

ZIOPHARM ONCOLOGY INC  
Form 10-Q  
November 06, 2017  
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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 September 30, 2017**

**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><br><b>(State or other jurisdiction of</b>    | <b>84-1475642</b><br><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 October 31, 2017, was 141,962,789 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 finance our operations and business initiatives and to continue as a going concern;

the sufficiency of our cash and investments and our expected uses of cash;

the progress, timing and results of preclinical and clinical trials involving our product candidates;

the progress of our research and development programs;

the costs and timing of the development and commercialization of our products;

additional planned regulatory filings for the approval and commercialization of our immuno-oncology product candidates;

whether any of our other therapeutic discovery and development efforts will advance further in pre clinical research or in the clinical trial process and whether and when, if at all, our product candidates will receive final approval from the U.S. Food and Drug Administration or equivalent foreign regulatory agencies and for which indications;

whether any other therapeutic products we develop will be successfully marketed if approved;

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

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

competition from other pharmaceutical and biotechnology companies;

the development of, and our ability to take advantage of, the market for our product candidates;

the anticipated amount, timing and accounting of deferred revenues, milestones and other payments under licensing, collaboration or acquisition agreements, research and development costs and other expenses;

the strength and enforceability of our intellectual property rights;

our assessment of the potential impact on our future revenues of health care reform legislation in the United States;

the timing and impact of measures worldwide designed to reduce health care costs;

the uncertainty of economic conditions in certain countries in Europe and Asia such as related to the United Kingdom's referendum in June 2016 in which voters approved an exit from the European Union, commonly referred to as "Brexit"; and general economic conditions.

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.

#### **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>September 30,<br/>2017</b> | <b>December 31,<br/>2016</b> |
|---|-------------------------------|------------------------------|
| <b>ASSETS</b>   |                               |                              |
| Current assets:   |                               |                              |
| Cash and cash equivalents   | \$ 84,406                     | \$ 81,053                    |
| Receivables   | 13                            | 21                           |
| Prepaid expenses and other current assets   | 30,469                        | 23,810                       |
| Total current assets  | 114,888                       | 104,884                      |
| Property and equipment, net   | 1,047                         | 843                          |
| Deposits  | 128                           | 128                          |
| Other non-current assets  | 496                           | 493                          |
| Total assets  | \$ 116,559                    | \$ 106,348                   |
| <b>LIABILITIES, PREFERRED STOCK AND STOCKHOLDERS<br/>DEFICIT</b>  |                               |                              |
| Current liabilities:  |                               |                              |
| Accounts payable  | \$ 1,524                      | \$ 156                       |
| Accrued expenses  | 10,110                        | 9,109                        |
| Deferred revenue - current portion  | 6,389                         | 6,389                        |
| Deferred rent - current portion   | 166                           | 155                          |
| Total current liabilities   | 18,189                        | 15,809                       |
| Deferred revenue, net of current portion  | 36,736                        | 41,528                       |
| Deferred rent, net of current portion   | 14                            | 126                          |
| Derivative liabilities  | 2,350                         | 862                          |
| Total liabilities   | 57,289                        | 58,325                       |
| Commitments and contingencies (Note 6)  |                               |                              |
| Preferred stock, \$0.001 par value, 30,000,000 shares authorized  |                               |                              |
| Series 1 preferred stock, \$1,200 stated value; 250,000 designated; 116,127 and 106,184 shares issued and outstanding at September 30, 2017 and | 139,065                       | 125,321                      |

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December 31, 2016, respectively; liquidation value of \$139.4 million and \$127.4 million at September 30, 2017 and December 31, 2016, respectively

|   |            |            |
|---|------------|------------|
| Stockholders' deficit:  |            |            |
| Common stock, \$0.001 par value; 250,000,000 shares authorized; 141,962,789 and 132,376,670 shares issued and outstanding at September 30, 2017 and December 31, 2016, respectively |            |            |
|   | 142        | 132        |
| Additional paid-in capital - common stock   | 619,232    | 580,567    |
| Accumulated deficit   | (699,169)  | (657,997)  |
| Total stockholders' deficit   | (79,795)   | (77,298)   |
| Total liabilities and stockholders' deficit   | \$ 116,559 | \$ 106,348 |

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<br/>September 30,</b> |             | <b>For The Nine Months Ended<br/>September 30,</b> |              |
|---|---|-------------|--|--------------|
|   | <b>2017</b>   | <b>2016</b> | <b>2017</b>  | <b>2016</b>  |
| Collaboration revenue   | \$ 1,598  | \$ 1,598    | \$ 4,792   | \$ 5,264     |
| Operating expenses:   |   |             |  |              |
| Research and development  | 11,105  | 8,975       | 33,903   | 148,402      |
| General and administrative  | 3,571   | 3,537       | 10,946   | 11,058       |
| Total operating expenses  | 14,676  | 12,512      | 44,849   | 159,460      |
| Loss from operations  | (13,078)  | (10,914)    | (40,057)   | (154,196)    |
| Other income (expense), net   | 175   | 39          | 299  | 102          |
| Change in fair value of derivative liabilities  | 202   | 21          | (1,292)  | 21           |
| Net loss  | \$ (12,701)   | \$ (10,854) | \$ (41,050)  | \$ (154,073) |
| Preferred stock dividends   | \$ (4,903)  | \$ (3,591)  | \$ (13,939)  | \$ (3,591)   |
| Net loss applicable to common stockholders  | \$ (17,604)   | \$ (14,445) | \$ (54,989)  | \$ (157,664) |
| Basic and diluted net loss per share  | \$ (0.13)   | \$ (0.11)   | \$ (0.41)  | \$ (1.21)    |
| Weighted average common shares outstanding used to compute basic and diluted net loss per share | 140,632,297   | 130,496,035 | 135,689,364  | 130,347,370  |

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



Table of Contents**ZIOPHARM Oncology, Inc.****STATEMENT OF STOCKHOLDERS DEFICIT****For the Nine Months Ended September 30, 2017****(unaudited)****(in thousands, except share and per share data)**

|  | <b>Series 1 Preferred<br/>Stock - Mezzanine</b> |               | <b>Common Stock</b> |               | <b>Additional Paid In<br/>Capital Common Stock</b> |              | <b>Accumulated<br/>Deficit</b> | <b>Total Stockholders<br/>Deficit</b> |
|--|---|---------------|---------------------|---------------|--|--------------|--------------------------------|---------------------------------------|
|  | <b>Shares</b>                                   | <b>Amount</b> | <b>Shares</b>       | <b>Amount</b> |  |              |                                |                                       |
| Balance at<br>December 31, 2016  | 106,184   | \$ 125,321    | 132,376,670         | \$ 132        | \$ 580,567   | \$ (657,997) | \$ (77,298)                    |                                       |
| Cumulative effect<br>adjustment (Note 3)   |   |               |                     |               | 122  | (122)        |                                |                                       |
| Exercise of employee<br>stock options  |   |               | 26,047              | 1             | 98   |              | 99                             |                                       |
| Stock-based<br>compensation  |   |               |                     |               | 6,165  |              | 6,165                          |                                       |
| Restricted stock<br>buy-back at vesting to<br>cover taxes                              |   |               | (148,666)           | (1)           | (1,041)  |              | (1,042)                        |                                       |
| Issuance of common<br>stock, net of<br>commissions and<br>expenses of<br>\$2.7 million |   |               | 9,708,738           | 10            | 47,260   |              | 47,270                         |                                       |
| Preferred stock<br>dividends   | 9,943   | 13,744        |                     |               | (13,939)   |              | (13,939)                       |                                       |
| Net loss   |   |               |                     |               |  | (41,050)     | (41,050)                       |                                       |
| Balance at<br>September 30, 2017   | 116,127   | \$ 139,065    | 141,962,789         | \$ 142        | \$ 619,232   | \$ (699,169) | \$ (79,795)                    |                                       |

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 Nine Months<br/>Ended September 30,</b> |              |
|--|--|--------------|
|  | <b>2017</b>  | <b>2016</b>  |
| Cash flows from operating activities:  |  |              |
| Net loss   | \$ (41,050)  | \$ (154,073) |
| Adjustments to reconcile net loss to net cash used in operating activities:              |  |              |
| Depreciation and amortization  | 259  | 227          |
| Stock-based compensation   | 6,165  | 6,094        |
| Preferred stock issued in exchange for a license agreement                               |  | 118,936      |
| Change in fair value of derivative liabilities   | 1,292  | (21)         |
| Issuance of common stock in a license agreement  |  | 87           |
| Change in operating assets and liabilities:  |  |              |
| (Increase) decrease in:  |  |              |
| Receivables  | 8  | 421          |
| Prepaid expenses and other current assets  | (6,660)  | (9,611)      |
| Other noncurrent assets  | (3)  | 1            |
| Increase (decrease) in:  |  |              |
| Accounts payable   | 1,368  | (194)        |
| Accrued expenses   | 1,002  | (1,542)      |
| Deferred revenue   | (4,792)  | (5,264)      |
| Deferred rent  | (102)  | (322)        |
| Net cash used in operating activities  | (42,513)   | (45,261)     |
| Cash flows from investing activities:  |  |              |
| Purchases of property and equipment  | (461)  | (469)        |
| Net cash used in investing activities  | (461)  | (469)        |
| Cash flows from financing activities:  |  |              |
| Proceeds from exercise of stock options  | 99   | 551          |
| Repurchase of restricted common stock  | (1,042)  | (853)        |
| Repurchase of common stock   |  | (2)          |
| Proceeds from issuance of common stock, net of commissions and expenses of \$2.7 million | 47,270   |              |
| Net cash provided by (used in) financing activities                                      | 46,327   | (304)        |
| Net decrease in cash and cash equivalents  | 3,353  | (46,034)     |

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|  |           |            |
|--|-----------|------------|
| Cash and cash equivalents, beginning of period                                 | 81,053    | 140,717    |
| Cash and cash equivalents, end of period                                       | \$ 84,406 | \$ 94,683  |
| <b>Supplementary disclosure of cash flow information:</b>                      |           |            |
| Cash paid for interest   | \$        | \$         |
| Cash paid for income taxes   | \$        | \$         |
| <b>Supplementary disclosure of noncash investing and financing activities:</b> |           |            |
| Series 1 preferred stock issued as consideration for a license agreement       | \$        | \$ 119,045 |
| Payment of Series 1 preferred stock dividends in preferred stock               | \$ 13,939 | \$ 3,591   |

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 or the Company, is a biopharmaceutical company seeking to develop, acquire, and commercialize, on its own or with partners, a diverse portfolio of immuno-oncology therapies.

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

The Company has operated at a loss since its inception in 2003 and has minimal revenues to date. The Company anticipates that its losses will continue for the foreseeable future. As of September 30, 2017, the Company has approximately \$84.4 million of cash and cash equivalents. At September 30, 2017, the Company's accumulated deficit was approximately \$699.2 million. Given its development plans, the Company anticipates its cash resources will be sufficient to fund its operations into the fourth quarter of 2018. The Company will need to raise additional capital, whether through a sale of equity or debt securities, licensing arrangements, asset sales, additional product collaborations or other means, to complete the development and commercialization of its product candidates, to support its ongoing activities and to continue as a going concern. The forecast of cash requirements 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 including changes in the Company's business strategy and direction of its research and development efforts, competitive and technical advances, regulatory changes or other developments.

The Company has based its estimates on assumptions that may prove to be wrong, and its expenses could prove to be significantly higher than it currently anticipates. Management does not know whether additional financing will be on terms favorable or acceptable to the Company when needed, if at all. There can be no assurance that any such financing can be realized by the Company, or if realized, what the terms thereof may be, or that any amount that the Company is able to raise will be adequate to support the Company's working capital requirements until it achieves profitable operations. If adequate additional funds are not available when required, or if the Company is unsuccessful in entering into collaboration or partnership agreements for further development of its product candidates, management may need to curtail its current development efforts and cut operating costs in order to conserve its cash. Based on the forecast, management determined that there is substantial doubt regarding the Company's 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, 2016, included in the Company's Annual Report on Form 10-K for the fiscal year ended December 31, 2016 filed with the SEC on February 16, 2017, or the Form 10-K.

The interim financial statements do not include all of the information and footnotes required by GAAP for complete financial statements, as allowed by the relevant SEC rules and regulations; however, the Company believes that its disclosures are adequate to ensure that the information presented is not misleading.

The results disclosed in the statements of operations for the three and nine months ended September 30, 2017 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;

fair value measurements of stock based compensation, warrants 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. Financings**

On May 11, 2017, the Company sold in an underwritten public offering an aggregate of 9,708,738 shares of its common stock. The price to the public in the offering was \$5.15 per share, and the underwriters agreed to purchase the shares from the Company pursuant to the underwriting agreement at a purchase price of \$4.893 per share. The offering was made pursuant to the Company's effective registration statement on Form S-3ASR (File No. 333-201826) previously filed with the SEC, and a prospectus supplement thereunder. The net proceeds from the offering were approximately \$47.3 million after deducting underwriting commissions and estimated offering expenses payable by the Company.

### 3. Summary of Significant Accounting Policies

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.

#### *New Accounting Pronouncements*

In May 2014, the Financial Accounting Standards Board, or FASB, issued ASU 2014-09, *Revenue from Contracts with Customers* (Topic 606) (ASU 2014-09), which clarifies the principles for recognizing revenue and develops a common revenue standard for U.S. GAAP and International Financial Reporting Standards, or IFRS. This standard removes inconsistencies and weaknesses between U.S. GAAP and IFRS in revenue requirements, provides a more robust framework for addressing revenue issues, improves comparability of revenue recognition practices across entities, industries, jurisdictions, and capital markets, provides more useful information to users of financial statements through improved disclosure requirements, and simplifies the preparation of financial statements by reducing the number of requirements to which an entity must refer. This update is effective for annual periods beginning after December 15, 2017, including interim periods within that reporting period and early application is not permitted. We expect to adopt this standard using the modified retrospective approach on January 1, 2018. We are in the process of completing our assessment and anticipate that the implementation will result in a decrease to collaboration revenues and an increase to deferred revenue. We continue to review the impact that this new standard will have on collaboration and license arrangements as well our financial statement disclosures.

