recognize 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.



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**ZIOPHARM Oncology, Inc.**

**NOTES TO FINANCIAL STATEMENTS (unaudited)**

**5. Revenue Recognition (continued)**

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 contract 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 judgement to determine the standalone selling price for each performance obligation identified in each contract. The key assumptions utilized in determining the standalone selling price for each performance obligation may include forecasted revenues, development timelines, estimated research and development costs, discount rates, likelihood of exercise and probabilities of technical and regulatory success.

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

As it relates to the Ares Trading License and Collaboration 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 describe above, the transaction price of \$57.5 million was allocated to the performance obligations based on their relative standalone selling prices.

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 or for the period ended March 31, 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.

The first performance obligation includes three initial targets, two of which were substantially complete at March 31, 2018. Revenue recognized to date relates to these two targets. The remaining contract liability related to these two targets is \$476 thousand and is expected to be recognized within the next twelve months. The third target included in the first performance obligation has not yet been identified; revenue recognition will be deferred until the time that the work on the project begins. No revenue has been recognized related to the material rights as the option for the material right has not yet been exercised.

Table of Contents**ZIOPHARM Oncology, Inc.****NOTES TO FINANCIAL STATEMENTS (unaudited)****5. Revenue Recognition (continued)**

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

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

The amount by which each financial statement line item is affected in the current reporting period by Topic 606 as compared with the guidance that was in effect prior to adoption is disclosed below.

Description	Impact of Topic 606 Adoption on the Balance Sheet as of March 31, 2018		
	As reported under Topic 606	Adjustments	Balances without adoption of Topic 606
Contract liability, current portion	\$ 476	\$ (5,913)	\$ 6,389
Contract liability, net of current portion	\$ 49,037	\$ 15,495	\$ 33,542
Accumulated deficit	\$ (736,593)	\$ 9,582	\$ (746,175)

Table of Contents**ZIOPHARM Oncology, Inc.****NOTES TO FINANCIAL STATEMENTS (unaudited)****5. Revenue Recognition (continued)**

Description	Impact of Topic 606 Adoption on the Statement of Operations for the Three Months Ended March 31, 2018		
	As reported under Topic 606	Adjustments	Balances without adoption of Topic 606
Collaboration revenue	\$ 146	\$ (1,451)	\$ 1,597
Net loss applicable to common shareholders	\$ (21,140)	\$ (1,451)	\$ (19,689)
Basic and diluted net loss per share	\$ (0.15)	\$ (0.01)	\$ (0.14)

Description	Impact of Topic 606 Adoption on the Statement of Cash Flows for the Three Months Ended March 31, 2018		
	As reported under Topic 606	Adjustments	Balances without adoption of Topic 606
Net loss applicable to common shareholders	\$ (21,140)	\$ (1,451)	\$ (19,689)
Changes in contract liability	\$ (146)	\$ 1,451	\$ (1,597)

The most significant change above relates to the Company's collaboration revenue, which to date has been exclusively generated from its collaboration arrangement with Ares Trading S.A. and Precigen, previously Intrexon (Note 6). Under ASC 605, the Company accounted for the up-front payment over the estimated period of performance of the research and development services which were estimated to be 9 years. In connection with the adoption of Topic 606, the Company uses a proportional performance model which depicts the Company's performance in transferring control to the customer. The Company concluded that it will utilize a cost-based input method to measure progress because such method best reflects the satisfaction of the performance obligation. In applying the cost-based input method of revenue recognition, the Company uses actual costs incurred relative to the budgeted costs to complete the research programs. These costs consist primarily of internal full-time equivalent effort and third-party contract costs. Revenue is recognized based on actual costs incurred as a percentage of total budgeted costs. As a result, although the performance obligations noted above and identified under Topic 606 were generally consistent with the units of account identified under ASC 605, the timing of the allocation of the transaction price to the identified performance obligations under Topic 606 differed from the allocations of consideration under ASC 605. Accordingly, the transaction price ultimately allocated to each performance obligation under Topic 606 differed from the amounts allocated under ASC 605.

The Company has a full valuation allowance so there was no effect on incomes taxes as a result of this change.



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**ZIOPHARM Oncology, Inc.**

**NOTES TO FINANCIAL STATEMENTS (unaudited)**

**6. Commitments and Contingencies**

**Operating Leases**

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

On October 17, 2013, the Company entered into a sublease agreement to lease all of its New York office space to a subtenant. The Company remains primarily liable to pay rent on the original lease. The Company recorded a loss on the sublease in the amount of \$729 thousand for the year ended December 31, 2013, representing the remaining contractual obligation of \$2.3 million, less \$1.6 million in payments from its subtenant. Total sublease loss was approximately \$31 thousand for each of the three month periods ending March 31, 2018 and 2017. The Company continues to maintain the \$388 thousand letter of credit in respect of the New York office space, which is recorded in other current assets on the balance sheets.

Prior to December 31, 2012, the Company entered into separate operating lease agreements for various spaces in a building in Boston, MA. In June 2012, the Company re-negotiated a master lease for the Company's Boston office space to incorporate all three lease agreements under the same master agreement, which was originally set to expire in August 2016. On December 21, 2015 and April 15, 2016, the Company renewed the sublease for the Company's corporate headquarters in Boston, MA through August 31, 2021. As of March 31, 2018, a security deposit of \$128 thousand is included in deposits on the balance sheet.

On January 30, 2018, the Company entered into a lease agreement for office space in Houston, TX at MD Anderson. Under the terms of the Houston lease agreement, 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. Upon signing the lease agreement, the Company expensed approximately \$40 thousand for rent expense for the period beginning in May 2015 through December 2017. The \$40 thousand for rent expense incurred from May 2015 through December 2017, and all future rent expense incurred in Houston, is being deducted from our prepayment at MD Anderson described in the license agreement section below.

Total rent expense was approximately \$176 thousand and \$172 thousand for the three months ended March 31, 2018 and 2017, respectively.

The Company records rent expense on a straight-line basis over the term of the lease. Accordingly, the Company has recorded a liability for deferred rent at March 31, 2018 and December 31, 2017 of \$105 thousand (\$102 thousand as is classified current and \$3 thousand as is classified long-term) and \$142 thousand (\$141 thousand as is classified current and \$1 thousand as is classified long-term), respectively, which is recorded in deferred rent on the balance sheets.



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**ZIOPHARM Oncology, Inc.**

**NOTES TO FINANCIAL STATEMENTS (unaudited)**

**6. Commitments and Contingencies (continued)**

License Agreements

*Exclusive Channel Partner Agreement with Precigen for the Cancer Programs*

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

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

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

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

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



Is being commercialized by the Company;

Has received regulatory approval;

Is a subject of an application for regulatory approval that is pending before the applicable regulatory authority; or

Is the subject of at least an ongoing Phase 2 clinical trial (in the case of a termination by Precigen due to an uncured breach or a voluntary termination by the Company), or an ongoing Phase 1 clinical trial in the field (in the case of a termination by us due to an uncured breach or a termination by Precigen following an unconsented assignment by the Company or its election not to pursue development of a Superior Therapy (as defined in the Channel Agreement)).

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

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**ZIOPHARM Oncology, Inc.**

**NOTES TO FINANCIAL STATEMENTS (unaudited)**

**6. Commitments and Contingencies (Continued)**

*Amendment of Collaborations with Precigen*

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

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

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

*Exclusive Channel Collaboration Agreement with Precigen for GvHD*

On September 28, 2015, the Company entered into the GvHD Agreement with Intrexon (now Precigen), whereby the Company would use Precigen's technology directed towards *in vivo* expression of effectors to research, develop and

commercialize products for use in the treatment or prevention of GvHD. The GvHD Agreement granted us a worldwide license to use specified patents and other intellectual property of Precigen in connection with the research, development, use, importing, manufacture, sale, and offer for sale of products developed under the GvHD Agreement.

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

In November 2017, as a result of an in-depth review of the Company's research and development portfolio, the determination was made that the pursuit of GvHD as an indication was not a material part of its corporate strategy and therefore have decided to stop pursuing the development of engineered cell therapy strategies, used either separately or in combination, for targeted treatment of GvHD. The Company has reverted the rights under the GvHD program back to Precigen and is in the process of winding down the related activities. The Company made this decision to focus its efforts and resources on the development of the Controlled IL-12 and Sleeping Beauty platforms for the treatment of oncology indications.

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**ZIOPHARM Oncology, Inc.**

**NOTES TO FINANCIAL STATEMENTS (unaudited)**

**6. Commitments and Contingencies (Continued)**

*License Agreement The University of Texas MD Anderson Cancer Center*

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

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

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

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

Pursuant to the Research and Development Agreement, the Company, Intrexon (now Precigen) and MD Anderson have agreed to form a joint steering committee that will oversee and manage the new and ongoing research programs.

As provided under the MD Anderson License, the Company provided funding for research and development activities in support of the research programs under the Research and Development Agreement for a period of three years and in an amount of no less than \$15.0 million and no greater than \$20.0 million per year. During the three months ended March 31, 2018, the Company made payments in the aggregate amount of \$2.7 million to MD Anderson compared to \$3.8 million during the three months ended March 31, 2017. The decrease in cash paid to MD Anderson during the first quarter of 2018 as compared to the same period in the prior year is a result of approved expenditures incurred by us being deducted from the January 2018 quarterly payment. As of March 31, 2018, MD Anderson had used \$9.5 million to offset costs incurred pursuant to the MD Anderson License and the Research and Development Agreement. The net balance of cash resources on hand at MD Anderson available to offset expenses and future costs is \$32.4 million, of which \$18.5 million is included in other current assets and the remaining \$13.9 million is included in non-current assets at March 31, 2018.

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**ZIOPHARM Oncology, Inc.**

**NOTES TO FINANCIAL STATEMENTS (unaudited)**

**6. Commitments and Contingencies (Continued)**

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 us and Precigen, if such breach has not been cured within 60 days of receiving such notice. In addition, the MD Anderson License will terminate upon the occurrence of certain insolvency events for both the Company and Precigen and may be terminated by the mutual written agreement of the Company, Precigen, and MD Anderson.