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**ZIOPHARM Oncology, Inc.**

**NOTES TO FINANCIAL STATEMENTS (unaudited)**

**3. Summary of Significant Accounting Policies (continued)**

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

In March 2016, the FASB issued ASU No. 2016-09, Compensation – Stock Compensation (Topic 718): *Improvements to Employee Share-Based Accounting*, or ASU 2016-09, to require changes to several areas of employee share-based payment accounting in an effort to simplify share-based reporting. ASU 2016-09 is effective for annual reporting periods beginning after December 15, 2016, including interim reporting periods within each annual reporting period. The Company adopted this standard on January 1, 2017. The update revises requirements in the following areas: minimum statutory withholding, accounting for income taxes, and forfeitures. Prior to adoption, the Company recognized share-based compensation, net of estimated forfeitures, over the vesting period of the grant. Upon adoption of ASU 2016-09, the Company elected to change its accounting policy to recognize forfeitures as they occur. The new forfeiture policy election was adopted using a modified retrospective approach with a cumulative effect adjustment recorded to retained earnings as of January 1, 2017. The update requires the Company to recognize the income tax effect of awards in the income statement when the awards vest or are settled. It also allows the Company to repurchase more of an employee's shares than it can today for tax withholding purposes without triggering a liability. The income tax related items had no effect on the current period presentation and the Company maintains a full valuation allowance against its deferred tax assets.

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

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



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

Table of Contents**ZIOPHARM Oncology, Inc.****NOTES TO FINANCIAL STATEMENTS (unaudited)****4. 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 September 30, 2017 and December 31, 2016 were as follows:

*(\$ in thousands)*

| Description            | Balance as of<br>September 30, 2017 | Fair Value Measurements at Reporting Date Using<br>Quoted Prices in<br>Active Markets for |  |   |
|------------------------|-------------------------------------|---|--|---|
|                        |                                     | Identical<br>Assets/Liabilities<br>(Level 1)  | Significant Other<br>Inputs<br>(Level 2) | Significant<br>Unobservable Inputs<br>(Level 3) |
| <b>Assets:</b>         |                                     |   |  |   |
| Cash equivalents       | \$ 79,488                           | \$ 79,488   | \$                                       | \$  |
| <b>Liabilities:</b>    |                                     |   |  |   |
| Derivative liabilities | \$ (2,350)                          | \$  | \$                                       | \$ (2,350)                                      |



Table of Contents**ZIOPHARM Oncology, Inc.****NOTES TO FINANCIAL STATEMENTS (unaudited)****4. Fair Value Measurements (continued)**

(\$ in thousands)

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

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

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

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

## 5. 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 September 30, 2017 and 2016 consisted of the following:

|                           | September 30, |            |
|---------------------------|---------------|------------|
|                           | 2017          | 2016       |
| Stock options             | 3,622,335     | 3,448,070  |
| Unvested restricted stock | 1,330,492     | 1,236,388  |
| Preferred stock           | 22,398,582    | 22,564,685 |
|                           | 27,351,409    | 27,249,143 |

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**ZIOPHARM Oncology, Inc.**

**NOTES TO FINANCIAL STATEMENTS (unaudited)**

**5. Net Loss per Share (continued)**

The Series 1 preferred stock automatically converts into shares of common stock upon the date the first approval in the United States of (i) a ZIOPHARM Product, as defined in and developed under the Exclusive Channel Partner Agreement dated as of January 6, 2011 and as amended from time to time, by and between the Company and Intrexon, 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 September 30, 2017, the Series 1 preferred stock would convert into 22,398,582 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.

**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 non-current assets on the balance sheet as of September 30, 2017 and December 31, 2016. The lease for office space in New York, NY expires in October 2018.

On October 17, 2013, the Company entered into a sublease agreement to lease all of its New York office space to a subtenant. The Company remains primarily liable to pay rent on the original lease. The Company recorded a loss on the sublease in the amount of \$729 thousand for the year ended December 31, 2013, representing the remaining contractual obligation of \$2.3 million, less \$1.6 million in payments from its subtenant. The Company continues to maintain the \$388 thousand letter of credit in respect of the New York office space and recorded in other non-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 September 30, 2017, and December 31, 2016, a total security deposit of \$128 thousand is included in deposits on the balance sheet.

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Total rent expense was approximately \$177 thousand and \$545 thousand for the three and nine months ended September 30 2017, respectively. Total rent expense for the three and nine months ended September 30, 2016 was \$109 thousand and \$231 thousand, 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 September 30, 2017 and December 31, 2016 of \$180 thousand (\$166 thousand current and \$14 thousand long-term) and \$281 thousand (\$155 thousand current and \$126 thousand 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 Intrexon Corporation for the Cancer Programs*

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

The Channel Agreement grants the Company a worldwide license to use patents and other intellectual property of Intrexon in connection with the research, development, use, importing, manufacture, sale, and offer for sale of products involving DNA administered to humans for expression of anti-cancer effectors for the purpose of treatment or prophylaxis of cancer, which 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 Intrexon's written consent.

Under the Channel Agreement, and subject to certain exceptions, the Company is responsible for, among other things, the performance of the Cancer Program, including the development, commercialization and certain aspects of manufacturing of ZIOPHARM Products. Intrexon 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 Intrexon's patents.

Subsequent to the the 2016 ECP Amendment, discussed below, and subject to certain expense allocations and other offsets provided in the Channel Agreement, the Company is obligated to pay Intrexon 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 Intrexon on a quarterly basis 50% of revenue obtained in that quarter from a sublicensor in the event of a sublicensing arrangement. In addition, in partial consideration for each party's execution and delivery of the Channel Agreement, the Company entered into a stock purchase agreement with Intrexon.

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



Is being commercialized by 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 Intrexon 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 the Company due to an uncured breach or a termination by Intrexon following an unconsented assignment by the Company or its election not to pursue development of a Superior Therapy (as defined in the Channel Agreement)).

The Company's obligation to pay 20% of net profits or revenue described above with respect to these retained products will survive termination of the Channel Agreement.

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**ZIOPHARM Oncology, Inc.**

**NOTES TO FINANCIAL STATEMENTS (unaudited)**

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

*Exclusive Channel Collaboration Agreement with Intrexon Corporation for Graft-Versus-Host Disease (GvHD)*

On September 28, 2015, the Company entered into the GvHD Agreement with Intrexon, whereby the Company will use Intrexon's technology directed towards *in vivo* expression of effectors to research, develop and commercialize products for use in the treatment or prevention of graft-versus-host disease, or GvHD. GvHD may occur after a bone marrow or stem cell transplant in which someone receives bone marrow tissue or cells from a donor. The new, transplanted cells regard the recipient's body as foreign. When this happens, the newly transplanted cells attack the recipient's body.

The exclusive collaboration, or the GvHD Program, will focus on the pursuit of the following engineered cell therapy strategies, used either separately or in combination, for the targeted treatment of GvHD: (i) the infusion of regulatory T cells expressing membrane-bound and/or soluble interleukin-2 and (ii) the deployment of orally delivered, genetically modified *L. lactis* that express interleukin-2 to modulate immune function. The GvHD Agreement establishes committees comprising Company and Intrexon representatives that will govern activities related to the GvHD Program in the areas of project establishment, chemistry, manufacturing and controls, clinical and regulatory matters, commercialization activities and intellectual property.

The GvHD Agreement grants the Company a worldwide license to use specified patents and other intellectual property of Intrexon in connection with the research, development, use, importing, manufacture, sale, and offer for sale of products developed under the GvHD Program, or the Products. Such license is exclusive with respect to any clinical development, selling, offering for sale or other commercialization of the Products, and otherwise is non-exclusive. Subject to limited exceptions, the Company may not sublicense the rights described without Intrexon's written consent.

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

The Company paid Intrexon a technology access fee of \$10.0 million in cash in October 2015 and will reimburse Intrexon for all research and development costs. Subject to certain expense allocations and other offsets provided in the GvHD Agreement, the GvHD Agreement also provides for equal sharing of the profits derived from the sale of the Products. 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.

During the first 24 months after September 28, 2015, the GvHD Agreement may be terminated by (i) either party in the event of a material breach by the other, except for the failure of the other party to use diligent efforts or to comply with any diligence obligations set forth in the GvHD Agreement and (ii) Intrexon under certain circumstances if the Company assigns its rights under the GvHD Agreement without Intrexon's consent. Following such twenty-four-month period, Intrexon may also terminate the GvHD Agreement if the Company elects not to pursue the development of the GvHD Program identified by Intrexon that is a Superior Therapy, as defined in the GvHD Agreement. Also following such period, the Company may voluntarily terminate the GvHD Agreement upon 90 days written notice to Intrexon.

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**ZIOPHARM Oncology, Inc.**

**NOTES TO FINANCIAL STATEMENTS (unaudited)**

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

Upon termination of the GvHD Agreement, the Company may continue to develop and commercialize any 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 Intrexon due to a Company uncured breach or a voluntary termination by the Company), or an ongoing Phase 1 clinical trial (in the case of a termination by the Company due to an Intrexon uncured breach or a termination by Intrexon following an unconsented assignment by the Company or the Company's election not to pursue development of a Superior Therapy).

The Company's obligation to pay 20% of net profits or revenue with respect to these retained products will survive termination of the GvHD Agreement.

*Amendment of Collaborations with Intrexon*

On March 27, 2015, the Company and Intrexon entered into an Exclusive Channel Partner Amendment, or 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 Intrexon/ZIOPHARM collaboration under the Channel Agreement. The ECP Amendment provides that Intrexon will pay to the Company fifty percent of all payments Intrexon 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 amending the Channel Agreement, and (2) the 2016 GvHD Amendment, amending the GvHD Agreement. The 2016 ECP Amendment reduced the royalty percentage that the Company will pay to Intrexon 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 will pay to Intrexon 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 Ares Trading S.A., or Ares Trading, a subsidiary of 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 agreed to issue to 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).

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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, 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 and Intrexon 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 Chief Executive Officer of the Company on May 7, 2015 and was formerly a tenured professor of pediatrics at MD Anderson and is now currently a visiting scientist under that institution's policies, as well as either co-exclusive or non-exclusive licenses under certain related technologies.

Pursuant to the terms of the MD Anderson License, MD Anderson received consideration consisting of \$50.0 million in shares of the Company's 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 of 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 and Intrexon entered into a letter agreement, or the Letter Agreement, pursuant to which MD Anderson received consideration of \$7.5 million in shares of the Company's 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 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 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 will provide 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 nine months ended September 30, 2017, the Company made payments in the aggregate amount of \$9.3 million to MD Anderson compared to \$11.3 million during the nine months ended September 30, 2016. The decrease in cash paid to MD Anderson during 2017 is a result of approved expenditures incurred by the Company being deducted from the April and July 2017 payment. As of September 30, 2017, MD Anderson had used \$6.2 million to offset costs incurred pursuant to the MD Anderson License and the Research and Development Agreement. The net balance of \$29.4 million is included in other current assets at September 30, 2017. The Company's final payment to MD Anderson is due in January 2018 and the Company will continue to assess the timing and expected use of the funds.

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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 and Intrexon shall then have a fully-paid up, royalty free, perpetual, irrevocable and sublicensable license to use the licensed intellectual property thereunder. After ten years from the date of the 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 Intrexon are not using commercially reasonable efforts to commercialize the licensed intellectual property on a case-by-case basis. After five years from the date of the MD Anderson License and subject to a 180-day cure period, MD Anderson will have the right to terminate the MD Anderson License with respect to specific technology(ies) funded by the government or subject to a third party contract if the Company and Intrexon are not meeting the diligence requirements in such funding agreement or contract, as applicable. MD Anderson may also terminate the agreement with written notice upon material breach by the Company and Intrexon, if such breach has not been cured within 60 days of receiving such notice. In addition, the MD Anderson License will terminate upon the occurrence of certain insolvency events for both the Company and Intrexon and may be terminated by the mutual written agreement of the Company, Intrexon 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 and MD Anderson entered into a Registration Rights Agreement, or the Registration Rights Agreement, pursuant to which the Company agreed to file a resale registration statement, or the Registration Statement, registering the resale of the License Shares, the Incentive Shares and any other shares of the Company's common stock held by MD Anderson on the date that the Registration Statement is filed. Under the terms of the Registration Rights Agreement, the Company is obligated to maintain the effectiveness of the Registration Statement until all securities therein are sold or are otherwise can be sold pursuant to Rule 144, without any restrictions. A prospectus supplement under the Company's already effective registration statement on Form S-3 (File No. 333-201826) was filed on April 1, 2015 in satisfaction of the Company's 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 and Intrexon 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 expects to perform multiple preclinical development programs, each consisting of the development of one product candidate, pursuant to the agreement. The Company and Intrexon 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 Intrexon.

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**ZIOPHARM Oncology, Inc.**

**NOTES TO FINANCIAL STATEMENTS (unaudited)**

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

Intrexon is entitled to receive \$5.0 million 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 and nine months ended September 30, 2017, the Company has expensed \$718 thousand and \$994 thousand under the Ares Trading Agreement, respectively.

Ares Trading paid a non-refundable upfront fee of \$115.0 million to Intrexon as consideration for entry into the Ares Trading Agreement. Pursuant to the ECP Amendment, the Company was entitled to receive 50% of the upfront fee, or \$57.5 million, which the Company 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, or the FDA, or other global regulatory authorities. Commercial milestone payments are triggered when an approved pharmaceutical product reaches certain defined levels of net sales by the licensee. The Ares Trading Agreement also provides for up to \$50.0 million of one-time payments upon the achievement of certain technical milestones evidenced by the initiation of a defined phase of clinical research. All development, regulatory and technical milestones are considered substantive on the basis of the contingent nature of the milestone, specifically reviewing factors such as the scientific, clinical, regulatory, commercial and other risks that must be overcome to achieve the milestone as well as the level of effort and investment required. Accordingly, such amounts will be recognized as revenue in full in the period in which the associated milestone is achieved, assuming all other revenue recognition criteria are met. All commercial milestones will be accounted for in the same manner as royalties and recorded as revenue upon achievement of the milestone, assuming all other revenue recognition criteria are met. The next potential milestone payment that Intrexon 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, Intrexon 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. Intrexon will pay 50% of all milestone and royalty payments that it receives under the Ares Trading Agreement to the Company 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 the Company.

The Company considered FASB Accounting Standards Codification 605-25, *Multiple-Element Arrangements*, in evaluating the appropriate accounting for the Ares Trading Agreement. In accordance with this guidance, the Company identified the license and research and development services as the Company's deliverables in the

arrangement. The Company concluded that the license does not have standalone value independent from the research and development services. Accordingly, the Ares Trading Agreement is accounted for by the Company as a single unit of accounting. The \$57.5 million upfront payment received by the Company was recorded as deferred revenue and is being recognized over the estimated period of performance of the research and development services which are currently estimated to be nine years, beginning with the commencement of the research and development services. During the three and nine months ended September 30, 2017 and 2016, the Company recognized \$1.6 million, each quarter, of revenue related to the Ares Trading Agreement. As of September 30, 2017, the remaining balance of deferred revenue associated with the upfront payment is \$43.1 million, of which \$6.4 million is current and \$36.7 million is classified as long-term. As of December 31, 2016, the remaining balance of deferred revenue associated with the upfront payment was \$47.9 million, of which \$6.4 million was current and \$41.5 million was classified as long term.

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

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

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**Table of Contents****ZIOPHARM Oncology, Inc.****NOTES TO FINANCIAL STATEMENTS (unaudited)****6. Commitments and Contingencies (Continued)**

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

*Collaboration Agreement with Solasia Pharma K.K.*

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

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

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**ZIOPHARM Oncology, Inc.**

**NOTES TO FINANCIAL STATEMENTS (unaudited)**

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

*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. One remaining royalty payment of \$250 thousand is due 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 nine months ended September 30, 2017 and 2016.

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

On January 10, 2017, the Company announced the signing of a Cooperative Research and Development Agreement, or CRADA, with the National Cancer Institute, or NCI, for the development of adoptive cell transfer, or ACT,-based immunotherapies genetically modified using the *Sleeping Beauty*, or 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, or 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 for this CRADA is \$5.6 million over the next three years, payable in \$625 thousand payments on a quarterly basis. During the nine months ended September 30, 2017, the Company paid and expensed three payments totaling \$1.9 million.

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**ZIOPHARM Oncology, Inc.**

**NOTES TO FINANCIAL STATEMENTS (unaudited)**

**7. Related Party Transactions**

***Collaborations with Intrexon***

On January 6, 2011, the Company entered into the Channel Agreement with Intrexon (Note 6). A director of the Company, Randal J. Kirk, is the CEO, 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 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 entered into with Ares Trading, on March 27, 2015. The ECP Amendment provided that Intrexon will pay to the Company 50% of all payments that Intrexon 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.

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**ZIOPHARM Oncology, Inc.**

**NOTES TO FINANCIAL STATEMENTS (unaudited)**

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

On September 28, 2015, the Company entered into the GvHD Agreement with Intrexon, whereby the Company will use Intrexon'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 Intrexon a technology access fee of \$10.0 million in cash in October 2015 and will reimburse Intrexon for all research and development costs. Subject to certain expense allocations and other offsets provided in the ECC Agreement, the ECC Agreement also provides for equal sharing of the profits derived from the sale of the Products.

On June 29, 2016, the Company entered into the 2016 ECP Amendment, with Intrexon, 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 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 will pay to Intrexon 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 September 30, 2017, the Company issued an aggregate of 3,414 shares of Series 1 preferred stock to Intrexon, the holder of all of the outstanding shares of the Company's Series 1 preferred stock, as monthly dividend payments. The Company recorded such shares of Series 1 preferred stock at a fair value of \$4.9 million, which is a component of temporary equity and recorded a gain on the change of the derivative liabilities in the amount of \$202 thousand. See Notes 4 and 9 for additional discussion regarding the accounting for and valuation of these derivative financial instruments.



During the three months ended September 30, 2017 and 2016, the Company expensed \$5.6 million and \$4.9 million, respectively, for services performed by Intrexon. During the nine months ended September 30, 2017 and 2016, the Company expensed \$16.8 million and \$17.0 million, respectively, for services performed by Intrexon. As of September 30, 2017 and December 31, 2016, the Company recorded \$5.5 million and \$3.4 million, respectively, in current liabilities on its balance sheet for amounts due to Intrexon.

***Collaboration with Intrexon and MD Anderson***

On January 13, 2015, the Company, together with Intrexon, 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 Intrexon 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 nine months ending September 30, 2017, the Company made three quarterly payments totaling \$9.3 million, bringing the total aggregate payments to \$35.6 million under this arrangement.

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<br/>ended September 30,</b> |             | <b>For the nine months<br/>ended September 30,</b> |             |
|----------------------------------|---|-------------|--|-------------|
|                                  | <b>2017</b>   | <b>2016</b> | <b>2017</b>  | <b>2016</b> |
| Research and development         | \$ 615  | \$ 505      | \$ 1,772   | \$ 1,398    |
| General and administrative       | 1,467   | 1,514       | 4,393  | 4,696       |
| Stock-based compensation expense | \$ 2,082  | \$ 2,019    | \$ 6,165   | \$ 6,094    |

The Company granted 593,500 and 859,000 stock options during the three and nine months ended September 30, 2017 with a weighted-average grant date fair value of \$4.29 and \$4.34 per share, respectively. The Company granted an aggregate of 21,300 and 157,300 stock options during the three and nine months ended September 30, 2016 with a weighted-average grant date fair value of \$3.71 and \$5.36 per share, respectively.

For the three months ended September 30, 2017 and 2016, 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 September 30,</b> |                |
|-------------------------|---|----------------|
|                         | <b>2017</b>                                     | <b>2016</b>    |
| Risk-free interest rate | 1.88 - 2.01%                                    | 1.27 - 1.37%   |
| Expected life in years  | 6   | 6              |
| Expected volatility     | 80.82 - 80.95%                                  | 79.26 - 79.34% |
| Expected dividend yield | 0   | 0              |

The Company adopted 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.

Table of Contents**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 nine months ended September 30, 2017 is as follows:

|   | <b>Number<br/>of<br/>Shares</b> | <b>Weighted-<br/>Average Exercise<br/>Price</b> | <b>Weighted-<br/>Average<br/>Contractual<br/>Term (Years)</b> | <b>Aggregate<br/>Intrinsic Value</b> |
|---|---------------------------------|---|---|--------------------------------------|
| Outstanding, December 31, 2016          | 3,465,335                       | \$ 5.07   |   |                                      |
| Granted                                 | 359,000                         | 6.28  |   |                                      |
| Exercised                               | (80,000)                        | 4.85  |   |                                      |
| Cancelled                               | (122,000)                       | 6.64  |   |                                      |
| Outstanding, September 30, 2017         | 3,622,335                       | \$ 5.14   | 6.22  | \$ 5,657                             |
| Options exercisable, September 30, 2017 | 2,696,835                       | \$ 4.62   | 5.39  | \$ 5,215                             |
| Options exercisable, December 31, 2016  | 2,671,835                       | \$ 4.40   | 5.88  | \$ 3,383                             |
| Options available for future grant      | 1,540,760                       |   |   |                                      |

At September 30, 2017, 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 1.71 years.

In September 2017, the Company granted an option for 500,000 shares of its common stock, with an exercise price of \$6.16 per share, and vesting one third on the next three grant date anniversaries. This option was granted outside of the 2012 plan and therefore, is not included in the table above. The grant date fair value was \$2.2 million. As of September 30, 2017, all 500,000 options are outstanding with a remaining contractual life of 10.0 years.

A summary of the status of unvested restricted stock for the nine months ended September 30, 2017 is as follows:

|                               | <b>Number of Shares</b> | <b>Weighted-Average<br/>Grant Date Fair Value</b> |
|-------------------------------|-------------------------|---|
| Non-vested, December 31, 2016 | 1,680,492               | \$ 7.49   |
| Granted                       |                         |   |

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|                                |           |    |      |
|--------------------------------|-----------|----|------|
| Vested                         | (350,000) |    | 9.35 |
| Cancelled                      |           |    |      |
| Non-vested, September 30, 2017 | 1,330,492 | \$ | 9.46 |

At September 30, 2017, total unrecognized compensation costs related to unvested restricted stock outstanding amounted to \$6.0 million. The cost is expected to be recognized over a weighted-average period of 1.33 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 (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 Value**

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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**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 \$0.7 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 \$118.4 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.

During the three months ended September 30, 2017, the Company issued an aggregate of 3,414 shares of Series 1 preferred stock to Intrexon, the holder of all of the outstanding shares of its Series 1 preferred stock, as monthly dividend payments. The Company recorded such shares of Series 1 preferred stock at a fair value of \$4.9 million, which is a component of temporary equity and recorded a gain on the change in fair value of the derivative liabilities in the amount of \$202 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 |
| September 30, 2017:      |                        |            |
| Derivative liabilities   | Liabilities            | \$ 2,350   |

The change in the derivative liability for the three months ended September 30, 2017 consisted of the following:

| <i>(\$ in thousands)</i>                       |            |
|--|------------|
|  | Fair Value |
| Balance, June 30, 2017                         | \$ 2,480   |
| Dividends                                      | 72         |
| Change in fair value of derivative liabilities | (202)      |
| Balance, September 30, 2017                    | \$ 2,350   |

The fair value of the Series 1 preferred stock dividends were 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:

|                         | September 30, 2017 | December 31, 2016 |
|-------------------------|--------------------|-------------------|
| Risk-free interest rate | 1.72%              | 1.69%             |
| Expected dividend rate  | 0                  | 0                 |
| Expected volatility     | 70.20%             | 72.70%            |



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

See Notes 4 and 9 for additional discussion regarding the accounting for and valuation of these derivative financial instruments.

**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. In particular, statements contained in this Form 10-Q, 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. These statements relate to our future plans, objectives, expectations and intentions and may be identified by words such as may, will, should, expects, plans, anticipates, intends, targets, projects, contemplates, believes, seeks, goals, estimates, predict, continue or similar words. 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 identified below, under Part II, Item 1A. Risk Factors and elsewhere herein. Therefore, actual results may differ materially and adversely from those expressed in any forward-looking statements. We undertake no obligation to revise or update any forward-looking statements for any reason.

**Company Overview**

ZIOPHARM Oncology, Inc. is a biopharmaceutical company seeking to develop, acquire and commercialize, on its own or with partners, a diverse portfolio of immuno-oncology therapies. We are currently focused on developing therapeutics 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 and graft-versus-host-disease (GvHD), a type of auto-immune disease. Pursuant to two exclusive channel partner agreements, or Channel Agreements with Intrexon Corporation, or Intrexon, we obtained certain exclusive rights to Intrexon's technologies for use in the fields of oncology and GvHD.

The technologies represent an industrialized engineering approach for molecular and cell biology and gene control. They employ an inducible gene-delivery system, or switch, that enables controlled *in vivo* expression of genes that produce therapeutic proteins to treat cancer. We and Intrexon refer to this switch as the RheoSwitch Therapeutic System®, or RTS®, platform. Our initial product candidate being developed using the immuno-oncology platform is Ad-RTS-IL-12 + veledimex, a clinical-stage product that we license from Intrexon under the Channel Agreement in the field of oncology.

Ad-RTS-IL-12 + veledimex uses our gene delivery system to produce interleukin-12, or IL-12, a potent, naturally occurring anti-cancer protein. 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. Additionally, expression of functional IL-12 in human subjects by direct intratumoral injection of Ad-RTS-hIL-12 + veledimex is further demonstrated by the generation of downstream interferon gamma, or IFN-g.

On November 6, 2017, the Company announced details regarding four abstracts being presented as part of the 22<sup>nd</sup> Annual Meeting and Education Day of the Society for Neuro-Oncology (SNO). E. Antonio Chiocca, M.D., Ph.D. will present an e-talk, entitled, A Phase 1 study of Ad-RTS-hIL-12 + veledimex in adult recurrent glioblastoma on Saturday, November 18, 2017. John A Barrett Ph.D., Ziopharm Vice President of Research and Development/Translational Medicine. will present two oral presentations; the first, entitled, Controlled expression of

IL-12 improves survival in glioma by activating the immune response in mice and humans will be presented on Sunday, November 19, 2017; the second, entitled, Controlled local expression of IL-12 as gene therapy concomitant with systemic chemotherapy improves survival in glioma will be presented on Sunday, November 19, 2017. Stewart Goldman, MD, will present a poster, entitled Phase 1 study of Ad-RTS-hIL-12 + veledimex in pediatric brain tumors on Friday, November 17, 2017.

On October 16, 2017, we announced that the first patient has been dosed in a new Phase 1 study 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 in the cortex, while the second is comprised of pediatric patients with diffuse intrinsic pontine glioma (DIPG). This Phase 1 study 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.

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On September 18, 2017 we announced updated data from a subset of patients in its Phase 1 multicenter study of Ad-RTS-hIL-12 + veledimex in patients with recurrent or progressive glioblastoma (GBM) was presented by E. Antonio Chiocca, M.D., Ph.D., Harvey W. Cushing Professor of Neurosurgery, Department of Surgery, Harvard Medical School, Surgical Director, Center for Neuro-oncology, Dana-Farber Cancer Institute, Chairman, Neurosurgery, Brigham and Women's Hospital and Co-Director, Institute for the Neurosciences, Brigham and Women's Hospital at the 79<sup>th</sup> Annual Meeting of the American Academy of Neurological Surgery (AAcNS) in Santa Barbara, CA. Dr. Chiocca's oral presentation, included detail on three biopsied patients that were shown to have pseudo-progression rather than tumor progression. Pseudo-progression may be seen in post-treatment imaging studies of the brain, where the tumor site appears larger compared to baseline, but these changes were shown to be due to infiltration of immune cells, as evidenced by subsequent biopsies. Importantly, some GBM lesions on repeated MRI scans showed evidence of similar progression, later followed by regression, which is consistent with immune-mediated anti-tumor effects, the postulated mechanism of action underlying Ad-RTS-hIL-12 + veledimex.

On September 28, 2017, we announced the appointment of David Mauney, M.D., as our Executive Vice President and Chief Business Officer. Dr. Mauney has assumed leadership of our corporate development and investor strategy functions, and, as of November 6, 2017, he has also assumed the role of interim Chief Operating Officer, reporting directly to Laurence Cooper, M.D., Ph.D., our Chief Executive Officer.

On June 28, 2017, we announced the initiation of a stereotactic treatment cohort in our Phase 1 study of Ad-RTS-hIL-12 + veledimex in rGBM. The stereotactic study arm serves as a runway to clinical studies of controlled IL-12 gene therapy in pediatric patients and in adult patients in combination with checkpoint inhibitors. The stereotactic cohort will include patients with rGBM that are not scheduled to undergo surgical resection to assess the safety and tolerability of a single dose of Ad-RTS-hIL-12 administered via injection and activated with orally-administered veledimex (initially, 20 mg QD, days 1-14). By introducing stereotactic administration, we broaden the population of patients who may be eligible for treatment, including children with DIPG, a rapidly fatal and inoperable form of brain cancer. Additionally, preclinical studies of this tunable IL-12 gene therapy in combination with an immune checkpoint inhibitor have yielded promising results, notably a 100 percent survival rate was observed in a cohort of the treated mice, and we will be advancing this approach into the clinic in the next few months.

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At the 2017 American Society of Clinical Oncology Annual Meeting held in June, the Company reported encouraging results from patients receiving intratumoral Ad-RTS-hIL-12 with 20 mg of orally-administered veledimex (n = 15) following craniotomy, with a median overall survival (mOS) of 12.5 months comparing favorably to historical controls. The mOS compares favorably with the survival of patients in other studies who received approved medications and device for the treatment of rGBM.