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

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

*Ares Trading License and Collaboration Agreement*

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

therapeutic, palliative or diagnostic use for cancer in humans.

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

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**ZIOPHARM Oncology, Inc.**

**NOTES TO FINANCIAL STATEMENTS (unaudited)**

**6. Commitments and Contingencies (Continued)**

Precigen is entitled to receive \$5.0 million, from Ares Trading, payable in equal quarterly installments over two years for each identified product candidate, which will be used to fund discovery work. The Company is responsible for costs exceeding the quarterly installments and all other costs of the preclinical research and development. For the three months ended March 31, 2018, the Company has expensed \$36 thousand under the Ares Trading Agreement.

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

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

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

See Note 5 for detail of the accounting for the Ares Trading Agreement.



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

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

*Collaboration Agreement with Solasia Pharma K.K.*

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

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**ZIOPHARM Oncology, Inc.**

**NOTES TO FINANCIAL STATEMENTS (unaudited)**

**6. Commitments and Contingencies (Continued)**

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.

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

On March 28, 2016, Solasia initiated a multi-center pivotal clinical trial intended to provide substantial evidence of efficacy necessary to support the filing of an application for an NDA for darinaparsin in certain of the territories assigned to Solasia. The initiation of the trial on March 28, 2016 triggered a \$1.0 million milestone payment from Solasia to 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).

*License Agreement with Baxter Healthcare S.A.*

On November 3, 2006, the Company entered into a definitive Asset Purchase Agreement for indibulin and a License Agreement to proprietary nanosuspension technology with affiliates of Baxter Healthcare S.A. The purchase included the entire indibulin intellectual property portfolio as well as existing drug substance and capsule inventories. The final royalty payment of \$250 thousand was paid in November 2017. The terms of the Asset Purchase Agreement included an upfront cash payment and an additional payment for existing inventory. No payments were made during the three months ended March 31, 2018 and 2017.

*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 (CRADA) with the National Cancer Institute (NCI) for the development of adoptive cell transfer (ACT)-based immunotherapies genetically modified using the *Sleeping Beauty* (SB) transposon/transposase system to express

TCRs for the treatment of solid tumors. The principal goal of the CRADA is to develop and evaluate ACT for patients with advanced cancers using autologous peripheral blood lymphocytes (PBL) genetically modified using the non-viral SB system to express TCRs that recognize specific immunogenic mutations, or neoantigens, expressed within a patient's cancer. Clinical evaluations of the ability of these SB-engineered PBL to express TCRs reactive against cancer mutations to mediate cancer regression in patients with metastatic disease will be performed. Research conducted under the CRADA will be at the direction of Steven A. Rosenberg, M.D., Ph.D., Chief of the Surgery Branch at the NCI, in collaboration with researchers at the Company and Intrexon. The Company's remaining obligation, as of March 31, 2018, for this CRADA is \$4.4 million over the next two years, payable in \$625 thousand payments on a quarterly basis. During the quarter ended March 31, 2018, the Company made and expensed one payment of \$625 thousand.

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**ZIOPHARM Oncology, Inc.**

**NOTES TO FINANCIAL STATEMENTS (unaudited)**

**7. Related Party Transactions**

***Collaborations with Intrexon/ Precigen***

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

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

On March 27, 2015, the Company and Intrexon (now Precigen) entered into a Second Amendment to the Exclusive Channel Partner Agreement amending the Channel Agreement, which is referred to as the ECP Amendment. The ECP Amendment modified the scope of the parties' collaboration under the Channel Agreement in connection with the Ares Trading Agreement, which the Company and Intrexon (now Precigen) entered into with Ares Trading, on March 27, 2015. The ECP Amendment provided that Intrexon (now Precigen) will pay to the Company 50% of all payments that Precigen receives for upfronts, milestones and royalties under the Ares Trading Agreement (Note 6). The Amendment also reduces Intrexon's aggregate commitment under a Stock Purchase Agreement that the parties executed in connection with the initial Channel Agreement to purchase the Company's common stock from \$50.0 million to \$43.5 million, which has been satisfied.

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

On September 28, 2015, the Company entered into the GvHD Agreement with Precigen, whereby the Company was granted the right to use Precigen's technology directed towards *in vivo* expression of biologics to research, develop and commercialize products for use in the treatment or prevention of graft-versus-host disease, or GvHD (Note 6). The Company paid Precigen a technology access fee of \$10.0 million in cash in October 2015 and agreed to reimburse Precigen for all research and development costs under the GvHD Agreement.

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**ZIOPHARM Oncology, Inc.**

**NOTES TO FINANCIAL STATEMENTS (unaudited)**

**7. Related Party Transactions (continued)**

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

In consideration for the execution and delivery of the 2016 ECP Amendment and the 2016 GvHD Amendment, the Company issued Intrexon 100,000 shares of its Series 1 preferred stock. Each share of the Company's Series 1 preferred stock has a stated value of \$1,200, subject to appropriate adjustment in the event of any stock dividend, stock split, combination or other recapitalization, and certain other rights, preferences, privileges and obligations (Note 9). The holders of the shares of Series 1 preferred stock are entitled to receive a monthly dividend, payable in additional shares of Series 1 preferred stock, equal to \$12.00 per preferred share held by such holder per month divided by the stated value of the preferred shares, rounded down to the nearest whole share.

During the 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. See Notes 8 and 9 for additional discussion regarding the accounting for and valuation of these derivative financial instruments.

During the three months ended March 31, 2018, and 2017, the Company expensed \$2.8 million and \$6.1 million, respectively, for services performed by Precigen. As of March 31, 2018, and 2017, the Company recorded \$2.8 million and \$6.1 million, respectively, in current liabilities on its balance sheet for amounts due to Intrexon.

***Collaboration with Precigen and MD Anderson***

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

Precigen hold an exclusive, worldwide license to certain technologies owned and licensed by MD Anderson, including technologies relating to novel CAR<sup>+</sup> T-cell therapies arising from the laboratory of Laurence Cooper, M.D., Ph.D., who is now the Company's Chief Executive Officer and was formerly a professor of pediatrics at MD Anderson and now currently a visiting scientist under that institution's policies, as well as either co-exclusive or non-exclusive licenses under certain related technologies. In partial consideration for entering into the MD Anderson License, the Company issued MD Anderson an aggregate of 11,722,163 shares of common stock for which the Company incurred a \$67.3 million charge recorded in 2015. The Company has determined that the rights acquired in the MD Anderson License represent in-process research and development with no alternative future use. During the three months ending March 31, 2018, the Company made the final quarterly payment of \$2.7 million under the research and development agreement, bringing the total aggregate payments to \$41.9 million.

Table of Contents**ZIOPHARM Oncology, Inc.****NOTES TO FINANCIAL STATEMENTS (unaudited)****8. Stock-Based Compensation**

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

<i>(in thousands)</i>	<b>For the three months ended March 31,</b>	
	<b>2018</b>	<b>2017</b>
Research and development	\$ 603	\$ 560
General and administrative	3,056	1,464
<b>Stock-based compensation expense</b>	<b>\$ 3,659</b>	<b>\$ 2,024</b>

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 granted an aggregate of 117,000 stock options during the three months ended March 31, 2017 with a weighted-average grant date fair value of \$4.48 per share.

On February 15, 2018, the Company extended the contractual life of 751,667 fully vested stock options held by one officer of the Company by an additional 9 months. Additionally, on March 12, 2018, the Company extended the contractual life of 117,500 fully vested stock options held by a director. These extensions resulted in additional stock compensation expense of \$481 thousand in the three months ended March 31, 2018.

For the three months ended March 31, 2018 and 2017, the fair value of stock options was estimated on the date of grant using a Black-Scholes option valuation model with the following assumptions:

	<b>For the three months ended March 31,</b>	
	<b>2018</b>	<b>2017</b>
Risk-free interest rate	2.56 - 2.74%	2.04 - 2.23%
Expected life in years	6	6
Expected volatility	80.75 - 81.10%	80.31 - 80.90%
Expected dividend yield	0	0

The Company accounts for forfeitures under ASU 2016-09 Stock Compensation (Topic 718): Improvement to Employee Share-Based Payment Accounting, effective January 1, 2017. The update revises requirements in the following areas: minimum statutory withholding, accounting for income taxes, and forfeitures. Prior to adoption, the Company recognized share-based compensation, net of estimated forfeitures, over the vesting period of the grant. Upon adoption of ASU 2016-09, the Company elected to change its accounting policy to recognize forfeitures as they occur. The new forfeiture policy election was adopted using a modified retrospective approach with a cumulative effect adjustment of \$122 thousand recorded to accumulated deficit as of January 1, 2017.





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## ZIOPHARM Oncology, Inc.

## NOTES TO FINANCIAL STATEMENTS (unaudited)

## 8. Stock-Based Compensation (continued)

Stock option activity under the Company's stock option plan for the three months ended March 31, 2018 is as follows:

<i>(in thousands, except share and per share data)</i>	Number of Shares	Weighted- Average Exercise Price	Weighted- Average Contractual Term (Years)	Aggregate Intrinsic Value
Outstanding, December 31, 2017	3,852,135	\$ 5.12		
Granted	7,500	4.27		
Exercised				
Cancelled	(36,667)	5.93		
Outstanding, March 31, 2018	3,822,968	\$ 5.08	6.20	\$ 1,020
Options exercisable, March 31, 2018	2,951,502	\$ 4.83	5.36	\$ 1,019
Options exercisable, December 31, 2017	2,925,502	\$ 5.12	5.58	\$ 1,152
Options available for future grant	403,962			

At March 31, 2018, total unrecognized compensation costs related to unvested stock options outstanding amounted to \$5.0 million. The cost is expected to be recognized over a weighted-average period of 1.70 years.

A summary of the status of unvested restricted stock for the three months ended March 31, 2018 is as follows:

	Number of Shares	Weighted-Average Grant Date Fair Value
Non-vested, December 31, 2017	1,808,559	\$ 5.74
Granted		
Vested	(205,491)	5.38
Cancelled	(70,867)	5.07
Non-vested, March 31, 2018	1,532,201	\$ 5.82

At March 31, 2018, total unrecognized compensation costs related to unvested restricted stock outstanding amounted to \$7.9 million. The cost is expected to be recognized over a weighted-average period of 1.48 years.