In support of the mOS data, the Company has provided three lines of evidence to show why patients with rGBM may benefit from Ad-RTS-hIL-12 + veledimex. The first is that patients who received low dose systemic corticosteroids for post-operative management have a much better survival rate than those who received elevated systemic corticosteroids, as the latter presumably interferes with immune activation. The second mOS appears directly correlated to a ratio of CD8<sup>+</sup>/FOXP3<sup>+</sup> (effector/suppressor) T cells measured in peripheral blood which is consistent with IL-12-mediated cellular immune activation. The third is that biopsies of three patients 22 weeks after completion of veledimex showed new infiltration of CD8<sup>+</sup> T cells which produce IFN-gamma which is attributed to the effects of IL-12, as well the evidence of the imaging phenomenon known as pseudo-progression, a confirmatory response to the immune activation by IL-12.

The Company is pleased with the recent confirmatory evidence of mechanism of action underlying the observed therapeutic effect and continues to progress towards a registration study for Ad-RTS-hIL-12 + veledimex for rGBM. Based on guidance from U.S. and European regulatory authorities on such a registration study, the Company is planning to initiate a randomized control trial by the end of 2017. The Company remains in active discussions with multiple potential collaborators relative to the execution of the registration study of Ad-RTS-hIL-12 + veledimex.

Pursuant to our Channel Agreement for the cancer program, in January 2015, we and Intrexon obtained an exclusive, worldwide license to certain additional immuno-oncology technologies owned and licensed by The University of Texas MD Anderson Cancer Center, or MD Anderson, including technologies relating to novel chimeric antigen receptors, or CARs, natural killer cells, or NK cells and T-cell receptors, or TCRs. We refer to this as the MD Anderson License. We plan to use these technologies to develop genetically modified T cells and other immune cells that will target and kill cancer cells using viral and non-viral approaches to gene transfer. Regarding our non-viral gene transfer approach, we are using *Sleeping Beauty*, or SB, a transposon/transposase system under the MD Anderson License to express CAR in clinical trials to render T cells specific for CD19. This approach differs from that of many of our competitors in that it does not rely on virus for gene transfer. We believe product manufacturing using the SB approach will be simpler, faster, and less costly than viral manufacturing. The initial associated trials using the first-generation CAR with a four-week manufacturing process showed favorable progression-free survival, or PFS, and/or overall survival when patient- and donor-derived CAR T cells, or CAR<sup>+</sup> T, were infused after hematopoietic stem-cell transplantation, or HSCT. All patients receiving autologous SB-modified T cells had non-Hodgkin lymphoma, or NHL, and most patients receiving allogeneic CAR<sup>+</sup> T cells had acute lymphoblastic leukemia, or ALL. The safety data associated with patients who received SB-modified T cells is reassuring. A summary of the initial clinical experience using SB-modified CD19-specific CAR<sup>+</sup> T cells in patients with NHL and ALL was published in the *Journal of Clinical Investigation* in September 2016. In addition to survival of the recipients, these trials demonstrated that the infused T cells persisted for lengths of time that compared favorably with T cells genetically modified with virus to express CAR.

We are currently enrolling patients for 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. A patient with multiple-relapsed B-cell ALL received CD19-specific CAR<sup>+</sup> T cells produced with a three-week manufacturing process and achieved a complete remission with normalization of positron emission tomography computed tomography, or PET/CT, tumor imaging lasting approximately six months. At the 2016 Annual Meeting of the ASGCT, we presented preclinical data in a mouse tumor model showing improved survival with

treatment using CAR<sup>+</sup> T cells with reduced time in culture (approximately two weeks as compared to the four weeks needed for previous first-generation CAR<sup>+</sup> T process). Our second-generation CD19 trial underway is accomplishing important aims: (1) testing of the revised CAR design to lengthen CAR<sup>+</sup> T cell persistence (2) shortening the manufacturing process from four to as short as two weeks and (3) establishing continued safety of SB-modified T cells in patients. The Company expects to stop enrollment in this study in 2018, as the third-generation study commences. Updates on patients who were enrolled in our first generation trials and second generation trial, and the respective persistence of infused CAR<sup>+</sup> T cells will be presented in posters at the 2017 American Society of Hematology Annual Meeting, or ASH in December.

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The learnings from these first and second-generation trials form the basis of our third-generation phase 1 trial, which is designed to leverage SB CAR<sup>+</sup> T cells co-expressing a membrane-bound version of the cytokine interleukin (IL)-15, or mbIL15, and employing a SB non-viral manufacturing process of less than 2 days. We anticipate entering the clinic with our mbIL-15 product candidate and its shortened manufacturing process, which we are calling point-of-care (P-O-C), in 2018.

IL-15 is a critical cytokine for cell proliferation, maintaining cells in a younger, less differentiated state. A point-of-care process delivers genetically modified T cells with superior proliferative potential *in vivo*, or inside of the body. We believe that data presented at the 2016 American Society of Hematology Meeting, or ASH, supported by an earlier 2016 publication in the Proceedings of the National Academy of Sciences, indicated promising results: third generation SB CAR<sup>+</sup> T cells demonstrated that a single, low dose of T cells co-expressing a CD19-specific CAR and mbIL15 resulted in sustained *in vivo* persistence that produced potent anti-tumor effects and superior leukemia-free survival. These clinical and preclinical data support the Company's point-of-care plans to rapidly infuse SB CAR<sup>+</sup> T cells in a Phase 1 trial. With the intent to administer clinical-grade SB CAR<sup>+</sup> T cells loaded with mb-IL-15, with a manufacturing process of less than 2 days, this non-viral CAR-T approach has the potential to outpace viral-based methods in terms of time to treatment and cost. We anticipate undertaking an investigator-led study utilizing point-of-care to generate CD19-specific T cells at MDACC in 2018. Control systems are also being developed such as the RTS<sup>®</sup> for receptor and/or cytokine expression, as well as for the conditional ablation of genetically modified cells using a kill switch. The Company has decided to initially launch the P-O-C program without the RTS<sup>®</sup> switch and will instead use a kill switch for control. A poster at the 2017 Annual Meeting of ASH will present further preclinical *in vitro* and *in vivo* data on the intended CD19 mbIL15 point-of-care target. We anticipate future CAR<sup>+</sup> T programs from the Company may also utilize the P-O-C manufacturing approach.

The company has reprioritized its pipeline and intends to enhance its focus and resources towards advancing the point-of-care CAR<sup>+</sup>T target to the clinic. We will continue efforts to genetically modify allogeneic NK cells to improve their persistence and anti-tumor efficacy, but we have decided to pause further development of the Off-the-shelf (OTS) non-genetically modified primary NK program for AML.

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On May 2, 2017, we announced that an investigator-initiated Investigational New Drug, or IND, application for a Phase 1 study of CD33-specific CAR<sup>+</sup> T therapy for treatment of relapsed or refractory acute myeloid leukemia, or AML was active. The CD33-specific CAR<sup>+</sup> T cells also incorporate a kill switch designed to eliminate the modified T cells after infusion under potential adverse safety conditions. A poster detailing preclinical data supportive of the CD33 CAR<sup>+</sup> T therapy will be presented at the 2017 Annual Meeting of ASH in December. The Phase 1 study is open to enrollment.

The Company is also developing T cell therapies for solid tumor targets. Only a minority of tumor antigens are on the surface and able to be targeted by CARs, while most tumor-derived antigens are within the cell and will likely need to be targeted by TCRs. Therefore, we are developing approaches to target solid tumors using T cells genetically modified with the SB system to express TCRs for recognition of neoantigens. Data demonstrating the ability to generate T cells with patient-specific TCRs against neoantigens utilizing the SB system were published in Molecular Therapy in 2016. We also presented further preclinical information regarding the targeting of solid tumors at the 2016 Annual Meeting of ASH.

On January 10, 2017, the Company announced the signing of a Cooperative Research and Development Agreement, or CRADA, with the National Cancer Institute, or NCI, for the development of adoptive cell transfer, or ACT)-based immunotherapies genetically modified using the 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, or 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 will conduct 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 the Company and Intrexon. Preparations for the clinical trial are underway at the NCI. Following validation of the manufacturing process, we anticipate submission of the IND in the first quarter of 2018.

On March 27, 2015, we entered into a global collaboration with Intrexon focused exclusively on CAR<sup>+</sup> T, products with Ares Trading, or Ares, a biopharmaceutical division of Merck KGaA, which we refer to as the Ares Trading Agreement. Intrexon will share the economic provisions of this collaboration equally with us, including an upfront payment of \$115.0 million that was received in July 2015, milestones and royalties. Under this collaboration, Ares has already selected two CAR<sup>+</sup> T targets for which we are performing certain research activities that are, in part, funded by Ares. Pursuant to the terms of an amendment to our Channel Agreement with Intrexon, which we refer to as the ECP Amendment, that we entered into at the time of the Ares Trading Agreement, we will be responsible for any additional research and development expenditure beyond the funding provided by Ares. Once these candidates reach investigational new drug stage, the programs will be transferred to Ares for clinical development and commercialization. We and Intrexon will also independently conduct research and development on other CAR<sup>+</sup> T candidates, with Ares having the opportunity during clinical development to opt-in to these candidates for additional payments to us and Intrexon. We and Intrexon, in the exclusive partnership with Ares, are progressing development of the two CAR<sup>+</sup> T targets, utilizing our key technologies for regulating cytokine expression, the proprietary RTS<sup>®</sup> platform and mbIL15.

On September 28, 2015, we entered into a new exclusive channel collaboration agreement, or the GvHD Agreement, with Intrexon to develop therapies for the treatment and/or prevention of GvHD, a major complication of allogeneic HSCT, which significantly impairs the quality of life and survival of many recipients. Allogeneic HSCT is used for the treatment of various diseases including hematological malignancies, immunological deficiencies as well as non-malignant conditions.



We believe that the combined expertise and knowledge gained from our research programs with Intrexon in adoptive T-cell therapies and cytokine modulation for the treatment of cancer positions us well to develop and implement therapeutic approaches addressing an area of high unmet medical need for patients with GvHD. Through the GvHD Agreement, we and Intrexon plan to pursue engineered cell therapy strategies, used either separately or in combination, for targeted prevention and/or treatment of GvHD. The first approach under consideration is the engineering of Tregs. An update of preclinical research on the gene-modified Tregs will be provided in a poster at the 2017 Annual Meeting of ASH. The second approach is expected to utilize the deployment of Intrexon's orally delivered microbe-based ActoBiotics® therapeutics, based on *Lactococcus lactis*, to modulate immune function.

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**Table of Contents*****Enabling Technology***

Our approach to immuno-oncology and GvHD entails the application of engineering principles to biological systems for the purpose of designing and constructing new biological systems or redesigning/modifying existing biological systems. Biological systems are governed by DNA, the building block of gene programs, which control cellular processes by coding for the production of proteins and other molecules that have a functional purpose and by regulating the activities of these molecules. This regulation occurs via complex biochemical and cellular reactions working through intricate cell signaling pathways, and control over these molecules modifies the output of biological systems. Our approach to immuno-oncology and GvHD 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.

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

On September 28, 2015, we entered into the GvHD Agreement with Intrexon to develop therapies for the treatment and/or prevention of GvHD, a major complication of allogeneic HSCT, which significantly impairs the quality of life and survival of many recipients. Some of the technologies used to generate product candidates for immuno-oncology have potential application for GvHD. These include the ability to genetically modify cells using viral and non-viral approaches and the application of RTS® to control gene expression, such as cytokines. Some of these methodologies, as well as our expertise in bioprocessing, are being investigated to generate regulatory T cells, or Tregs. In addition, we are generating genetically modified *L lactis* to alter the inflammatory milieu of patients with GvHD, especially of the gastrointestinal tract. These modifications are facilitated through collaboration with ActoBiotics®, a division of Intrexon.

More detailed descriptions of our clinical development plans for each of these programs are set forth below under the caption *Product Candidates*.

***Immuno-oncology***

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

using immunotherapies, or therapies that activate the immune system.

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On January 13, 2015, we, together with Intrexon, entered into a license agreement with MD Anderson, which we refer to as the MD Anderson License. Pursuant to the MD Anderson License, we and Intrexon hold an exclusive, worldwide license to certain technologies owned and licensed by MD Anderson, including technologies relating to novel CAR<sup>+</sup> T cell therapies arising from the laboratory of Laurence Cooper, M.D., Ph.D., who was then a tenured professor at MD Anderson and is now our Chief Executive Officer, as well as either co-exclusive or non-exclusive licenses under certain related technologies.

Combining the non-viral genetic engineering technologies, we licensed from MD Anderson together with Intrexon's industrialized approach to gene engineering and cell control, we believe we can reprogram T cells to express a particular CAR or TCR construct that will enable the T cell and/or NK cell to recognize and target cancer cells. CAR<sup>+</sup> T cells target cell surface tumor antigens, such as CD19, that exist on cancer cells and that are independent of human leukocyte antigens, or HLAs, and which we refer to as public antigens. TCR-expressing T cells target tumor antigens that are dependent on HLAs and which we refer to as private antigens and include neoantigens. NK cells target tumors with loss or differences of HLAs, or tumors with no defined antigens. Most CAR<sup>+</sup> and TCR<sup>+</sup> genetically modified T cells currently being developed by competitors are autologous, or derived from the patient's own mononuclear white blood cells, and gene engineered with viral technology. As a result, the patient's blood must be harvested, shipped to a centralized manufacturing facility where the isolated mononuclear white blood cells are modified using a virus to express the CAR or TCR, and then shipped back to the hospital and infused into the patient. The process can take weeks and is labor intensive and costly. Currently, this complex technique can only be done in sophisticated laboratories. We believe we will be able to manufacture genetically modified cells using viral and non-viral methods. The latter may result in a reduced cost of manufacturing, particularly as we develop processes to eliminate the requirements for cell propagation and activation, thereby facilitating a shortened manufacturing process, which can be implemented at multiple points-of-care. Our non-viral methods, which we believe are customizable, fast, and less costly than other gene transfer approaches, together with our industrialized, scalable engineering approach, are expected to enable highly efficient and less costly manufacturing approaches to gene-engineered, cell-based therapy. In addition, our proprietary RTS<sup>®</sup> and/or kill switches may give us the ability to control *in vivo* gene expression of CAR or TCR or cytokine on T cells and/or NK cells, which we believe could result in significantly lower toxicity compared to other products currently in development.

### ***Cancer Overview***

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

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

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

According to the American Cancer Society, it is estimated that about 1,688,780 new cases of cancer are expected to be diagnosed in 2017 and about 600,920 Americans are expected to die from cancer in 2017. The cost of treating cancer is significant. The Agency for Healthcare Research and Quality estimates that the direct medical cost of cancer in 2014 was \$87.8 billion.