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**ZIOPHARM Oncology, Inc.**

**NOTES TO FINANCIAL STATEMENTS (unaudited)**

**9. Preferred Stock**

The Company has 30,000,000 shares of preferred stock authorized, of which, 250,000 shares are designated as Series 1 preferred stock.

On June 29, 2016, the Company entered into the 2016 ECP Amendment and 2016 GvHD Amendment with Intrexon (now Precigen) (see 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 has a stated value of \$1,200, subject to appropriate adjustment in the event of any stock dividend, stock split, combination or other recapitalization. The Series 1 preferred stock has the following rights and preferences and certain other rights, preferences, privileges and obligations.

**Conversion**

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

**Dividends**

The Series 1 preferred stock provides for a monthly dividend, payable in additional shares of Series 1 preferred stock, equal to \$12.00 per share, per month divided by the stated value per share, or the PIK Dividend; provided, that if any shares of Series 1 preferred stock are not converted on the Conversion Event Date (discussed below), then the rate of the PIK Dividend on all remaining unconverted shares of Series 1 preferred stock shall automatically increase from \$12.00 to \$24.00 per share, per month.

**Liquidation Preference**

In the event of any voluntary or involuntary liquidation, dissolution or winding up of the Company or a change of control or sale, lease transfer or exclusive license of all or substantially all of the Company's assets prior to the conversion of the Series 1 preferred stock into shares of common stock, then the Series 1 preferred stock will participate in the proceeds of the transaction on a pro rata basis along with common stock, treating the Series 1

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

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**Table of Contents****ZIOPHARM Oncology, Inc.****NOTES TO FINANCIAL STATEMENTS (unaudited)****9. Preferred Stock (continued)****Voting Rights**

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

**Analysis**

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

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

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

During the 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 its 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. (Note 10).

**Table of Contents****ZIOPHARM Oncology, Inc.****NOTES TO FINANCIAL STATEMENTS (unaudited)****10. Derivative Financial Instruments**

The Company determined that certain embedded features related to the Series 1 preferred stock are derivative financial instruments.

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

<i>(\$ in thousands)</i>		
Liability derivatives:	Balance Sheet Location	Fair Value
March 31, 2018:		
Derivative liabilities	Liabilities	\$ 2,469

The change in the derivative liability for the three months ended March 31, 2018 consisted of the following:

<i>(\$ in thousands)</i>		Fair Value
Balance, December 31, 2017		\$ 2,424
Dividends		73
Change in fair value		(28)
Balance, March 31, 2018		\$ 2,469

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

	March 31, 2018	December 31, 2017
Risk-free interest rate	2.50%	1.92 - 2.12%
Expected dividend rate	0	0
Expected volatility	80.30%	68.7 - 80.4%

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Preferred stock conversion limit - percentage of outstanding common stock	19.90%	19.90%
Preferred conversion floor price	\$ 1.00	\$ 1.00

See Notes 5 and 8 for additional discussion regarding the accounting for and valuation of these derivative financial instruments.



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**Table of Contents****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, predicts, potential and continue or similar words. In particular, statements contained in this Quarterly Report, including but not limited to, statements regarding the costs and timing of our clinical trials and of the development and commercialization of our pipeline products and services; the sufficiency of our cash, investments 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 such statements.

**Business Overview**

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

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

Control of IL-12 is achieved from a replication-incompetent adenoviral (AD) vector administered via a single injection of virus into the brain tumor and engineered to conditionally express human IL-12 (hIL-12). The conditional expression of hIL-12 is modulated with the RheoSwitch Therapeutic System® (RTS®) by the small molecule vededimex, an activator ligand orally administered which has been shown to cross the blood-brain barrier. A Phase 1 trial in patients at high risk for death due to disease progression produced data demonstrating the safety of controlled

local expression of IL-12 and showed that local IL-12 expression can improve the survival of patients with recurrent glioblastoma, or rGBM. The mechanism by which these patients developed an anti-tumor effect is due to IL-12 turning cold tumors hot as shown from repeat biopsies that revealed an increased and sustained infiltrate of activated T-cells producing interferon gamma (IFN-g) within the brain-tumor lesion. These data are consistent with biopsy data from patients with breast cancer and melanoma that also showed IL-12 turning cold tumors hot, which could have a profound impact on oncology therapy in general.

Initially, we are developing this controlled IL-12 therapy as a monotherapy for adults and children with recurrent brain tumors as well as exploring stereotactic administration.. In addition, we are pursuing the development of controlled IL-12 combined with a checkpoint inhibitor, for which a Phase 1 trial in rGBM has been initiated. The potential for exploring combination therapy with checkpoint inhibitor(s) in additional oncology indications is also being explored.

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

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

### *Program Updates*

#### *Controlled IL-12 Platform*

We have decided to further develop our controlled IL-12 platform as monotherapy and in combination with immune checkpoint inhibitor(s) in rGBM and are exploring other oncology indication(s). This decision was based on the Company's demonstration that recombinant IL-12 produced from within the tumor following Ad-RTS-hIL-12 therapy can favorably change the tumor microenvironment from weeks to months by recruiting and activating T cells. This activity likely contributes to anti-tumor effects and supports our enthusiasm for exploring the potential of the IL-12 platform across multiple tumor types. In January 2018, we provided updates on the continued development of our Controlled IL-12 platform and development programs for the treatment of brain cancer at the J.P. Morgan Healthcare Conference. We announced the initiation of a Phase I clinical trial to evaluate Ad-RTS-hIL-12 plus veledimex in combination with OPDIVO® (nivolumab), an immune checkpoint, or PD-1 inhibitor, in adult patients with rGBM. In order to pursue these additional clinical studies in other indications, we have elected to delay the initiation of our Pivotal study. We had designed a Phase 3 randomized control trial to evaluate Controlled IL-12 for the treatment of patients with rGBM following meetings with U.S. and European regulatory authorities, and we are completing execution of Chemistry Manufacturing and Control (CMC) technical requirements.

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

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

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**Table of Contents***Sleeping Beauty (SB) Platform*

In December 2017, we delivered multiple presentations on our adoptive cell therapy programs and application of the SB technology at the 59<sup>th</sup> American Society of Hematology (ASH) Annual Meeting and Exposition in Atlanta. We presented on the advancement of our SB platform towards point-of-care (P-O-C) for very rapid manufacturing of genetically modified CAR<sup>+</sup> T cells. Data presented from first- and second-generation SB clinical trials demonstrate tolerability, disease response, long-term survival and persistence of infused CD19-specific CAR<sup>+</sup> T cells. Preclinical studies presented at ASH and at the Keystone Symposia in February 2018 showed that P-O-C CAR<sup>+</sup> T cells co-expressing membrane-bound interleukin-15 (mbIL15) and a control switch manufactured within two days do not require activation or propagation in tissue culture to achieve anti-tumor effects and prolonged T-cell survival in mice. Building on these data, subject to regulatory clearance, we plan to initiate an investigator-led first P-O-C clinical trial in the second half of 2018 at MD Anderson. We have announced that an investigational new drug application has been submitted to the U.S. Food and Drug Administration, or FDA, by MD Anderson to initiate a Phase 1 trial to evaluate the point-of-care technology for the investigational treatment of CD19<sup>+</sup> leukemia and lymphoma.

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

*Platform Technologies*

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

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



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

Controlled IL-12: An immune system master regulator which weaponizes the immune system delivered in a tunable dose and turns cold tumors hot ;

*Sleeping Beauty*: A non-viral genetic manipulation that empowers and directs T cells to fight cancer.

***Product Candidates***

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

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**Table of Contents***Controlled IL-12 Platform**Background*

Ad-RTS-hIL-12 plus veledimex, our most advanced product candidate, uses our gene delivery system to produce IL-12, a potent, naturally occurring anti-cancer protein. We have developed a replication-incompetent adenoviral vector, Ad-RTS-hIL-12, administered intra-tumorally under the control of a switch referred to as the RTS expression platform. Activation of the switch and therefore conditional gene expression and subsequent IL-12 protein production is tightly controlled by the activator ligand, veledimex, delivered to the patient as an oral capsule. When veledimex is administered to a patient, the switch is turned on and IL-12 are produced; when veledimex is withdrawn, the switch is turned off and production of recombinant IL-12 ceases. Furthermore, the amount of IL-12 produced is proportional to the dosing of veledimex. The recombinant IL-12 appears to be biologically active as for example, it can stimulate production of the body's own interferon-gamma (IFN-g). IL-12 is a potent pro-inflammatory cytokine capable of reversing immune escape mechanisms and improving the function of tumor fighting natural killer, or NK, and T cells. We have found direct evidence of sustained and deep infiltration of activated T cells in previously cold tumors (i.e. turning cold tumors such as rGBM and breast cancer hot) following administration of Ad-RTS-hIL-12 plus veledimex; the presence of such T-cells has furthermore been sustained months after administration of the Ad-RTS-hIL-12 plus veledimex. Gliomas represent a unique form of aggressive cancer that spreads loco-regionally and are particularly well suited to IL-12 local therapy.

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

*Glioblastoma Market*

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

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

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

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

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

The primary objective of the Phase 1 trial is to determine the safety and tolerability of a single intratumoral Ad-RTS-hIL-12 injection activated upon dosing with oral veledimex. Secondary objectives are to determine the maximum tolerated dose, the immune responses elicited, and assessment of biologic response. The study has enrolled patients at doses ranging from 10 mg to 40 mg of veledimex. We expect to continue to enroll patients at the 20 mg dose level this year in an expansion study to the existing Phase 1 trial. The trial is designed to further evaluate the monotherapy in patients who have not received bevacizumab for their disease and are not receiving steroids for the 4 weeks prior to therapy initiation.

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

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

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

Immunohistochemistry analyses from three of three patient biopsies after completion of veledimex demonstrated that IL-12 activates and sustains an immune response in rGBM;

All three biopsies of brain cancer lesions demonstrated evidence of an anti-tumor response with extensive infiltration of CD8<sup>+</sup> T cells within the rGBM;

Biopsies all showed sustained (greater than 4 months) production of IFN-g, a cytokine crucial to arming an immune response in the tumor microenvironment;

Ratio of circulating killer CD8<sup>+</sup> T cells to suppressor FOXP3<sup>+</sup> T cells appeared to correlate with survival;



IFN-g was undetectable in the blood at the time of biopsies while observed in the tumor providing further evidence of a sustained on-target response;

Expression levels of both PD-1 and PD-L1 were upregulated in all the biopsies, which suggests added potential efficacy for combining Ad-RTS-hIL-12 plus veledimex with an immune checkpoint inhibitor; Dr. Chiocca, the 2017 President of the Society for Neuro-Oncology, was the lead author of this presentation.

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

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

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We continue to engage in partnership discussions for further development in this indication and are collecting additional clinical data from the open Phase 1 trial, including a combination study with an immune checkpoint inhibitor (iCPI).

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

### *Pediatrics*

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

### *Combination therapy*

Our enthusiasm about Controlled IL-12 as a platform has recently increased based on emerging clinical data demonstrating that this cytokine recruits immune cells such as T-cells into rGBM turning cold tumor sites hot for long periods of time. As the Phase 1 survival data matured over the latter half of 2017, we saw compelling evidence from biopsies, taken more than four months after administration of Ad-RTS-hIL-12 plus veledimex, demonstrating that Controlled IL-12 causes a sustained influx of activated killer (CD8<sup>+</sup>) T cells into brain tumors and upregulated expression of PD-1/PDL-1 biomarkers.

We have previously reported, in May 2016 at the Annual Meeting of the American Society of Gene and Cell Therapy, or ASGCT, preclinical trials suggesting that combination of Ad-RTS-hIL-12 plus veledimex with iCPIs improves the anti-tumor effect. We believe these data support a first-in-human study combining Ad-RTS-hIL-12 + veledimex with an iCPI, such as targeting PD-1, for the investigational treatment of rGBM.

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

### *Other indications*

Ad-RTS-hIL-12 plus veledimex has been evaluated in four clinical trials prior to shifting our focus to brain cancer. The first, a Phase 1/2 study for the treatment of metastatic melanoma, and the second, a Phase 2 study for the treatment of unresectable recurrent or metastatic breast cancer. We have also concluded enrollment of a single-center Phase 1b/2 study, following standard chemotherapy, for the treatment of patients with locally advanced or metastatic breast cancer. In January 2017, we announced that we paused the breast cancer studies after successfully collecting the desired biomarker data. As a result of further correlative studies including sustained CD8<sup>+</sup> T cell infiltration and production of intratumoral IFN-g (ESMO 2016) in the tumor, in other words turning "cold tumors hot", we plan to further develop Ad-RTS-hIL-12 plus veledimex in both monotherapy as well as in combination with immune

checkpoint inhibitor(s) and are exploring other oncology indications, including breast cancer.

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**Table of Contents***Sleeping Beauty-Modified T-cell Platform*

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

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

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

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

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

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

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**Table of Contents***Hematologic and solid tumor malignancy market*

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

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

**Clinical Development of CAR<sup>+</sup> T**

Through the MD Anderson License, we entered the clinic with three CAR<sup>+</sup> T therapies in 2015 utilizing the non-viral genetic modification capabilities of the SB system. Two of these trials are with first generation technologies, the results from which were published in the *Journal of Clinical Investigation* in September 2016. An update on patients in the first-generation trials was presented in a poster at the 2017 Annual Meeting of ASH. The trials demonstrated that first-generation SB-modified CD19-specific CAR<sup>+</sup> T cells appear to provide long term cancer control when infused after hematopoietic stem-cell transplantation (HSCT) for patients with advanced CD19<sup>+</sup> malignancies and could be detected years after administration in some recipients. All seven patients with advanced CD19<sup>+</sup> non-Hodgkin's lymphoma (NHL) that received autologous T-cells were alive at a median survival of 40 months since infusion. We reported the proportion of patients who were alive was 100% and progression free was 86%. For 19 patients with advanced CD19<sup>+</sup> acute lymphoblastic leukemia (ALL) and NHL infused with allogeneic T-cells following HSCT, nine patients were alive with a median survival of 31 months. The proportion of patients reported alive was 49% and the proportion of patients that were progression free was 32%. Of the subset of eight patients who received donor-derived T-cells after haploidentical HSCT, the proportion of patients who were alive was 63% and the proportion of patients that were progression free was 50%. These survival rates compare favorably with historical data for patients receiving HSCT alone (i.e. without CAR-T). Patients receiving autologous HSCT have been reported to have a 3-year progression free survival (PFS) of 49%. Patients receiving allogeneic HSCT have been reported to have a 1-year overall survival (OS) of 20-34%, and haploidentical (haplo) allogeneic HSCT patients have a 3-year OS of 37% and disease free survival (DFS) of 31%. Persistence of circulating SB-modified CAR<sup>+</sup> T cells was demonstrated at two years in an autologous and allogeneic patient and for four years in two autologous patients.

We are currently enrolling patients in an investigator-led Phase 1 study using second-generation CD19-specific CAR<sup>+</sup> T cells with a revised CAR structure in patients with advanced lymphoid malignancies at MD Anderson. Our second-generation CD19 trial employs a revised CAR design and shortened manufacturing process advancement, with culturing times as short as two weeks. A summary of this ongoing trial was presented by Dr. Partow Kebriaei of MDACC in a presentation at the 2017 Annual Meeting of ASH in December. Interim data from the trial demonstrated that autologous T-cells infused after lymphodepleting chemotherapy could be detected, and exhibited anti-tumor effects and an encouraging safety profile in patients with relapsed/refractory CD19<sup>+</sup> malignancies. Complete responses at one month were reported in four of eight patients with either ALL (n=5), chronic lymphocytic leukemia

(n=1), or diffuse large B-cell lymphoma (n=2), with two morphologic complete responses at three months. Follow-up blood tests demonstrated sustained persistence of infused T-cells and targeting of malignant and normal B cells. There were no dose limiting toxicities with only grade 1 or 2 adverse events being reported. T-cell dose escalation continues. We anticipate stopping enrollment in this trial in 2018 as our third-generation trial moves forward in the clinic.

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

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

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

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**Table of Contents****Clinical Development of TCR**

Cancer immunotherapy generally offers limited clinical benefit without coordinated strategies to mitigate the immunosuppressive nature of the tumor microenvironment. Tumor-associated antigens (TAAs) on the surface of solid tumors represents an attractive target for CAR-based T-cell therapy if expression is restricted to tumor cells. Because CARs directly bind to antigens independent of the human leukocyte antigen (HLA) system, an advantage of this approach is that one CAR design with a particular specificity may target a particular cancer diagnosis shared by multiple individuals. However, these types of TAAs on the cancer cell surface are not common. In contrast, it is increasingly recognized that neoantigens (or sometimes referred to as mutation-specific proteins), which are selectively expressed within solid tumors as they result from cancer-specific mutations, are more prevalent targets for T-cell therapy. Thus, neoantigens might serve as attractive targets than TAAs if they can be targeted by T-cell receptors (TCRs), which in contrast to CARs, recognize antigens processed through HLA. The problem to be overcome is that neoantigens are typically different between patients with cancer, thus the TCRs targeting a neoantigen are different for different recipients of T-cell therapy. One way to target neoantigens is to genetically modify T cells with TCRs to recognize neoantigens. Since many neoantigens may be expressed within a tumor, preference is given to target a subset of antigens that are tied to the formation of the tumor. In other words, to target driver mutations. We believe that our non-viral platform is well suited for targeting neoantigens as the SB system has the potential for the very rapid production of TCR-modified T cells such as under P-O-C. This approach to the clinical production of TCR-modified T cells may be cost-effective, and is expected to be customizable so that patients can receive TCR-modified T cells personalized for their cancer. Therefore, we are pursuing a discovery program in TCR therapies for neoantigen targets.

On January 10, 2017, we announced the signing of a CRADA with the NCI for the development of ACT-based immunotherapies genetically modified using the SB transposon/transposase system to express TCRs for the treatment of solid tumors. The principal goal of the CRADA is to develop and evaluate ACT for patients with advanced cancers using autologous PBL genetically modified using the non-viral SB system to express TCRs that recognize specific immunogenic mutations, or neoantigens, expressed within a patient's cancer. We plan to perform clinical evaluations of the ability of these SB-engineered PBL to express TCRs reactive against cancer mutations to mediate cancer regression in patients with metastatic disease. Research conducted under the CRADA will be at the direction of Steven A. Rosenberg, M.D., Ph.D., Chief of the Surgery Branch at the NCI, in collaboration with researchers at Ziopharm and Precigen. Preparations for the clinical trial are underway at the NCI. Following validation of the manufacturing process, we anticipate submission of the IND and initiation of the clinical trial in 2018.

**Preclinical Development**

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

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



**Table of Contents****Financial Overview****Overview of Results of Operations****Three Months Ended March 31, 2018 Compared to Three Months Ended March 31, 2017**

**Revenue.** Revenue during the three months ended March 31, 2018 and 2017 was as follows:

(\$ in thousands)	Three months ended		Change
	March 31, 2018	March 31, 2017	
Collaboration revenue	\$ 146	\$ 1,597	\$(1,451) -91%

Revenue for the three months ended March 31, 2018 decreased, compared to revenue for the three months ended March 31, 2017 due to the adoption of ASU 2014-09 (Note 2, Summary of Significant Accounting Policies). During the three months ended March 31, 2018, the Company recognized \$146 thousand of revenue related to the Ares Trading Agreement. As of March 31, 2018, the remaining balance of contract liability associated with the upfront payment is \$49.5 million, of which \$476 thousand is classified as current and \$49.0 million is classified as long-term. During the three months ended March 31, 2017, the Company recognized \$1.6 million of revenue related to the Ares Trading Agreement. As of December 31, 2017, the remaining balance of contract liability (formerly deferred revenue) associated with the upfront payment was \$41.5 million, of which \$6.4 million is current and \$35.1 million is classified as long-term.