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**Table of Contents***Cancer Treatments*

Major treatments for cancer include surgery, radiotherapy, chemotherapy and immunotherapy. Newer approaches such as anti-angiogenic and targeted therapies are rapidly evolving. While there are many experimental treatments under investigation, including DNA and other immunological-based therapies, we believe the prevalence of cancer will remain a significant unmet medical need. Many therapies, including combination approaches, with different mechanisms of action may be needed to overcome tumor escape. In addition to monotherapy treatment in GBM, our approach to cancer treatment includes applying multiple modality and multi-delivery approaches that encompass viral and non-viral mechanisms, differentiating us from many other companies in the field of adoptive cellular therapy today.

*Market Opportunities*

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 (OS) of 6-7 months, while OS in patients who have failed temozolomide and bevacizumab, or equivalent salvage chemotherapy, is approximately 3-5 months. Given the poor overall prognosis and lack of effective treatments, new therapeutic approaches for malignant gliomas are needed. In children, the incidence of brain cancer is approximately 4.84 per 100,000, according to the National Cancer Institute. 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 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.

It is estimated that there are nearly three million women living in the United States with a history of invasive breast cancer, and an additional 226,870 women were diagnosed in 2012. Approximately 50% of women diagnosed with primary breast cancer will eventually relapse and develop metastatic or advanced disease. In addition, around 10% of patients present with metastatic disease at first diagnosis. The five year relative survival rate for women diagnosed with localized breast cancer is 98.6%; survival declines to 83.8% for regional stage and to 23.3% for distant stage. In addition to stage, factors that influence survival include tumor grade, hormone receptor status, and human epidermal growth factor receptor 2 (HER2) status.

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

It is estimated that in 2016 more than 15.5 million people in the U.S. were living with, or are in remission from some form of cancer. Approximately 1,688,780 new cancer cases are expected to be diagnosed in the US in 2017 according to the American Cancer Society. Of these, the majority will be 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.

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***GvHD Overview***

GvHD is a major complication of allogeneic HSCT, which significantly impairs the quality of life and survival of many recipients. Allogeneic HSCT is an increasingly important treatment of various diseases including hematological malignancies, immunological deficiencies as well as non-malignant conditions, and is considered to be the most effective form of tumor immunotherapy available to date. However, GvHD, when immune (graft) cells in a transplant patient recognize their engrafted host as foreign and attack the patient's (host) cells, remains a major source of morbidity and mortality following allogeneic HSCT. During development of GvHD, activation of various immune cells, especially donor T cells, leads to damage of target organs including skin, liver, hematopoietic system, and of particular importance, gut.

There were approximately 23,000 allogeneic HSCT procedures in the U.S. and Europe in 2013. Approximately 40% to 60% of HSCT recipients develop GvHD, either acute or chronic. Immunosuppressive agents and systemic steroids routinely used to treat GvHD have limited efficacy and toxicity; patients with steroid-resistant acute GvHD have a dismal prognosis, with mortality rates in excess of 90%, defining the need for safer, more effective therapies. New ways of treating and preventing GvHD have the potential to increase the market opportunity through (1) broadening of patient eligibility to receive allogeneic HSCT and (2) increasing the number of effective donor/recipient combinations.



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***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.

**Immuno-oncology programs:**

***Ad-RTS-IL-12 + veledimex***

Ad-RTS-IL-12 + veledimex, our most advanced product candidate, uses our gene delivery system to produce IL-12, a potent, naturally occurring anti-cancer protein. More specifically, IL-12 is a potent immunostimulatory cytokine which activates and recruits dendritic cells that facilitate the cross-priming of tumor antigen-specific T cells. We have developed an adenoviral vector, Ad-RTS-IL-12, administered intra-tumorally under the control of the RheoSwitch Therapeutic System® (RTS®) expression platform. Gene expression and subsequent IL-12 protein production is tightly controlled by the activator ligand, veledimex.

Ad-RTS-IL-12 + veledimex has been evaluated in two Phase 2 studies, the first for the treatment of metastatic melanoma, and the second for the treatment of unresectable recurrent or metastatic breast cancer. 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.

***Ad-RTS-IL-12 + veledimex for metastatic breast cancer***

On April 27, 2015, we announced the initiation of a Phase 1b/2 study of Ad-RTS-hIL-12 + veledimex following standard chemotherapy for the treatment of patients with locally advanced or metastatic breast cancer. The study was conducted at the Memorial Sloan Kettering Cancer Center in New York and evaluated improving the patient's response at 12 weeks. A poster presentation of this study titled, Phase 1b/2 study of intra-tumoral Ad-RTS-hIL-12 + veledimex in patients with chemotherapy-responsive locally advanced or metastatic breast cancer, was presented at the San Antonio Breast Cancer Symposium, in San Antonio, Texas in December 2015. We also presented updated information on the study at the 2016 ASCO meeting in June 2016.

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We presented an update of the study at the European Society for Medical Oncology (ESMO) Congress in October 2016 in Copenhagen, Denmark. As of August 30, 2016, a total of nine patients were available for initial assessment. Results showed that Ad-RTS-hIL-12 + 7 days of veledimex consistently elicited production of IL-12, which in turn produced IFN $\gamma$ . It was notable that the intratumoral influx of CD8<sup>+</sup> T cells and IFN $\gamma$  were present six weeks after completion of veledimex, consistent with the ability of Ad-RTS-hIL-12 to favorably impact the tumor environment over the long term. In two patients, Ad-RTS-hIL-12 + veledimex provided a meaningful drug holiday, with durable responses for 18 and 35 weeks. In all patients, disease control rate (DCR) was 44% at Week 6 and 22% at Week 12. Overall response rate (ORR), defined as achieving a partial response (PR) or better, was 11% at Week 12. Most toxicities promptly reversed upon discontinuation of veledimex, including cytokine release syndrome (grade 1-2 CRS), observed in six of nine patients. The higher than expected incidence of CRS was likely related to CYP-3A4 drug interactions with veledimex (80 mg), which resulted in enhanced peak cytokine expression.

The Company announced at JP Morgan on January 11, 2017 that we are pausing the breast cancer study after successful completion of the desired biomarker data.

### *Ad-RTS-IL-12 + veledimex for recurrent glioma*

We initiated a multi-center Phase 1 study in patients with recurrent or progressive GBM or Grade III malignant glioma, a form of brain cancer, in June 2015. On July 23, 2015, the U.S. Food and Drug Administration, or the FDA, granted orphan drug designation for Ad-RTS-IL-12 + veledimex for the treatment of malignant glioma. 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.

We reported biologic data from this Phase 1 study in our presentation titled, Intra-tumoral regulated expression of IL-12 as a gene therapy approach to treatment of glioma, at the Society for Neuro-Oncology (SNO) 20th Annual Scientific Meeting, November 19-22, 2015 in San Antonio, TX. On February 24, 2016, we announced the successful completion of the initial dosing cohort and that the first patient had been dosed in the next succeeding cohort of the GBM study. In addition to Ad-RTS-IL-12 + veledimex as monotherapy, we have undertaken preclinical studies that suggest we may be able to combine this viral-based immunotherapy with an immune checkpoint inhibitor, or iCPI, to improve the anti-tumor effect for recurrent GBM. In May 2016, we presented the preclinical data from these preclinical studies at the Annual Meeting of the American Society of Gene and Cell Therapy, or ASGCT, and we believe the data supports the first-in-human application of combining Ad-RTS-IL-12 + veledimex with an iCPI for investigational treatment of rGBM.

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Our ongoing Phase 1, multi-center, dose-escalation study of the gene therapy candidate Ad-RTS-hIL-12 + orally administered veledimex in patients with recurrent or progressive GBM, was presented at the ASCO annual meeting in June 2016. On June 27, 2016, we announced the successful completion of enrollment in the first and second dosing cohorts. In August 2016, we completed enrollment of the third cohort of the study.

The primary objective of the Phase 1 study 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 first cohort of seven patients received 20 mg doses of veledimex, the second cohort of six patients received 40 mg doses of veledimex, and the third cohort of four patients received 30 mg doses of veledimex to refine the effect of activating the immune response within the tumor. The resultant immunologic activity that followed IL-12 expression from the brain tumor suggested that no further dose escalation would be necessary and the optimal dosing may be reached sooner than initially anticipated. An expansion cohort to enroll an additional eight patients at 20 mg has also been completed.

Data from 11 patients with recurrent high-grade gliomas were presented at the 2016 ASCO Annual Meeting in June 2016. All of these patients had failed at least two prior lines of therapy and underwent partial resection leaving residual tumors, in certain cases with significant tumor burden. Ad-RTS-hIL-12 was administered through direct injection into the brain tumor at the time of surgery and veledimex was taken orally to activate the production of IL-12 from the tumor site and stimulate an immune response. No enrollment restrictions were imposed for tumor size or location within the supratentorial space.

As of May 18, 2016, the date of data collection for the ASCO presentation, overall median follow-up was 6.2 months, with 10 of 11 patients alive. IL-12 in the bloodstream was measured and was found to be proportional to the amount of veledimex administered, demonstrating that this orally delivered activator crossed the blood brain barrier to turn on the RheoSwitch® technology in a dose-dependent manner.

It is established that the measurement of progression-free survival, or PFS, with immunotherapy may not correlate directly with overall survival, or OS. For purposes of the data that we presented at the ASCO annual meeting in 2016, all pseudoprogression/progression were assumed to trigger progressive disease for PFS analysis by Response Assessment for Neuro-Oncology, or RANO. However, clinical benefit, including long-term survival and tumor regression, can still occur after initial disease progression or after the appearance of new lesions in the Immunotherapy Response Assessment for Neuro-Oncology, or iRANO.

Overall, Ad-RTS-hIL-12 + veledimex was well tolerated, with a higher incidence of grade 3 or greater adverse events in the 40 mg cohort. All serious adverse events and Grade 3 related toxicities were rapidly reversible upon discontinuation of veledimex. The most common related adverse events included headache, nausea/vomiting, fever, white blood cell/leukocyte count decrease, platelet count decrease, liver function test increase and cytokine release syndrome. For patients who have experienced multiple recurrences of GBM, as the patients in our study have, prognoses are particularly poor. As of July 19, 2016, median follow-up in the first dose cohort from our study was 8 months, and the overall survival remains very encouraging in a population with an expected overall survival of 3 to 5 months for patients that have failed temozolomide and bevacizumab, or equivalent salvage chemotherapy.

We presented further interim updates on the progress of the Phase 1 GBM study, including longer-term survival follow-up, at the SNO 21<sup>st</sup> Annual Scientific Meeting in November 2016, in a poster entitled, Phase 1 study of intratumoral viral delivery of Ad-RTS-hIL-12 + oral veledimex is well tolerated and suggests survival benefit in recurrent high grade glioma, demonstrating median overall survival of 12.8 months, with 11 of 17 patients alive. Survival rates at 6, 9, and 12 months for patients with multiple recurrences prior to administration of Ad-RTS-hIL-12

were 100%, 86%, and 71%, respectively, in the 20 mg cohort, and 87%, 65%, and 54%, respectively, for all subjects. In addition, a nonclinical poster was also presented at SNO in November entitled "Local regulated IL-12 expression as an immunotherapy for the treatment of pontine glioma". Based on pre-clinical data in a pontine mouse model of Ad-RTS-IL-12 + veledimex presented at SNO November 2016, the Company has initiated a Phase 1 study in the treatment of brain tumors in children.

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At the 35<sup>th</sup> Annual J.P. Morgan Healthcare Conference on January 11, 2017, we presented further Phase 1 GBM study data. Based on tolerability and survival benefit (median OS=12.7 months, n=15), 20 mg was selected for an expansion cohort, and we are following patients' overall survival data. Ad-RTS-hIL-12 + veledimex was well tolerated and suggests a survival benefit over historical controls at 6, 9, and 12 months (median OS=9.6 months, n=25). Toxicities were tolerable, predictable and reversible upon discontinuing veledimex. There is a strong positive correlation between veledimex dose, blood-brain barrier penetration, and IL-12 production. These data demonstrate that the RTS<sup>®</sup> gene switch works in humans, toggling not only as a switch to turn on and off the production of IL-12, but also as a rheostat to control the level of IL-12.

At the 2017 American Society of Clinical Oncology (ASCO) Annual Meeting in Chicago, we presented on June 5<sup>th</sup> updated results from our Phase 1 multicenter study of Ad-RTS-hIL-12 + veledimex including the 20 mg expansion cohort in patients with recurrent or progressive GBM. The Company reported results from 25 patients with recurrent or progressive Grade III or IV glioma enrolled in three veledimex dosing cohorts (20 mg, n = 15; 30 mg, n = 4; and 40 mg, n = 6). Subjects with recurrent or progressive Grade III or IV glioma undergoing resection were injected intratumorally with Ad  $2 \times 10^{11}$  viral particles and received daily oral activator veledimex for 15 doses. As of May 24, 2017, the cutoff date for the ASCO presentation, median overall survival (mOS) of all patients receiving intratumoral Ad-RTS-hIL-12 with 20 mg of orally-administered veledimex was maintained at 12.5 months, with a mean follow-up time of 9.2 months. The majority of patients in the 20 mg cohort had 2 or more recurrences prior to entry in the study, indicating very advanced disease.

On March 27, 2017, the Company announced the receipt of positive guidance from an End-of-Phase 2 meeting with the U.S. Food and Drug Administration (FDA) for Ad-RTS-hIL-12 + veledimex for the investigational treatment of recurrent GBM.

As a result of a series of discussion with regulators, key opinion leaders and various other stakeholders, the Company believes that a randomized controlled trial is likely an effective mean to create shareholder value. Although some regulators have indicated a willingness to entertain a single-arm study, other regulators representing key markets are requiring a randomized trial design. The Company priorities are to accelerate partnership discussions and/or raise additional funds to further advance the program. With a commercialization path in view, we continue to actively engage broad discussions around financial strategies to bring this important therapeutic candidate to the market.

*CAR, NK and TCR cells*

We are actively pursuing viral and non-viral genetic engineering technologies and approaches to cell propagation to develop novel CAR<sup>+</sup> T, NK and TCR therapies. Combining this technology with Intrexon's industrialized synthetic biologic engineering and clinically tested and validated RTS modules and/or kill switches, represents a differentiated approach to genetically modified T cells and other immune cells, such as NK cells. Employing novel cell engineering techniques and multigenic gene programs, we expect to implement next-generation, non-viral and viral adoptive cellular therapies based on specialized cytokines, CARs and TCRs targeting both hematologic malignancies and solid tumors. The ability to genetically modify immune cells using non-viral and viral-based technologies enables us to express other genes in addition to immunoreceptors (CARs and TCRs) to redirect specificity.

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The platform we, together with Intrexon, exclusively licensed from MD Anderson uses the *Sleeping Beauty*, or SB, non-viral genetic modification system to generate and characterize new CAR<sup>+</sup> T and TCR designs, which enables a high-throughput approach to evaluate genetically modified immune cells in oncology. These CAR and TCR molecules are evaluated based on measurements of T-cell function, phenotype, and genotype. We believe this non-viral gene transfer using the SB system is unique in the field of oncology and may avoid the expense and manufacturing difficulty associated with creating T cells engineered to express CAR and TCR using viral vectors. After electroporation, the transposon/transposase employed by *Sleeping Beauty* improves the efficiency of integration of donor plasmids used to express CAR and other transgenes in T cells. The SB system combined with activating and propagating cells (AaPC) can selectively propagate and thus yield CAR-expressing T cells suitable for human applications. The Company is evaluating co-culture on AaPC for some human applications of CAR- and TCR-modified T cells. Elimination of co-culture on AaPC is contemplated in our technology referred to as point-of-care (P-O-C) to rapidly manufacture genetically modified T cells in 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. The addition of mbIL15 endows CAR-expressing younger T cells with an ability to be long-lived after infusion. Associated preclinical data were presented at both the May 2016 ASGCT meeting and the December 2016 annual meeting of ASH; additional data will be presented at the December 2017 annual meeting of ASH. The ability of CAR<sup>+</sup> T cells to signal via recombinant IL-15 raises the possibility that lymphodepleting chemotherapy may not be needed. One of the outcomes of reducing the endogenous T-cell mass with chemotherapy is the freeing up of endogenous IL-15 which may not be necessary with the administration of CAR<sup>+</sup> T cells co-expressing mbIL15.

The Company expects to build upon these data to co-express immunoreceptors with cytokines and to leverage its ability to control expression with RheoSwitch Therapeutic System<sup>®</sup> (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> works as a controllable switch in humans. By combining the most clinically advanced non-viral gene integration platform, SB to co-express CAR and mbIL15, and possibly in the future, the transcriptional switch system, RTS<sup>®</sup>, we will use our point-of-care approach to significantly shorten the time to manufacture T cells. Using this unique set of genetic engineering tools, the Company can employ a broad immunotherapy approach against cancers.

## CAR

Through the MD Anderson License, the Company 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 will be presented in a poster at the 2017 Annual Meeting of ASH.

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. A patient with multiple-relapsed B-cell ALL who received CD19-specific CAR<sup>+</sup> T cells produced with a three-week manufacturing process, achieved a complete remission with normalization of positron emission tomography-computed tomograph, or PET/CT, tumor imaging lasting approximately six months. At the 2016 Annual Meeting of the ASGCT, we presented preclinical data in a mouse tumor model showing improved survival with treatment using CAR<sup>+</sup> T cells with reduced time in culture (approximately two weeks as compared to the four weeks needed for previous first-generation CAR<sup>+</sup>T process). Our second-generation CD19 trial is underway, and employs a revised CAR design and shortened manufacturing process advancement, with culturing times as short as two weeks. A summary of this ongoing trial will be presented in a poster at the 2017 Annual Meeting of ASH. We anticipate stopping enrollment in this trial in 2018.



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In the preclinical setting, the time to administration of third-generation SB CAR<sup>+</sup> T cells co-expressing a membrane-bound version of the cytokine IL-15, or mbIL15 has been reduced to less than two days. This shortened very rapid manufacturing process, referred to as point-of-care, delivers genetically modified T cells with superior proliferative potential *in vivo*. We believe that data presented at the December 2016 annual meeting of ASH, supported by an earlier publication in the Proceedings of the National Academy of Sciences in November 2016 indicated promising results: third generation SB CAR<sup>+</sup> T cells 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. Additional preclinical data will be provided in a poster at the 2017 Annual Meeting of ASH. These clinical and preclinical data support the Company's P-O-C plans to very rapidly infuse SB CAR<sup>+</sup> T cells in a Phase 1 trial in 2018. With the intent to administer clinical-grade SB CAR<sup>+</sup> T cells in less than 48 hours, this non-viral CAR-T approach has the potential to outpace viral-based methods in terms of time to treatment and cost. The P-O-C technology is based on the non-viral gene transfer to stably integrate both CAR and mbIL15 with a switch.

On July 12, 2016, we announced that, after receiving feedback from the U.S. National Institutes of Health Office of Biotechnology Activities Recombinant DNA Advisory Committee, we anticipated progressing plans for a 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 2016 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 showed that these CAR-T cells were able to eliminate 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. Additional preclinical data on this program will be presented in a poster at the 2017 Annual Meeting of ASH. This Phase 1 clinical trial is now open for enrollment at MD Anderson. The anticipated clinical data will help establish that CD33 can be targeted by CAR on genetically modified T cells which will provide a foundation for considering then advancing this program under point-of-care.

**NK Cell**

The company has reprioritized its pipeline and intends to enhance its focus and resources towards advancing the P-O-C to the clinic. As a result, the Company has decided to pause further development of the OTS non-genetically modified primary NK program for AML. Instead, the company will continue efforts to genetically modify allogeneic NK cells to improve their persistence and anti-tumor efficacy.



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**Table of Contents****TCR**

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

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 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. Preparations for the clinical trial are underway at the NCI. Following validation of the manufacturing process, we anticipate submission of the IND in the first quarter of 2018.

***GvHD Program***

GvHD may occur after a bone marrow or stem cell transplant in which someone receives bone marrow tissue or cells from a donor. The new, transplanted cells regard the recipient's body as foreign. When this happens, the newly transplanted cells attack the recipient's body. We, together with Intrexon, are initiating a research program focused on addressing the underlying pathologies of GvHD through Intrexon's engineered cell platforms. The exclusive collaboration, or the GvHD Program, will focus on the pursuit of the following engineered cell therapy strategies, used either separately or in combination, for the targeted treatment of GvHD: (i) the infusion of regulatory T cells, such as expressing, membrane-bound and/or soluble interleukin-2 and (ii) the deployment of orally delivered, genetically modified *L. lactis* that express cytokines such as interleukin-2 to modulate immune function. We believe these strategies have the potential to broaden the number of patients eligible to receive allogeneic HSCT and also increase the number of effective donor/recipient combinations. Preclinical data from the regulatory T-cell program will be presented in a poster at the 2017 Annual Meeting of ASH.

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*Milestones*

We achieved and expect to achieve the following milestones in 2017:

Intra-tumoral IL-12 RheoSwitch® programs:

Update clinical data from Phase 1 of Ad-RTS-hIL-12 + veledimex for recurrent GBM was presented at ASCO

Update clinical data from Phase 1 of Ad-RTS-hIL-12 + veledimex for recurrent GBM to be presented at SNO

Initiate pivotal clinical trial for recurrent GBM

Initiate stereotactic administration of Ad-RTS-hIL-12 + veledimex for recurrent GBM

Initiate combination study of Ad-RTS-hIL-12 + veledimex with iCPI (anti-PD-1) for recurrent GBM

Initiate Phase 1 study in the treatment of brain tumors in children

CAR<sup>+</sup> T programs:

Continue CD19-specific CAR<sup>+</sup> T second-generation clinical study, enrolling patients under shortened manufacturing

Advance CD19 third generation mbIL15 towards a Phase 1 clinical study evaluating P-O-C

Initiate a CD33-specific CAR<sup>+</sup> T clinical study in adults and children for relapsed or refractory AML

Advance CAR<sup>+</sup> T-cell preclinical studies under a shortened manufacturing process towards P-O-C

TCR programs:

Execute CRADA with NCI utilizing *Sleeping Beauty* to generate T cells targeting neoantigens for treatment of patients with solid tumor malignancies

Advance development of process for delivering personalized gene-modified T-cell products against neoantigens

NK cell programs:

Advance development of genetically modified NK cells with improved persistence and potency

GvHD programs:

Advance preclinical studies

We are also evaluating additional potential preclinical candidates and continuing discovery efforts aimed at identifying other potential product candidates under our Channel Agreement and GvHD Agreement with Intrexon. In addition, we may seek to enhance our pipeline in immuno-oncology through focused strategic transactions, which may include acquisitions, partnerships and in-licensing activities.

*Small-molecule program*

In addition to our immuno-oncology programs, we maintain certain rights to a small-molecule program, darinaparsin, which we are no longer developing directly. We entered into an amended and restated global licensing agreement with Solasia Pharma K.K., or Solasia, on July 31, 2014, granting Solasia an exclusive worldwide license to develop and commercialize darinaparsin, and related organoarsenic molecules, in both intravenous and oral forms in all indications for human use. In exchange, we will be eligible to receive from Solasia development- and sales-based milestones, a royalty on net sales of darinaparsin, once commercialized, and a percentage of any sublicense revenues generated by Solasia. 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 a new drug approval in certain of the territories assigned to Solasia. The start of this trial triggered a \$1.0 million milestone payment to us which was subsequently paid to MD Anderson under the terms of the MD Anderson License. The Company has consulted with Solasia to determine additional development plans and has continued to support our business partnership over the past twelve months.

**Table of Contents****Financial Overview****Overview of Results of Operations****Three and Nine Months Ended September 30, 2017 Compared to Three and nine months Ended September 30, 2016**

**Revenue.** Revenue during the three and nine months ended September 30, 2017 and 2016 was as follows:

| (\$ in thousands)     | Three months ended<br>September 30, |          |        | Nine months ended<br>September 30, |          |              |
|-----------------------|-------------------------------------|----------|--------|------------------------------------|----------|--------------|
|                       | 2017                                | 2016     | Change | 2017                               | 2016     | Change       |
| Collaboration revenue | \$ 1,598                            | \$ 1,598 | \$ 0%  | \$ 4,792                           | \$ 5,264 | \$ (472) -9% |

Revenue for the three months ended September 30, 2017 remained unchanged compared to revenue for the three months ended September 30, 2016. During each of the three months ended September 30, 2017 and 2016, we recognized \$1.6 million in revenue under the Ares Trading Agreement (Note 6, Commitments and Contingencies).

Revenue for the nine months ended September 30, 2017 decreased, compared to revenue for the nine months ended September 30, 2016. During the nine months ended September 30, 2016, we recognized \$272 thousand in revenue as part of normal amortization of a \$5.0 million upfront payment received in March 2011 under the Solasia agreement (Note 6, Commitments and Contingencies). The \$5.0 million upfront payment received in March 2011 was amortized over the period of our research and development effort, which was completed in March 2016. Additionally, during the nine months ended September 30, 2016, we recognized \$200 thousand from our 2015 license agreement with Predictive Therapeutics for Palifosfamide. The revenue recognized under both the Solasia and Predictive agreements was fully recognized in 2016.

Deferred revenue of \$43.1 million is comprised entirely of revenue to be recognized under the Ares Trading Agreement which will be earned over the period of effort, estimated to be nine years.

**Research and development expenses.** Research and development expenses during the three and nine months ended September 30, 2017 and 2016 were as follows:

| (\$ in thousands)        | Three months ended<br>September 30, |          |              | Nine months ended<br>September 30, |            |                   |
|--------------------------|-------------------------------------|----------|--------------|------------------------------------|------------|-------------------|
|                          | 2017                                | 2016     | Change       | 2017                               | 2016       | Change            |
| Research and development | \$ 11,105                           | \$ 8,975 | \$ 2,130 24% | \$ 33,903                          | \$ 148,402 | \$ (114,499) -77% |

Research and development expenses for the three months ended September 30, 2017 increased by \$2.1 million, as compared to the three months ended September 30, 2016. The increase in research and development expenses for the three months ended September 30, 2017 is primarily due to an increase of \$1.1 million to support our ongoing trials, an increase of \$0.4 million related to our CRADA entered into on January 2017 with the National Cancer Institute, and an increase of \$0.6 million in research and development operating expenses related to increased headcount during the three months ended September 30, 2017.

Research and development expenses for the nine months ended September 30, 2017 decreased by \$116.0 million, as compared to the nine months ended September 30, 2016. The decrease in research and development expenses for the nine months ended September 30, 2017 is primarily due to the commitment to issue Series 1 preferred stock at fair value under the 2016 ECP Amendment and 2016 GvHD Amendment with Intrexon (Note 5) resulting in a \$119.0 million non-cash charge during the nine months ended September 30, 2016 that was not incurred during the nine months ended September 30, 2017. The \$119.0 million non-cash charge, in the prior year, was offset by an increase of \$1.6 million related to our CRADA entered into on January 2017 with the National Cancer Institute, an increase of \$0.4 million to support our ongoing trials and an increase of \$2.1 million in research and development operating expenses related to increased headcount during the three months ended September 30, 2017.

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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 nine months ended September 30, 2017, our clinical stage projects included a Phase 1 study with Ad-RTS-IL-12 + veledimex in progressive glioblastoma; a Phase 1b/2 study with Ad-RTS-IL-12 + veledimex in metastatic breast cancer; an investigator-led Phase 1 study infusing our 2nd generation CD19-specific CAR<sup>+</sup> T cells in patients with advanced lymphoid malignancies; and an investigator-led Phase 1 trial infusing the Company's CD33-specific CAR<sup>+</sup> T therapy for relapsed or refractory acute myeloid leukemia. The expenses incurred by us to third parties for our Phase 1 study with Ad-RTS-IL-12 + veledimex in progressive glioblastoma were \$0.6 million for the three months ended September 30, 2017, and \$3.6 million from the project's inception in June 2015 through September 30, 2017. There were no expenses incurred by us to third parties for our Phase 1b/2 study with Ad-RTS-IL-12 + veledimex in metastatic breast cancer for the three months ended September 30, 2017, and \$0.8 million from the project's inception in April 2015 through September 30, 2017. The expenses incurred by us to third parties for our investigator-led Phase 1 study infusing our 2nd generation CD19-specific CAR<sup>+</sup> T cells in patients with advanced lymphoid malignancies were \$0.7 million for the three months ended September 30, 2017 and \$2.6 million from the project's inception in December 2015 through September 30, 2017. The expenses incurred by us to third parties for our investigator-led Phase 1 trial infusing the Company's CD33-specific CAR<sup>+</sup> T therapy for relapsed or refractory acute myeloid leukemia were \$0.5 million for the three months ended September 30, 2017 and the project's inception in September 2017 through September 30, 2017.

Our future research and development expenses in support of our current and future programs will be subject to numerous uncertainties in timing and cost to completion. We test potential products in numerous preclinical studies for safety, toxicology and efficacy. We may conduct multiple clinical trials for each product. As we obtain results from trials, we may elect to discontinue or delay clinical trials for certain products 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 and nine months ended September 30, 2017 and 2016 were as follows:

|                            | Three months ended |                    |          | Nine months ended  |                    |              |
|----------------------------|--------------------|--------------------|----------|--------------------|--------------------|--------------|
|                            | September 30, 2017 | September 30, 2016 | Change   | September 30, 2017 | September 30, 2016 | Change       |
| <b>(\$ in thousands)</b>   |                    |                    |          |                    |                    |              |
| General and administrative | \$ 3,571           | \$ 3,537           | \$ 34 1% | \$ 10,946          | \$ 11,058          | \$ (112) -1% |

General and administrative expenses for the three months ended September 30, 2017 remained relatively the same as compared to the three months ended September 30, 2016. The slight increase for the three months ended September 30, 2017 was primarily due to a increases in employee related expenses in comparison to the three months ended September 30, 2016.