**Research and development expenses.** Research and development expenses during the three months ended March 31, 2018 and 2017 were as follows:

(\$ in thousands)	Three months ended		Change
	March 31, 2018	March 31, 2017	
Research and development	\$ 10,183	\$ 11,967	\$(1,784) -15%

Research and development expenses for the three months ended March 31, 2018 decreased by \$1.8 million, as compared to the three months ended March 31, 2017. The decrease in research and development expenses for the three months ended March 31, 2018 is primarily due to decreases of \$1.0 million in Gene Therapy programs, \$0.7 million in GvHD related expenses, and \$0.3 million in Cell Therapy program spending. These decreases related to program costs were offset by an increase of \$0.2 million related to stock compensation, salary and employee related expenses, and contracted outside service costs during the three months ended March 31, 2018.

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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, 2018, our clinical stage projects included a Phase 1 trial with Ad-RTS-IL-12 + veledimex in progressive glioblastoma; a Phase 1b/2 trial with Ad-RTS-IL-12 + veledimex in metastatic breast cancer; an investigator-led Phase 1 trial infusing our 2nd generation CD19-specific CAR<sup>+</sup> T cells in patients with advanced lymphoid malignancies; an investigator-led Phase 1 trial infusing our CD33-specific CAR<sup>+</sup> T therapy for relapsed or refractory acute myeloid leukemia; and a Phase 1 trial of Ad-RTS-hIL-12 with veledimex for the treatment of pediatric brain tumors. The expenses incurred by us to third parties for our Phase 1 trial with Ad-RTS-IL-12 + veledimex in progressive glioblastoma were \$0.3 million for the three months ended March 31, 2018, and \$4.7 million from the project's inception in June 2015 through March 31, 2018. There were no expenses incurred by us to third parties for our Phase 1b/2 trial with Ad-RTS-IL-12 + veledimex in metastatic breast cancer for the three months ended March 31, 2018, and expenses from the project's inception in April 2015 through March 31, 2018 were \$0.8 million. The expenses incurred by us to third parties for our investigator-led Phase 1 trial infusing our 2nd generation CD19-specific CAR<sup>+</sup> T cells in patients with advanced lymphoid malignancies were \$1.1 million for the three months ended March 31, 2018 and \$3.9 million from the project's inception in December 2015 through March 31, 2018. The expenses incurred by us to third parties for our investigator-led Phase 1 trial infusing our CD33-specific CAR<sup>+</sup> T therapy for relapsed or refractory acute myeloid leukemia were \$1.5 million for the three months ended March 31, 2018 and \$2.9 million from the project's inception in September 2017 through March 31, 2018. The expenses incurred by us to third parties for our investigator-led Phase 1 trial of Ad-RTS-hIL-12 with veledimex for the treatment of pediatric brain tumors were \$0.6 million for the three months ended March 31, 2018 and \$1.2 million from the project's inception in October 2017 through March 31, 2018.

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 patients;

The number of patients that ultimately participate in the trials;

The duration of patient follow-up to ensure the absence of long-term product-related adverse events; and

The efficacy and safety profile of the product.

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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, 2018 and 2017 were as follows:

	Three months ended			Change
	March 31,			
	2018	2017		
<b>(\$ in thousands)</b>				
General and administrative	\$ 6,159	\$ 3,595	\$ 2,564	71%

General and administrative expenses for the three months ended March 31, 2018 increased by \$2.6 million, as compared to the three months ended March 31, 2017. The increase for the three months ended March 31, 2018 was primarily due to an increase of \$2.2 million in stock compensation and employee related expenses incurred in the three months ended March 31, 2018 relating to stock option modifications for a departing officer and director. Additionally, contracted outside service expenses and other operating expense costs increased by \$0.4 million in comparison to the three months ended March 31, 2017.

**Other income (expense).** Other income (expense) for the three months ended March 31, 2018 and 2017 were as follows:

	Three months ended			Change
	March 31,			
	2018	2017		
<b>(\$ in thousands)</b>				
Other income (expense), net	\$ 148	\$ 38	\$ 110	289%
Change in derivative value	28	(1,560)	1,588	(102%)
<b>Total</b>	<b>\$ 176</b>	<b>\$ (1,522)</b>		

The increase in other expense for the three months ended March 31, 2018, compared to the three months ended March 31, 2017, was due primarily to interest received on our cash balance. The Company recorded a gain on the change of the derivative liabilities in the amount of \$28 thousand for the quarter ended March 31, 2018.

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**Liquidity and Capital Resources**

As of March 31, 2018, we have approximately \$51.1 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 2019 and currently have no committed sources of additional capital. The forecast of cash resources is forward-looking information that involves risks and uncertainties, and the actual amount of our expenses could vary materially and adversely as a result of a number of factors. We have based our estimates on assumptions that may prove to be wrong, and our expenses could prove to be significantly higher than we currently anticipate. Management does not know whether additional financing will be on terms favorable or acceptable to us when needed, if at all. If adequate additional funds are not available when required, or if we are unsuccessful in entering into partnership agreements for further development of our products, management may need to curtail development efforts. Based on the forecast, management determined that there is substantial doubt regarding our ability to continue as a going concern. As a result, our independent registered accounting firm has expressed substantial doubt as to our ability to continue as a going concern in their report dated March 1, 2018 included in our Annual Report on the Form 10-K for the fiscal year ended December 31, 2017.

Although all human clinical trials are expensive and difficult to design and implement, we believe that due to complexity, costs associated with clinical trials for synthetic biology immuno-oncology are greater than the corresponding costs associated with clinical trials for small-molecule candidates.

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

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

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The following table summarizes our net decrease in cash, cash equivalents, and restricted cash for the three months ended March 31, 2018 and 2017:

(\$ in thousands)	Three months ended	
	2018	2017
Net cash provided by (used in):		
Operating activities	\$ (18,957)	\$ (14,277)
Investing activities	(150)	(358)
Financing activities	(731)	29
Net increase (decrease) in cash, cash equivalents, and restricted cash	\$ (19,838)	\$ (14,606)

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

Non-cash operating items such as depreciation and amortization, stock-based compensation and common and preferred stock issued in exchange for license agreements;

Changes in operating assets and liabilities, which reflect timing differences between the receipt and payment of cash associated with transactions and when they are recognized in results of operations; and

Changes associated with the fair value of our derivative liabilities.

Net cash used in operating activities for the three months ended March 31, 2018 was \$19.0 million, as compared to net cash used in operating activities of \$14.3 million for the three months ended March 31, 2017. 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. The net cash used in operating activities for the three months ended March 31, 2017 was primarily due to our net loss of \$15.5 million, offset by the change in prepaid expenses of \$2.4 million and change in accrued expenses and other liabilities of \$19 thousand.

Net cash used in investing activities was \$150 thousand for the three months ended March 31, 2018 compared to \$358 thousand for the three months ended March 31, 2017. The change was due to an increase in offsite equipment purchased to support our CAR programs at MD Anderson incurred during the three months ended March 31, 2017.

Net cash used in financing activities was \$730 thousand for the three months ended March 31, 2018 compared to \$29 thousand provided by financing activities for the three months ended March 31, 2017. The \$760 thousand decrease in cash provided by financing activities is primarily attributable to restricted stock buy back to cover taxes on stock exercises.



**Table of Contents****Operating capital and capital expenditure requirements**

We anticipate that losses will continue for the foreseeable future. At March 31, 2018, our accumulated deficit was approximately \$736.6 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, 2018 was \$62.0 million, consisting of \$72.1 million in current assets and \$10.1 million in current liabilities. Working capital as of December 31, 2017 was \$69.9 million, consisting of \$90.8 million in current assets and \$20.9 million in current liabilities.

**Contractual obligations**

The following table summarizes our outstanding obligations as of March 31, 2018 and the effect those obligations are expected to have on our liquidity and cash flows in future periods:

(\$ in thousands)	Total	Less than			More than
		1 year	2 - 3 years	4 - 5 years	5 years
Operating leases	\$ 2,774	\$ 1,006	\$ 1,464	\$ 304	\$
CRADAs	\$ 4,375	2,500	1,875		
<b>Total</b>	<b>\$ 7,149</b>	<b>\$ 3,506</b>	<b>\$ 3,339</b>	<b>\$ 304</b>	<b>\$</b>

Our commitments for operating leases relate to the lease for our corporate headquarters in Boston, Massachusetts, and office space in New York, New York and Houston, Texas. On December 21, 2015 and April 15, 2016, we renewed the sublease for our corporate headquarters in Boston, MA through August 31, 2021. Included in the above table are obligations for the subleased portion of our New York and Houston office space (see Note 6, Commitments and Contingencies). We expect to receive a total of \$195 thousand in the next year from our subtenants in the New York



office.

On January 10, 2017, we announced the signing of a CRADA with the NCI for the development of ACT-based immunotherapies genetically modified using the SB transposon/transposase system for the treatment of solid tumors. Our obligation for the CRADA is reflected above with \$2.5 million in the column Less than 1 Year and \$1.9 million in the column 2 - 3 Years.

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### **Off-balance sheet arrangements**

During the three months ended March 31, 2018 and 2017, 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, 2017, 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, 2018. See note 2, Summary of Significant Accounting Policies, for a discussion of our adoption of ASU 2014-09 relating to revenue recognition.

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

### **Item 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, 2018 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 our contracts and properly account for revenue 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 standards.

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### **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, 2018, 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, 2017. 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, 2017, as filed with the Securities and Exchange Commission.