General and administrative expenses for the nine months ended September 30, 2017 decreased by \$0.1 million, as compared to the nine months ended September 30, 2016. The decrease for the nine months ended September 30, 2017 was primarily due to a \$0.3 million decrease in stock compensation incurred in the year. The \$0.3 million decrease in stock compensation was offset by a \$0.2 million increase in employee related expenses for the nine months ended September 30, 2017.

**Other income (expense).** Other income (expense) for the three and nine months ended September 30, 2017 and 2016 were as follows:

|                             | Three months ended |                    |             | Nine months ended  |                    |              |
|-----------------------------|--------------------|--------------------|-------------|--------------------|--------------------|--------------|
|                             | September 30, 2017 | September 30, 2016 | Change      | September 30, 2017 | September 30, 2016 | Change       |
| <b>(\$ in thousands)</b>    |                    |                    |             |                    |                    |              |
| Other income (expense), net | \$ 175             | \$ 39              | \$ 136 349% | \$ 299             | \$ 102             | \$ 197 193%  |
| Change in derivative value  | 202                | 21                 | 181 100%    | (1,292)            | 21                 | (1,313) 100% |
| <b>Total</b>                | <b>\$ 377</b>      | <b>\$ 60</b>       |             | <b>\$ (993)</b>    | <b>\$ 123</b>      |              |

The increase in other income for the three and nine months ended September 30, 2017, compared to the three and nine months ended September 30, 2016, was due primarily to interest received on our cash balance. During the three months ended September 30, 2017 and 2016, the Company recorded a gain on the change in fair value of the derivative liabilities of \$202 thousand and \$21 thousand, respectively. During the nine months ended September 30,



2017 and 2016, the Company recorded a loss on the change in fair value of the derivative liabilities of \$1.3 million and a gain on the change in fair value of the derivative liabilities of \$21 thousand, respectively. These changes are derived from the number of outstanding shares of preferred stock and their respective valuations.

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### **Liquidity and Capital Resources**

As of September 30, 2017, we had approximately \$84.4 million in cash and cash equivalents, compared to \$81.1 million in cash and cash equivalents as of December 31, 2016. Given our current development plans, we anticipate that our current cash resources will be sufficient to fund our operations into the fourth quarter of 2018. We will need to raise additional capital, whether through a sale of equity or debt securities, licensing arrangements, asset sales, additional product collaborations or other means, to complete the development and commercialization of our product candidates, to support our ongoing activities and to continue as a going concern. The forecast of cash requirements is forward-looking information that involves risks and uncertainties, and the actual amount of our expenses could vary materially and adversely as a result of a number of factors including changes in our business strategy and direction of our research and development efforts, competitive and technical advances, regulatory changes or other developments.

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 the Company is unsuccessful in entering into collaboration or partnership agreements for further development of its products, management may need to curtail development efforts, delay, scale back or eliminate some or all our research and development programs and cut operating expenses in order to conserve our cash. 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 expressed substantial doubt as to our ability to continue as a going concern in their report dated February 16, 2017 included in our Form 10-K.

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 increase (decrease) in cash and cash equivalents for the nine months ended September 30, 2017 and 2016:

| (\$ in thousands)                                    | Nine months ended     |             |
|--|-----------------------|-------------|
|  | September 30,<br>2017 | 2016        |
| Net cash provided by (used in):                      |                       |             |
| Operating activities                                 | \$ (42,513)           | \$ (45,261) |
| Investing activities                                 | (461)                 | (469)       |
| Financing activities                                 | 46,327                | (304)       |
| Net increase (decrease) in cash and cash equivalents | \$ 3,353              | \$ (46,034) |

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 pursuant to the terms of 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 nine months ended September 30, 2017 was \$42.5 million, as compared to net cash used in operating activities of \$45.3 million for the nine months ended September 30, 2016. The net cash used in operating activities for the nine months ended September 30, 2017 was primarily a result of our net loss of \$41.1 million, offset by the change in prepaid expenses of \$6.7 million, and change in accrued expenses and other liabilities of \$2.5 million. The net cash used in operating activities for the nine months ended September 30, 2016 was primarily a result of our net loss of \$154.1 million, offset by the issuance of Series 1 Preferred Stock of \$119.0 million, the change in prepaid expenses of \$9.6 million and the change in accrued expenses and other liabilities of \$7.3 million.

Net cash used in investing activities was \$461 thousand for the nine months ended September 30, 2017 compared to \$469 thousand for the nine months ended September 30, 2016. The change was due to an increase in offsite equipment purchased to support our CAR programs at MD Anderson incurred during the nine months ended September 30, 2017.

Net cash provided by financing activities was \$46.3 million for the nine months ended September 30, 2017 compared to \$304 thousand used in financing activities for the nine months ended September 30, 2016. The \$47.3 million provided by financing activities during the nine months ended September 30, 2017 is a result of our May 2017 underwritten offering which is described in Note 2 to the accompanying financial statements.



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

We anticipate that losses will continue for the foreseeable future. At September 30, 2017, our accumulated deficit was approximately \$699.2 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 September 30, 2017 was \$96.7 million, consisting of \$114.9 million in current assets and \$18.2 million in current liabilities. Working capital as of December 31, 2016 was \$89.1 million, consisting of \$104.9 million in current assets and \$15.8 million in current liabilities.

**Contractual obligations**

The following table summarizes our outstanding obligations as of September 30, 2017 and the effect those obligations are expected to have on our liquidity and cash flows in future periods:

| (\$ in thousands)        | Total     | Less than<br>1 year | 2 - 3 years | 4 - 5 years | More than<br>5 years |
|--------------------------|-----------|---------------------|-------------|-------------|----------------------|
| Operating leases         | \$ 3,320  | \$ 1,193            | \$ 1,462    | \$ 665      | \$                   |
| CRADAs                   | 5,625     | 2,500               | 3,125       |             |                      |
| Royalty and license fees | 7,642     | 7,642               |             |             |                      |
| Total                    | \$ 16,587 | \$ 11,334           | \$ 4,587    | \$ 665      | \$                   |

Our commitments for operating leases relate to the lease for our corporate headquarters in Boston, MA, and office space in New York, NY. On December 21, 2015 and April 15, 2016, we renewed the sublease for our corporate headquarters in Boston, MA through August 31, 2021. Our commitments for royalty and license fees relate to our agreement with Baxter Healthcare Corporation for the purchase of the assets relating to indibulin. The remaining

contract installment payments to Baxter are comprised of a \$250 thousand payment on November 3, 2017. Included in the above table are obligations for the subleased portion of our New York office (See Note 6, Commitments and Contingencies). We expect to receive a total of \$334 thousand in the next year and \$28.0 thousand in the next 2-3 years from our subtenants in the New York office.

On January 13, 2015, we entered into the MD Anderson License as detailed in Note 6, Commitments and Contingencies. The agreement includes minimum quarterly payments of \$3.8 million less approved deductions included in the above table within Royalty and License Fees. Our obligations related to this agreement are payments of \$7.6 million in the column Less than 1 Year.

On January 10, 2017, we entered into a CRADA with the National Cancer Institute as detailed in Note 6, Commitments and Contingencies. The agreement includes minimum quarterly payments of \$625 thousand. Our obligations related to this agreement are payments of \$2.5 million in the column Less than 1 Year and \$3.2 million in the column 2 - 3 Years .

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**Off-balance sheet arrangements**

During the nine months ended September 30, 2017 and 2016, 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, 2016, 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 nine months ended September 30, 2017.

**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 conduct certain of our 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.

No change in our internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) occurred during the period covered by this Quarterly Report that has materially affected, or is reasonably likely to materially affect, our internal control over financial reporting.



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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 September 30, 2017, 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, 2016. 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, 2016, 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 novel chimeric antigen receptor, or CAR, T cell and natural killer, or NK, cell therapies as well as T cell Receptor, or 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 Intrexon, pursuant to the Channel Agreement and GvHD 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 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 Intrexon will yield satisfactory products that are safe and effective, scalable, or profitable. Moreover, public perception of therapy safety issues, including adoption of new therapeutics or novel approaches to treatment, may adversely influence the willingness of subjects to participate in clinical trials, or if approved, of physicians to subscribe to the novel treatment mechanics. Physicians, hospitals and third-party payors often are slow to adopt new products, technologies and treatment practices that require additional upfront costs and training. Physicians may not be willing to undergo training to adopt this novel and personalized therapy, may decide the therapy is too complex to adopt without appropriate training and may choose not to administer the therapy. Based on these and other factors, hospitals and payors may decide that the benefits of this new therapy do not or will not outweigh its costs.

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 and GvHD Agreement with Intrexon described the terms of our use of Intrexon's advanced transgene engineering platform for the controlled and precise cellular production of anti-cancer effectors and for the development of therapeutic approaches for GvHD. 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 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 Intrexon'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 investigational new drug applications, or 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.

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In addition, the results of the limited clinical trials conducted by us, Intrexon 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.

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

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

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

The biopharmaceutical industry, and the rapidly evolving market for developing genetically engineered T cells and NK cells in particular, is characterized by intense competition and rapid innovation. Genetically engineering T cells and NK cells faces significant competition in the CAR and TCR technology space from multiple companies and their collaborators, such as Novartis/University of Pennsylvania, Bluebird bio/Celgene/Baylor College of Medicine, Kite Pharma/National Cancer Institute, Juno Therapeutics/Fred Hutchinson Cancer Research Center/Memorial Sloan-Kettering Cancer Center/Seattle Children's Research Institute, Cellectis/Pfizer, Adaptimmune/GSK, Celgene, NantKwest, Gritstone, Neon, BioNTech, and Advaxis. We also face competition from non-cell based treatments offered by other companies such as Amgen, AstraZeneca, Bristol-Myers, Incyte, Merck, and Roche. In addition, our gene therapy, immuno-oncology products such as Ad-RTS-IL-12 + veledimex face competition from VBL Therapeutics, Immunocellular Therapeutics, Merck, Genentech, Bristol-Myers, Arbor Pharmaceuticals, Tocagen, OncoSec and Insys Therapeutics. 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 Intrexon 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 Intrexon. Any termination of these licenses could result in the loss of significant rights and could harm our ability to commercialize our product candidates. Disputes may also arise between us and these licensors regarding intellectual property subject to a license agreement, including those relating to:

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

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

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

whether we and/or Intrexon are complying with our diligence obligations with respect to the use of the licensed technology in relation to our development and commercialization of our potential products under the MD Anderson License; 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 Intrexon, on acceptable terms, we may be unable to successfully develop and commercialize the affected potential products. We are generally also subject to all of the same risks with respect to protection of intellectual property that we license as we are for intellectual property that we own. If we or our licensors fail to adequately protect this intellectual property, our ability to commercialize potential products under our applicable licenses could suffer.

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

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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 nine months ended September 30, 2017, we had a net loss of \$41.1 million, and, as of September 30, 2017, we have incurred approximately \$699.2 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 or GvHD Agreement with Intrexon, 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 September 30, 2017, we have approximately \$84.4 million of cash and cash equivalents. Given our development plans, we anticipate cash resources will be sufficient to fund our operations into the fourth quarter of 2018, and we have no committed sources of additional capital at this time. The forecast of cash resources is forward-looking information that involves risks and uncertainties, and the actual amount of our expenses could vary materially and adversely as a result of a number of factors. We have based our estimates on assumptions that may prove to be wrong,



and our expenses could prove to be significantly higher than we currently anticipate. Management does not know whether additional financing will be on terms favorable or acceptable to us when needed, if at all. If adequate additional funds are not available when required, or if we are unsuccessful in entering into partnership agreements for further development of our product candidates, management may need to curtail development efforts. Based on the forecast, management determined that there is substantial doubt regarding the Company's 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 February 16, 2017 included in our Form 10-K.

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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 September 30, 2017, we have incurred approximately \$699.2 million of accumulated deficit and had approximately \$84.4 million of cash and cash equivalents. Given our current development plans, we anticipate that our current cash resources will be sufficient to fund our operations into the fourth quarter of 2018. However, changes may occur that would consume our existing capital prior to then, including expansion of the scope of, and/or slower than expected progress of, our research and development efforts and changes in governmental regulation. Actual costs may ultimately vary from our current expectations, which could materially impact our use of capital and our forecast of the period of time through which our financial resources will be adequate to support our operations. Also our estimates include the advancement of our immuno-oncology product candidates in the clinic under our Channel Agreement and GvHD Agreement with Intrexon and our increased expenses as we begin to advance candidates pursuant to the MD Anderson License with MD Anderson and commence providing funding for certain research and development activities of MD Anderson pursuant to the terms of the MD Anderson License, and we expect that the costs associated with these and 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 an MMA or BLA, to the EMA or 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 adverse events, 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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***Our use of synthetic immuno-oncology to develop product candidates may become subject to increasing regulation in the future.***

Most of the laws and regulations concerning immuno-oncology relate to the end products produced using synthetic biology, but that may change. For example, the Presidential Commission for the Study of Bioethical Issues recommended in December 2010 that the federal government oversee, but not regulate, synthetic biology research. The Presidential Commission also recommended that the government lead an ongoing review of developments in the synthetic biology field and that the government conduct a reasonable risk assessment before the field release of synthetic organisms. Other findings and recommendations have been published by the Presidential Commission through 2014. Immuno-oncology may become subject to additional government regulations as a result of the recommendations, which could require us to incur significant additional capital and operating expenditures and other costs in complying with these laws and regulations.

***\*We will incur additional expenses in connection with our Channel Agreement and GvHD Agreement with Intrexon.***

The immuno-oncology platform, in which we have acquired rights for cancer indications and for the development of therapeutic approaches for GvHD from Intrexon, includes two existing product candidates. Upon entry into the Channel Agreement and GvHD Agreement with Intrexon, we assumed responsibility for the clinical development of these product candidates, and our cell therapy programs, which we expect will increase the level of our overall research and development expenses significantly going forward. Although all human clinical trials are expensive and difficult to design and implement, we believe that due to complexity, costs associated with clinical trials for 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 and GvHD 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 Intrexon products, the actual costs associated therewith may be significantly in excess of forecasted amounts. In addition to the amount and timing of expenses related to the clinical trials, our actual cash requirements may vary materially from our current expectations for a number of other factors that may include, but are not limited to, changes in the focus and direction of our development programs, competitive and technical advances, costs associated with the development of our product candidates and costs of filing, prosecuting, defending and enforcing our intellectual property rights. If we exhaust our capital reserves more quickly than anticipated, regardless of the reason, and we are unable to obtain additional financing on terms acceptable to us or at all, we will be unable to proceed with development of some or all of our product candidates on expected timelines and will be forced to prioritize among them.