#### **RISKS RELATED TO OUR BUSINESS**

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

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

obtaining regulatory approval from the FDA and other regulatory authorities that have very limited experience with the commercial development of genetically modified and/or unmodified T-cell and NK-cell therapies for cancer;

developing and deploying consistent and reliable processes for engineering a patient's and/or donor's T-cells or NK cells *ex vivo* and infusing the T-cells or NK cells back into the patient;

possibly conditioning patients with chemotherapy in conjunction with delivering each of the potential products, which may increase the risk of adverse side effects of the potential products;

educating medical personnel regarding the potential side effect profile of each of the potential products, such as the potential adverse side effects related to cytokine release;

addressing any competing technological and market developments;

developing processes for the safe administration of these potential products, including long-term follow-up for all patients who receive the potential products;

sourcing additional clinical and, if approved, commercial supplies for the materials used to manufacture and process the potential products;

developing a manufacturing process and distribution network with a cost of goods that allows for an attractive return on investment;

establishing sales and marketing capabilities after obtaining any regulatory approval to gain market acceptance;

developing therapies for types of cancers beyond those addressed by the current potential products;

maintaining and defending the intellectual property rights relating to any products we develop;

and not infringing the intellectual property rights, in particular, the patent rights, of third parties, including competitors, such as those developing T-cell and/or NK-cell therapies.

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

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

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

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

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

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

Satisfaction of these requirements will entail substantial time, effort and financial resources. Any time, effort and financial resources we expend on our Ad-RTS-IL-12 + veledimex and genetically modified and non-modified T-cell and NK-cell product candidates and other early-stage product candidate development programs may adversely affect our ability to continue development and commercialization of our immuno-oncology product candidates.

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

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

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

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

Several competitors are developing technology which enhances the immune response within the tumor microenvironment, thereby making cold tumors hot. Companies in this area include Nektar Therapeutics, Heat Biologics, and Advantagene as well as others.

Companies that sell marketed drugs for recurrent glioblastoma are Genentech and Roche with Avastin and Arbor Pharmaceuticals. Four companies have product candidates in Phase 3 development for the treatment of glioblastoma. Immunocellular Therapeutics, Tocagen, and DelMar. Other competitors with product candidates currently in Phase 2 clinical trials include Abbvie's Depatus-M (ABT-414) and DNA-2401, a conditionally replicative adenovirus being evaluated in combination with pembrolizumab (KEYTRUDA<sup>®</sup>) for recurrent glioblastoma by DNATrix and Merck. Duke University is enrolling a randomized Phase 2 study of oncolytic polio/rhinovirus recombinant (PVSRIPO) alone or in combination with lomustine in recurrent WHO Grade IV malignant glioma patients. Also, MedImmune/Astra-Zeneca's durvalumab was evaluated in a Phase 2 trial in patients with rGBM. In addition, OncoSec is advancing IL-12 for the treatment of melanoma and has generated Phase 2 data for ImmunoPulse<sup>®</sup> IL-12 in combination with pembrolizumab.

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

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



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

developing drugs and biopharmaceuticals;

undertaking preclinical testing and human clinical trials;

obtaining FDA and other regulatory approvals of drugs and biopharmaceuticals;

formulating and manufacturing drugs and biopharmaceuticals; and

launching, marketing, and selling drugs and biopharmaceuticals.

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

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

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

the scope of rights granted under the applicable license agreement and other interpretation-related issues;

whether and the extent to which our technology and processes, and the technology and processes of Precigen, MD Anderson and our other licensors, infringe on intellectual property of the licensor that is not subject to the applicable license agreement;

our right to sublicense patent and other rights to third parties pursuant to our relationships with our licensors and partners;

whether we and/or Precigen are complying with our diligence obligations with respect to the use of the licensed technology in relation to our development and commercialization of our potential products under the MD Anderson License; and

the allocation of ownership of inventions and know-how resulting from the joint creation or use of intellectual property by our licensors and by us.

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

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

We have not generated significant revenue and have incurred significant net losses in each year since our inception. For the three months ended March 31, 2018, we had a net loss of \$16.0 million, and, as of March 31, 2018, we have incurred approximately \$736.6 million of accumulated deficit since our inception in 2003. We expect to continue to incur significant operating expenditures and net losses. Further development of our product candidates, including product candidates that we may develop under our Channel Agreement with Precigen, pursuant to the MD Anderson License or pursuant to the Ares Trading Agreement, will likely require substantial increases in our expenses as we:

continue to undertake clinical trials for product candidates;

scale-up the formulation and manufacturing of our product candidates;

seek regulatory approvals for product candidates;

work with regulatory authorities to identify and address program-related inquiries;

implement additional internal systems and infrastructure;

hire additional personnel;

begin to advance candidates pursuant to the MD Anderson License; and

commence providing funding for certain research and development activities of MD Anderson pursuant to the terms of the MD Anderson License.

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

As of March 31, 2018, we have approximately \$51.1 million of cash and cash equivalents. Given our development plans, we anticipate cash resources will be sufficient to fund our operations into the second quarter of 2019, and we have no committed sources of additional capital at this time. The forecast of cash resources is forward-looking information that involves risks and uncertainties, and the actual amount of our expenses could vary materially and adversely as a result of a number of factors. We have based our estimates on assumptions that may prove to be wrong, and our expenses could prove to be significantly higher than we currently anticipate. Management does not know

whether additional financing will be on terms favorable or acceptable to us when needed, if at all. If adequate additional funds are not available when required, or if we are unsuccessful in entering into partnership agreements for further development of our product candidates, management may need to curtail development efforts. Based on the forecast, management determined that there is substantial doubt regarding our ability to continue as a going concern. As a result, our independent registered public accounting firm has expressed substantial doubt as to our ability to continue as a going concern in their report dated March 1, 2018 included in our Annual Report on Form 10-K for the fiscal year ended December 31, 2017.

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

As of March 31, 2018, we have incurred approximately \$736.6 million of accumulated deficit and had approximately \$51.1 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 2019. However, changes may occur that would consume our existing capital prior to then, including expansion of the scope of, and/or slower than expected progress of, our research and development efforts and changes in governmental regulation. Actual costs may ultimately vary from our current expectations, which could materially impact our use of capital and our forecast of the period of time through which our financial resources will be adequate to support our operations. Also our estimates include the advancement of our immuno-oncology product candidates in the clinic under our Channel Agreement with Precigen and our increased expenses as we begin to advance candidates pursuant to the MD Anderson License with MD Anderson and commence providing funding for certain research and development activities of MD Anderson pursuant to the terms of the MD Anderson License, and we expect that the costs associated with these and any additional product candidates we pursue will increase the level of our overall research and development expenses significantly going forward.

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

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

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

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

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

may be delayed by several factors, including:

Additional nonclinical data requests by regulatory agencies;

Unforeseen safety issues;

Determination of dosing issues;

Lack of effectiveness during clinical trials;

Slower than expected rates of patient recruitment and enrollment;

Inability to monitor patients adequately during or after treatment;

Inability or unwillingness of medical investigators to follow our clinical protocols; and

Regulatory determinations to temporarily or permanently cease enrollment for other reasons not related to patient safety.

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

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

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

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

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

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

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

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

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

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



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**Table of Contents*****We will incur additional expenses in connection with our Channel Agreement with Precigen.***

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

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

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

In June 2016, we amended our Channel Agreement and GvHD Agreement with Intrexon (now Precigen) in order to, among other things, reduce the royalty rate on operating profits payable by us to Precigen from 50% to 20%. In consideration for these amendments, we issued to Intrexon shares of our Series 1 preferred stock, \$0.001 par value per share, or Series 1 preferred stock, which include, among other things, a monthly dividend of 1% payable in additional shares of Series 1 preferred stock. If we fail to pay such dividends when due, it would affect our eligibility to file Registration Statements on Form S-3 and our status as a well-known seasoned issuer, which may increase the expense and time associated with both the filing and effectiveness of future registration statements and the consummation of future financing transactions or other offerings of our securities.

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

The shares of our Series 1 preferred stock include a monthly dividend of 1% which shall accrue and be paid each month in the form of additional shares of Series 1 preferred stock. For the three months ended March 31, 2018, we issued an aggregate of 3,624 shares, as dividends, of our Series 1 preferred stock to Intrexon, the holder of all the outstanding shares of our Series 1 preferred stock. As a result of the monthly dividend, the number of shares of outstanding Series 1 preferred stock will increase each month that they are outstanding. Since the number of shares of our common stock issuable upon conversion of the Series 1 preferred stock is based on the 20-day volume-weighted average price of our common stock immediately prior to the public announcement of the first approval in the United States of (i) a Ziopharm Product under the Channel Agreement, (ii) a Product under the GvHD Agreement or (iii) a Product under the Ares Trading Agreement, if, at the time of such public announcement, the 20-day volume-weighted

average price of our common stock has not increased by more than the cumulative amount of the dividends on the shares of Series 1 preferred stock that we originally issued to Intrexon, then our common stockholders may experience additional dilution as a result of the conversion of the Series 1 preferred stock into shares of our common stock.

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

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

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

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

amend our certificate of incorporation or the Certificate of Designation of the Series 1 preferred stock, in each case in a manner that adversely affects the powers, preferences or rights of the Series 1 preferred stock in a manner that is more adverse than the effect on any other class or series of our capital stock;

authorize, create, issue or obligate us to issue (by reclassification, merger or otherwise) any security (or any class or series thereof) that has any powers, preferences or rights senior to the Series 1 preferred stock with respect to the distribution of assets on the liquidation, dissolution or winding up of the Company, the

payment of dividends or rights of redemption; or

enter into any transaction (or series of related transactions) the effect of which would adversely affect the holders of the Series 1 preferred stock in a manner that is more adverse than the effect on any other class or series of our capital stock.

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

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

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

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

is being commercialized by us;

has received regulatory approval;

is a subject of an application for regulatory approval that is pending before the applicable regulatory authority; or

is the subject of at least an ongoing Phase 2 clinical trial (in the case of a termination by Precigen due to an uncured breach or a voluntary termination by us), or an ongoing Phase 1 clinical trial in the field (in the case of a termination by us due to an uncured breach or a termination by Precigen following an unconsented assignment by us or our election not to pursue development of a Superior Therapy).

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

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

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

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

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

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

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

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

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

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





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

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

Under the MD Anderson License, we, together with Precigen, received an exclusive, worldwide license to certain technologies owned and licensed by MD Anderson including technologies relating to novel CAR<sup>+</sup> T cell, NK cell and TCR cell therapies arising from the laboratory of Laurence Cooper, M.D., Ph.D., who was then at MD Anderson, as well as either co-exclusive or non-exclusive licenses under certain related technologies. When combined with Precigen's technology suite and Ziopharm's clinically tested R<sub>1</sub> Interleukin-12 modules, the resulting proprietary methods and technologies may help realize the promise of genetically modified CAR<sup>+</sup> T cell and other immune cells by controlling cell expansion and activation in the body, minimizing off-target and unwanted on-target effects and toxicity while maximizing therapeutic efficacy. The term of the MD Anderson License expires on the last to occur of (a) the expiration of all patents licensed thereunder, or (b) the twentieth anniversary of the date of the MD Anderson License; provided, however, that following the expiration of the term, 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. Subject to a 30-day cure period, MD Anderson has the right to terminate the MD Anderson License if we and Precigen fail to timely deliver the shares due in consideration for the MD Anderson License. MD Anderson may also terminate the agreement with written notice upon material breach by us or Precigen, if such breach has not been cured within 60 days of receiving such notice. In addition, the MD Anderson License will terminate upon the occurrence of certain insolvency events for both us or Precigen and may be terminated by the mutual written agreement of us, Precigen and MD Anderson.

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

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

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

Continuing to undertake preclinical development and clinical trials;

Participating in regulatory approval processes;

Formulating and manufacturing products; and

Conducting sales and marketing activities.

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

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

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

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

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

***We may not be able to successfully manage our growth.***

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

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

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

of operations.

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

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

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

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

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

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

Decreased demand for our product candidates;

Injury to our reputation;

Withdrawal of clinical trial participants;

Withdrawal of prior governmental approvals;

Costs of related litigation;

Substantial monetary awards to patients;

Product recalls;

Loss of revenue; and

The inability to commercialize our product candidates.

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

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

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

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

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

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

Delay commercialization of, and our ability to derive product revenues from, our product candidates;

Impose costly procedures on us; and

Diminish any competitive advantages that we may otherwise enjoy.

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

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

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

Our product candidates are in various stages of development and require extensive clinical testing. Notwithstanding our current clinical trial plans for each of our existing product candidates, we may not be able to commence additional

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

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

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



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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.

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

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

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

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

In addition, the clinical study requirements of the FDA, the EMA and other regulatory agencies and the criteria these regulators use to determine the safety and efficacy of a product candidate vary substantially according to the type, complexity, novelty and intended use and market of the potential products. The regulatory approval process for novel product candidates such as ours can be more expensive and take longer than for other, better known or extensively studied pharmaceutical or other product candidates. Currently, two gene therapy products, Glybera and Strimvelis, have received approval from the EMA. UniQure's Glybera, received marketing authorization from the EMA in 2012 but has struggled commercially as a result of high cost and limited demand. GlaxoSmithKline's Strimvelis was approved by the EMA in May 2016 and in March 2017 dosed its first patient. According to GlaxoSmithKline, delays in Strimvelis's commercialization were due to cross-border European reimbursement. These factors make it difficult to determine how long it will take or how much it will cost to obtain regulatory approvals for our product candidates in either the United States or Europe. Approvals by the EMA may not be indicative of what the FDA may require for approval. The FDA approved its first gene therapy, Luxturna, in December 2017.

Regulatory requirements governing gene and cell therapy products have changed frequently and may continue to change in the future. For example, the FDA has established the Office of Cellular, Tissue and Gene Therapies within its Center for Biologics Evaluation and Research, or CBER, to consolidate the review of gene therapy and related products, and the Cellular, Tissue and Gene Therapies Advisory Committee to advise CBER on its review. Gene therapy clinical trials conducted at institutions that receive funding for recombinant DNA research from the U.S. National Institutes of Health, or the NIH, are also subject to potential review by the NIH Office of Biotechnology Activities' Recombinant DNA Advisory Committee, or the RAC. Although the FDA decides whether individual gene therapy protocols may proceed, the RAC review process can impede the initiation of a clinical trial, even if the FDA has reviewed the trial and approved its initiation. Conversely, the FDA can put an IND on clinical hold even if the

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

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

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

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

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

We do not have experience in drug formulation or manufacturing of drugs or biologics and do not intend to establish our own manufacturing facilities. Although we will work closely with and rely upon Precigen on the manufacturing and scale-up of Precigen product candidates, we lack the resources and expertise to formulate or manufacture our own product candidates. We currently are contracting for the manufacture of our product candidates. We intend to contract with one or more manufacturers to manufacture, supply, store, and distribute drug supplies for our clinical trials. If a product candidate we develop or acquire in the future receives FDA approval, we will rely on one or more third-party contractors or Precigen to manufacture our products. Our anticipated future reliance on a limited number of third-party manufacturers exposes us to the following risks:

We may be unable to identify manufacturers on acceptable terms or at all because the number of potential manufacturers is limited and the FDA must approve any replacement contractor. This approval would require new testing and compliance inspections. In addition, a new manufacturer would have to be educated in, or develop substantially equivalent processes for, production of our products after receipt of FDA approval, if any.

Our third-party manufacturers might be unable to formulate and manufacture our products in the volume and of the quality required to meet our clinical needs and commercial needs, if any.

Our future contract manufacturers may not perform as agreed or may not remain in the contract manufacturing business for the time required to supply our clinical trials or to successfully produce, store, and distribute our products.

Drug manufacturers are subject to ongoing periodic unannounced inspection by the FDA, the Drug Enforcement Administration and corresponding state and foreign agencies to ensure strict compliance with current good manufacturing practices, or cGMP, and other government regulations and corresponding foreign standards. We do not have control over third-party manufacturers' compliance with these regulations and standards.

If any third-party manufacturer makes improvements in the manufacturing process for our products, we may not own, or may have to share, the intellectual property rights to the innovation.

Our third-party manufacturers may not be able to comply with cGMP regulations or similar regulatory requirements outside the United States. Our failure, or the failure of our third-party manufacturers, to comply with applicable regulations could result in sanctions being imposed on us, including clinical holds, fines, injunctions, civil penalties, delays, suspension or withdrawal of approvals, license revocation, seizures or recalls of drug candidates or products, operating restrictions and criminal prosecutions, any of which could significantly and adversely affect supplies of our products.

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

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

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

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

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

Litigation involving patients taking our product;

Restrictions on such products, manufacturers or manufacturing processes;

Restrictions on the labeling or marketing of a product;

Restrictions on product distribution or use;

Requirements to conduct post-marketing studies or clinical trials;

Warning letters;

Withdrawal of the products from the market;

Refusal to approve pending applications or supplements to approved applications that we submit;

Recall of products;

Fines, restitution or disgorgement of profits or revenues;

Suspension or withdrawal of marketing approvals;

Damage to relationships with existing and potential collaborators;

Unfavorable press coverage and damage to our reputation;

Refusal to permit the import or export of our products;

Product seizure; or

Injunctions or the imposition of civil or criminal penalties.

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



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**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.

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

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

Perceptions by members of the healthcare community, including physicians, about the safety and effectiveness of our drugs;

Pharmacological benefit and cost-effectiveness of our products relative to competing products;

Availability of coverage and adequate reimbursement for our products from government or other healthcare payors;

Effectiveness of marketing and distribution efforts by us and our licensees and distributors, if any; and

The price at which we sell our products.

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

***\*Our ability to generate product revenues will be diminished if our products do not obtain coverage 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 government and health administration authorities, private health maintenance organizations and health insurers and other third-party payors.

Patients who are prescribed medicine for the treatment of their conditions generally rely on third-party payors to reimburse all or part of the costs associated with their prescription drugs. Sufficient coverage and adequate reimbursement from third-party payors is critical to new product acceptance. Coverage decisions may depend upon clinical and economic standards that disfavor new drug products when more established or lower cost therapeutic alternatives are already available or subsequently become available. It is difficult to predict the coverage and reimbursement decisions that will be made by third-party payors for novel gene 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.

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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.

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

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

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

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

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

An increase in the statutory minimum rebates a manufacturer must pay under the Medicaid Drug Rebate Program to 23.1% and 13% of the average manufacturer price for most branded and generic drugs, respectively;

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

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

New methodologies by which rebates owed by manufacturers under the Medicaid Drug Rebate Program are calculated for drugs that are inhaled, infused, instilled, implanted or injected, and for drugs that are line extensions;

Expansion of eligibility criteria for Medicaid programs by, among other things, allowing states to offer Medicaid coverage to additional individuals with income at or below 133% of the Federal Poverty Level, thereby potentially increasing both the volume of sales and manufacturers' Medicaid rebate liability;

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

A new requirement to annually report drug samples that certain manufacturers and authorized distributors provide to physicians;

Expansion of healthcare fraud and abuse laws, including the False Claims Act and the Anti-Kickback Statute, new government investigative powers, and enhanced penalties for noncompliance;

A licensure framework for follow-on biologic products;

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

Establishment of a Center for Medicare & Medicaid Innovation at the Centers for Medicare & Medicaid Services, or CMS to test innovative payment and service delivery models to lower Medicare and Medicaid spending, potentially including prescription drug spending.

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We cannot predict the full impact of the ACA, as many of the reforms require the promulgation of detailed regulations implementing the statutory provisions, some of which have not yet fully occurred. Further, since its enactment there have been judicial and Congressional challenges to certain aspects of the ACA. As a result, there have been delays in the implementation of, and action taken to repeal or replace, certain aspects of the ACA. In January 2017, President Trump signed an Executive Order directing federal agencies with authorities and responsibilities under the ACA to waive, defer, grant exemptions from, or delay the implementation of any provision of the ACA that would impose a fiscal or regulatory burden on states, individuals, healthcare providers, health insurers, or manufacturers of pharmaceuticals or medical devices. More recently, the U.S. House of Representatives passed legislation known as the American Health Care Act of 2017, and Senate Republicans have released a draft bill known as the Better Care Reconciliation Act of 2017, each of which would repeal certain aspects of the ACA if ultimately enacted. The Senate Republicans also introduced legislation to repeal the ACA without companion legislation to replace it, and a skinny version of the Better Care Reconciliation Act of 2017. Each of these measures was rejected by the full Senate. The prospects for enactment of these legislative initiatives remain uncertain. Further, Congress will likely consider other legislation to replace elements of the ACA. We cannot know how efforts to repeal and replace the ACA or any future healthcare reform legislation will impact our business.