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

In June 2016, we amended our Channel Agreement and GvHD Agreement with Intrexon in order to, among other things, reduce the royalty rate on operating profits payable by us to Intrexon 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 September 30, 2017, we issued an aggregate of 3,414 shares, as dividends, of our Series 1 preferred stock to Intrexon, the holder of all the outstanding shares of our Series 1 preferred stock representing monthly dividends due from July 1, 2017 through September 30, 2017. For the year ended December 31, 2016, we issued an aggregate of 6,184 shares, as dividends, of our Series 1 preferred stock representing monthly dividends due from June 30, 2016 through December 31, 2016. 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 the Company's common stock for the 20-day period ending on the date of the public announcement such approval. We refer to this proportionate share allocated to the holders of Series 1 preferred stock as the Series 1 Liquidation Amount. In addition, the Company may elect to redeem the shares of Series 1 preferred stock in connection with or following a Deemed Liquidation Event at a price per share equal to the Series 1 Liquidation Amount. Since the conversion rate is based on the stated value of the shares of Series 1 preferred stock, which was initially \$120 million and increases at a rate of 1% per month, the holders of shares of our Series 1 preferred stock could receive a disproportionate amount of the proceeds of any voluntary or involuntary liquidation, dissolution or winding up of the Company or Deemed Liquidation Event if our stock price has not sufficiently increased prior to the time that their proportionate share is calculated. Further, pursuant to the terms of a Securities Issuance Agreement we entered into with Intrexon in connection with the issuance of the Series 1 preferred stock, we agreed that the holders of common stock issued upon the conversion of the shares of Series 1 preferred stock issued to Intrexon shall be entitled to piggy-back registration rights with respect to any common stock registered by us following such conversion.

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

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

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

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



payment of dividends or rights of redemption; or

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

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

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

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

Intrexon may terminate the Channel Agreement if we fail to use diligent efforts to develop and commercialize ZIOPHARM Products or if we elect not to pursue the development of a Cancer Program identified by Intrexon that is a Superior Therapy as defined in the Channel Agreement. We may voluntarily terminate the Channel Agreement upon 90 days written notice to Intrexon. Upon termination of the Channel Agreement, we may continue to develop and commercialize any ZIOPHARM Product that, at the time of 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 Intrexon due to an uncured breach or a voluntary termination by us), or an ongoing Phase 1 clinical trial in the field (in the case of a termination by us due to an uncured breach or a termination by Intrexon following an unconsented assignment by us or our election not to pursue development of a Superior Therapy);

Our obligation to pay 20% of net profits or revenue and 50% of sublicensing revenue or royalties with respect to these retained products will survive termination of the Channel Agreement, as described further in Note 6 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 Intrexon Corporation for the Cancer Programs*.

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 Agreements with Intrexon Corporation are based in part on early stage technology in the field of human oncologic and autoimmune therapeutics.***

Our Channel Agreements with Intrexon contemplate our use of Intrexon's advanced transgene engineering platform for the controlled and precise cellular production of anti-cancer effectors and for the development of therapeutic approaches for GvHD. 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 Intrexon's synthetic immuno-oncology platform for additional products targeting key pathways used by cancers to grow and metastasize, we may not be successful in developing and commercializing these products for a variety of reasons. The risk factors set forth herein that apply to our small molecule drug candidates, which are in various stages of development, also apply to product candidates that we seek to develop under our Channel Agreement with Intrexon.

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

The synthetic immuno-oncology platform, in which we have acquired rights for cancer indications and for the development of therapeutic approaches for GvHD from Intrexon, includes two existing product candidates. Upon entry into the Channel Agreements with Intrexon, we assumed responsibility for the clinical development of these product candidates, which we expect will increase the level of our overall research and development expenses significantly going forward. Although all human clinical trials are expensive and difficult to design and implement, we believe that due to complexity, costs associated with clinical trials for synthetic 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, prior to the adoption of our April 2013 workforce reduction plan, we added headcount in part to support our Channel Agreement endeavors, and we may need to do so again in the future which would add to our general and administrative expenses going forward.

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

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

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

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

Our obligation to pay 20% to 50% of net profits or revenue as described further in our Annual Report on Form 10-K under the heading *Business License Agreements, Intellectual Property and Other Agreements Exclusive Channel Partner Agreement with Intrexon Corporation* with respect to these retained products will survive termination of the Channel Agreement.

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

***We will incur additional expenses in connection with our License Agreement with The University of Texas M.D. Anderson Cancer Center***

Pursuant to the MD Anderson License with MD Anderson, we, together with Intrexon, obtained an exclusive, worldwide license to certain technologies owned and licensed by MD Anderson including technologies relating to novel CAR+ T cell, 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 Intrexon, 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. In addition, we also expect to enter into additional collaboration and technology transfer agreements with MD Anderson and Intrexon to accelerate technology and clinical development of these product candidates. We expect to increase the level of our overall research and development expenses significantly going forward as a result of each of these items.

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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 Intrexon by The University of Texas M.D. Anderson Cancer Center to technologies relating to novel chimeric antigen receptor, or CAR, T cell therapies and other related technologies.***

Under the MD Anderson License, we, together with Intrexon, received an exclusive, worldwide license to certain technologies owned and licensed by MD Anderson including technologies relating to novel CAR<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 Intrexon's technology suite and ZIOPHARM's clinically tested RheoSwitch Therapeutic System<sup>®</sup> 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, the Company and Intrexon shall then have a fully-paid up, royalty free, perpetual, irrevocable and sublicensable license to use the licensed intellectual property thereunder.

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

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

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

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

Continuing to undertake preclinical development and clinical trials;

Participating in regulatory approval 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, Caesar J. Belbel, our Executive Vice President and Chief Legal Officer, Dr. Francois Lebel, our Chief Medical Officer, and Executive Vice President of Research and Development and our principal scientific, regulatory, and medical advisors. Dr. Cooper s, Dr. Mauney s, Mr. Belbel s, and Dr. Lebel s employment are governed by written employment agreements. Dr. Cooper, Dr. Mauney, Mr. Belbel, and Dr. 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 Dr. Cooper, Dr. Mauney, Mr. Belbel, Dr. 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 NDAs or BLAs. We cannot be sure that we will ever obtain regulatory approval for any of our product candidates. Failure to obtain FDA approval for our product candidates will severely undermine our business by leaving us without a saleable product, and therefore without any potential revenue source, until another product candidate can be developed. There is no guarantee that we will ever be able to develop or acquire another product candidate or that we will obtain FDA approval if we are able to do so.

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

*Our product candidates are in various stages of clinical trials, which are very expensive and time-consuming. We cannot be certain when we will be able to submit 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 adverse events, we may be required to halt or delay further clinical development of our product candidates. The FDA, the EMA or other foreign regulatory authorities could order us to cease further development of or deny approval of our product candidates for any or all targeted indications.

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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 studies in support of approval of an NDA or BLA. Success in preclinical testing and early clinical trials does not ensure that later clinical trials will be successful, and we cannot be certain that the results of later clinical trials will replicate the results of prior clinical trials and preclinical testing. 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, no gene therapy products have been approved in the United States and only two products have been approved in 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 and GvHD. 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 studies 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.

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



reviewed the trial and approved its initiation. Conversely, the FDA can put an IND on clinical hold even if the RAC has provided a favorable review. 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 Intrexon on the manufacturing and scale-up of Intrexon product candidates, we lack the resources and expertise to formulate or manufacture our own product candidates. We currently are contracting for the manufacture of our product candidates. We intend to contract with one or more manufacturers to manufacture, supply, store, and distribute drug supplies for our clinical trials. If a product candidate we develop or acquire in the future receives FDA approval, we will rely on one or more third-party contractors or Intrexon to manufacture our products. Our anticipated future reliance on a limited number of third-party manufacturers exposes us to the following risks:

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

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

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

Drug manufacturers are subject to ongoing periodic unannounced inspection by the FDA, the Drug Enforcement Administration and corresponding state 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 adverse events or other problems with our products, manufacturers or manufacturing processes, or failure to comply with regulatory requirements, may yield various results, including:

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

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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 or adequate reimbursement from payors.***

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

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



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

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

***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.***

With the enactment of the Biologics Price Competition and Innovation Act of 2009, or BPCIA, as part of the Patient Protection and ACA, an abbreviated pathway for the approval of follow-on biological products was created. The new abbreviated regulatory pathway establishes legal authority for the FDA to review and approve biosimilar biologics, including the possible designation of a biosimilar as interchangeable with an existing brand product. Under the BPCIA, an application for a biosimilar product cannot be approved by the FDA until 12 years after the original branded product was approved under a BLA. However, there is a risk that the U.S. Congress could amend the BPCIA to significantly shorten this exclusivity period as previously proposed by President Obama, 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.



Although final implementation of the BPCIA is not yet complete, such FDA implementation could have a material adverse effect on the future commercial prospects for our product candidates.

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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 Intrexon technology, including the existing Intrexon product candidates, such as Ad-RTS-IL-12 + veledimex, and the GvHD program, 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 Intrexon, Intrexon has the sole right to conduct and control the filings, prosecution and maintenance of the patents and patent applications licensed to us. Although under the agreement Intrexon has agreed to consider in good faith and consult with us regarding any comments we may have regarding these patents and patent applications, we cannot guarantee that our comments will be solicited or followed. Under the MD Anderson License, future filings and applications require the agreement of each of MD Anderson, Intrexon and us, and MD Anderson has the right to control the preparation and filing of additional patent applications unless the parties agree that we or Intrexon may prosecute the application directly. Although under the agreement MD Anderson has agreed to review and incorporate any reasonable comments that we or Intrexon may have regarding these patents and patent applications, we cannot guarantee that our comments will be solicited or followed. Without direct control of the channel program patents and patent applications, we are dependent on Intrexon or MD Anderson, as applicable, to keep us advised of prosecution, particularly in foreign jurisdictions where prosecution information may not be publicly available. We anticipate that we, Intrexon and MD Anderson will file additional patent applications both in the United States and in other countries. However, we cannot predict or guarantee:

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

If and when patents will be issued;

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

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

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

and prosecution of patent applications, or to maintain the patents, covering technology that we license from third parties. We may also require the cooperation of our licensors in order to enforce the licensed patent rights, and such cooperation may not be provided. Therefore, these patents and applications may not be prosecuted and enforced in a manner consistent with the best interests of our business.

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

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

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

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

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

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

Our success also depends upon the skills, knowledge, and experience of our scientific and technical personnel, our consultants and advisors, as well as our licensors and contractors. To help protect our proprietary know-how and our inventions for which patents may be unobtainable or difficult to obtain, and to maintain our competitive position, we rely on trade secret protection and confidentiality agreements. To this end, it is our general policy to require our employees, consultants, advisors, and contractors to enter into agreements that prohibit the disclosure of confidential information and, where applicable, require disclosure and assignment to us of the ideas, developments, discoveries,

and inventions important to our business. These agreements may not provide adequate protection for our trade secrets, know-how or other proprietary information in the event of any unauthorized use or disclosure or the lawful development by others of such information. Moreover, we may not be able to obtain adequate remedies for any breaches of these agreements. Our trade secrets may also be obtained by third parties by other means, such as breaches of our physical or computer security systems. Enforcing a claim that a party illegally disclosed or misappropriated a trade secret is difficult, expensive and time-consuming, and the outcome is unpredictable. In addition, some courts inside and outside the United States are less willing or unwilling to protect trade secrets. If any of our trade secrets were to be lawfully obtained or independently developed by a competitor, we would have no right to prevent them, or those to whom they communicate it, from using that technology or information to compete with us. If any of our trade secrets, know-how or other proprietary information is disclosed, the value of our trade secrets, know-how and other proprietary rights would be significantly impaired and our business and competitive position would suffer.

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

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

Our commercial success depends upon our ability, and the ability of our collaborators, to develop, manufacture, market and sell our 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 and GvHD Agreement with Intrexon, is particularly complex. We are aware of numerous United States and foreign patents and pending patent applications of third parties that cover compositions, methods of use and methods of manufacture of synthetic 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 Intrexon is early-stage technology and we are in the process of designing and developing products using this technology. Although we will seek to avoid pursuing the development of products that may infringe any patent claims that we believe to be valid and enforceable, we may fail to do so. Moreover, given the breadth and number of claims in patents and pending patent applications in the field of synthetic immuno-oncology and the complexities and uncertainties associated with them, third parties may allege that we are infringing upon patent claims even if we do not believe such claims to be valid and enforceable.

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

discontinue or significantly delay commercialization and development of the affected products.

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

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

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

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

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

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

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

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

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

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

In addition, while it is our policy to require our employees and contractors who may be involved in the development of intellectual property to execute agreements assigning such intellectual property to us, we may be unsuccessful in executing such an agreement with each party who in fact develops intellectual property that we regard as our own. Our



and their assignment agreements may not be self-executing or may be breached, and we may be forced to bring claims against third parties, or defend claims they may bring against us, to determine the ownership of what we regard as our intellectual property.

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

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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 timing and amount of product sales, announcements of the status of development of our products, announcements of technological innovations or new therapeutic products by us or our competitors, announcements regarding collaborative agreements 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 NDA 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 September 30, 2017, our executive officers, directors and holders of five percent or more of our outstanding common stock, beneficially owned, in the aggregate, 20.4% 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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For the three months ended September 30, 2017, we issued an aggregate of 3,414 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 July 1, 2017 through September 30, 2017. 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*

None.

**Item 3. Defaults upon Senior Securities**

Not applicable.

**Item 4. Mine Safety Disclosures**

Not applicable.

**Item 5. Other Information**

None.

**Item 6. Exhibits**

| <b>Exhibit No.</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>Offer Letter by and between the Registrant and David M. Mauney, M.D. (incorporated by reference to the Registrant's Current Report on Form 8-K, SEC File No. 001-33038, filed September 28, 2017).</u>  |
| 10.2               | <u>Severance Agreement by and between the Registrant and David M. Mauney, M.D. (incorporated by reference to the Registrant's Current Report on Form 8-K, SEC File No. 001-33038, filed September 28, 2017).</u>   |
| 10.3               | <u>Inducement Award Agreement by and between the Registrant and David M. Mauney, M.D. (incorporated by reference to the Registrant's Current Report on Form 8-K, SEC File No. 001-33038,</u>   |

filed September 28, 2017).

|          |  |
|----------|--|
| 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: November 6, 2017

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

Senior Vice President -  
Finance, Chief Accounting

Officer and Treasurer  
*(Principal Financial Officer and Principal  
Accounting Officer)*  
Dated: November 6, 2017