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

In addition, other legislative changes have been proposed and adopted since the ACA was enacted. For example, in August 2011, President Obama signed into law the Budget Control Act of 2011, which, among other things, created the Joint Select Committee on Deficit Reduction to recommend proposals in spending reductions to Congress. The Joint Select Committee on Deficit Reduction did not achieve its targeted deficit reduction of at least \$1.2 trillion for the years 2013 through 2021, triggering the legislation's automatic reductions to several government programs. These reductions include aggregate reductions to Medicare payments to providers of 2% per fiscal year, which went into effect on April 1, 2013, and, due to subsequent legislative amendments, will stay in effect through 2025 unless additional Congressional action is taken. In January 2013, President Obama signed into law the American Taxpayer Relief Act of 2012, which, among other things, further reduced Medicare payments to several providers and increased the statute of limitations period for the government to recover overpayments to providers from three to five years. Further, there have been several recent U.S. Congressional inquiries and proposed bills designed to, among other things, bring more transparency to drug pricing, review the relationship between pricing and manufacturer patient programs, and reform government program reimbursement methodologies for drugs. The full impact of these new laws, as well as laws and other reform and cost containment measures that may be proposed and adopted in the future, remains uncertain, but may result in additional reductions in Medicare and other healthcare funding, which could have a material adverse effect on our future customers and accordingly, our ability to generate revenue, attain profitability, or commercialize our products.



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

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

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

Federal civil and criminal false claims laws and civil monetary penalty laws, which prohibit, among other things, individuals or entities from knowingly presenting, or causing to be presented, claims for payment from Medicare, Medicaid, or other third-party payors that are false or fraudulent;

The federal Health Insurance Portability and Accountability Act of 1996, or HIPAA, which created new federal criminal statutes that prohibit, among other things, executing a scheme to defraud any healthcare benefit program or making false statements relating to healthcare matters;

HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act of 2009, or HITECH, and its implementing regulations, which imposes certain requirements relating to the privacy, security and transmission of individually identifiable health information;

Requirements to report annually to CMS certain financial arrangements with physicians and teaching hospitals, as defined in the ACA and its implementing regulations, including reporting any transfer of value made or distributed to teaching hospitals, prescribers, and other healthcare providers and reporting any ownership and investment interests held by physicians and their immediate family members and applicable group purchasing organizations during the preceding calendar year; and

State and foreign law equivalents of each of the above federal laws, such as anti-kickback and false claims laws which may apply to items or services reimbursed by any third-party payor, including commercial insurers; state laws that require pharmaceutical companies to comply with the industry's voluntary compliance guidelines and the applicable compliance guidance promulgated by the federal government that otherwise restricts certain payments that may be made to healthcare providers and entities; state laws that require drug manufacturers to report information related to payments and other transfer of value to

physicians and other healthcare providers and entities; and state and foreign laws governing the privacy and security of health information in certain circumstances, many of which differ from each other in significant ways and often are not preempted by HIPAA, thus complicating compliance efforts.

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

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

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

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

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

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

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

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**RISKS RELATED TO OUR INTELLECTUAL PROPERTY**

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

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

To date, we have exclusive rights to certain U.S. and foreign intellectual property with respect to the Precigen technology, including the existing Precigen product candidates, such as Ad-RTS-IL-12 + veledimex, and with respect to CAR<sup>+</sup> T, NK and TCR cell therapies arising from the laboratory of Laurence Cooper, M.D., Ph.D., who was then at MD Anderson. Under our Channel Agreement with Precigen, Precigen has the sole right to conduct and control the filings, prosecution and maintenance of the patents and patent applications licensed to us. Although under the agreement Precigen has agreed to consider in good faith and consult with us regarding any comments we may have regarding these patents and patent applications, we cannot guarantee that our comments will be solicited or followed. Under the MD Anderson License, future filings and applications require the agreement of each of MD Anderson, Precigen and us, and MD Anderson has the right to control the preparation and filing of additional patent applications unless the parties agree that we or Precigen may prosecute the application directly. Although under the agreement MD Anderson has agreed to review and incorporate any reasonable comments that we or Precigen may have regarding these patents and patent applications, we cannot guarantee that our comments will be solicited or followed. Without direct control of the channel program patents and patent applications, we are dependent on Precigen or MD Anderson, as applicable, to keep us advised of prosecution, particularly in foreign jurisdictions where prosecution information may not be publicly available. We anticipate that we, Precigen and MD Anderson will file additional patent applications both in the United States and in other countries. However, we cannot predict or guarantee:

The degree and range of protection any patents will afford us against competitors, including whether third parties will find ways to invalidate or otherwise circumvent our patents;

If and when patents will be issued;

Whether or not others will obtain patents claiming subject matter related to or relevant to our product candidates; or

Whether we will need to initiate litigation or administrative proceedings that may be costly whether we win or lose.

The patent prosecution process is expensive and time-consuming, and we may not be able to file and prosecute all necessary or desirable patent applications at a reasonable cost, in a timely manner, or in all jurisdictions. It is also possible that we will fail to identify patentable aspects of our research and development output before it is too late to obtain patent protection. Moreover, in some circumstances, we do not have the right to control the preparation, filing and prosecution of patent applications, or to maintain the patents, covering technology that we license from third

parties. We may also require the cooperation of our licensors in order to enforce the licensed patent rights, and such cooperation may not be provided. Therefore, these patents and applications may not be prosecuted and enforced in a manner consistent with the best interests of our business.

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

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

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

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

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

patents protecting such candidates might expire before or shortly after such candidates are commercialized. As a result, our owned and licensed patent portfolio may not provide us with sufficient rights to exclude others from commercializing products similar or identical to ours.

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

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

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

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

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

Our research, development and commercialization activities, as well as any product candidates or products resulting from these activities, may infringe or be claimed to infringe patents or patent applications under which we do not hold



licenses or other rights. Patents do not protect its owner from a claim of infringement of another owner's patent. Therefore, our patent position cannot and does not provide any assurance that we are not infringing the patent rights of another.

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

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

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

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

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

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

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

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

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

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

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*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.

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**OTHER RISKS RELATED TO OUR COMPANY**

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

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

Price and volume fluctuations in the overall stock market;

Market conditions or trends in our industry or the economy as a whole;

Laboratory or clinical trial results;

Public concern as to the safety of drugs developed by us or others;

Changes in operating results and performance and stock market valuations of other biopharmaceutical companies generally, or those that develop and commercialize cancer drugs in particular;

The financial or operational projections we may provide to the public, any changes in these projections or our failure to meet these projections;

Comments by securities analysts or changes in financial estimates or ratings by any securities analysts who follow our common stock, our failure to meet these estimates or failure of those analysts to initiate or maintain coverage of our common stock;

The public's response to press releases or other public announcements by us or third parties, including our filings with the Securities Exchange Commission, or the SEC, and announcements of the status of development of our products, announcements of technological innovations or new therapeutic products by us or our competitors, announcements regarding collaborative agreements and other announcements relating to product development, litigation and intellectual property impacting us or our business;

Government regulation;

FDA determinations on the approval of a product candidate BLA submission;

The sustainability of an active trading market for our common stock;

Future sales of our common stock by our executive officers, directors and significant stockholders;

Announcements of mergers or acquisition transactions;

Our inclusion or deletion from certain stock indices;

Developments in patent or other proprietary rights;

Changes in reimbursement policies;

Announcements of medical innovations or new products by our competitors;

Announcements of changes in our senior management;

Other events or factors, including those resulting from war, incidents of terrorism, natural disasters or responses to these events; and

Changes in accounting principles.

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

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

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

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

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

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

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

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

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

As of March 31, 2018, our executive officers, directors and holders of five percent or more of our outstanding common stock, beneficially owned, in the aggregate, 21.0% 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.



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

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

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

**Table of Contents****Item 2. Unregistered Sale of Equity Securities and Use of Proceeds*****Unregistered Sale of Equity Securities and Use of Proceeds***

For the three months ended March 31, 2018, we issued an aggregate of 3,624 shares of Series 1 preferred stock to Intrexon Corporation, the holder of all of the outstanding shares of our Series 1 preferred stock, as dividends, representing monthly dividends due from January 1, 2018 through March 31, 2018. The issuances of the dividend shares were exempt from registration under Section 4(a)(2) of the Securities Act of 1933, as amended.

***Issuer Purchases of Equity Securities***

The following table provides information about our purchases of common stock for the three months ended March 31, 2018:

Period	Total Number of Shares Purchased	Average Price Paid Per Share
January 1 to January 31, 2018		\$
February 1 to February 28, 2018	188,233 <sup>(1)</sup>	\$ 3.88
March 1 to March 31, 2018		\$
Total	188,233	

<sup>(1)</sup> 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 the vesting of restricted 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.

**Table of Contents****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.

<b>Exhibit</b>	
<b>Number</b>	<b>Description</b>
3.1	<u>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).</u>
3.2	<u>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).</u>
3.3	<u>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).</u>
10.1	<u>Separation Agreement by and between the Registrant and Caesar J. Belbel dated as of February 15, 2018 (incorporated by reference to Exhibit 10.1 to the Registrant's Current Report on Form 8-K, SEC File No. 001-33038, filed February 22, 2018).</u>
31.1*	<u>Certification pursuant to Section 302 of the Sarbanes-Oxley Act of 2002</u>
31.2*	<u>Certification pursuant to Section 302 of the Sarbanes-Oxley Act of 2002</u>
32.1*	<u>Certifications pursuant to 18 U.S.C. Section 1350</u>
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.

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**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 10, 2018

By: /s/ Kevin G. Lafond  
Kevin G. Lafond

Senior Vice President, Chief Accounting

Officer and Treasurer  
*(Principal Financial and Accounting Officer)*  
Dated: May 10, 2018