

Karyopharm Therapeutics Inc.  
Form 10-Q  
May 10, 2018  
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**UNITED STATES**  
**SECURITIES AND EXCHANGE COMMISSION**  
**Washington, D.C. 20549**

**FORM 10-Q**

**(Mark One)**

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

**For the quarterly period ended March 31, 2018**

**OR**

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

**For the transition period from \_\_\_\_\_ to \_\_\_\_\_**

**Commission file number: 001-36167**

**Karyopharm Therapeutics Inc.**

**(Exact name of registrant as specified in its charter)**

**Delaware**  
**(State or other jurisdiction of**  
**incorporation or organization)**

**26-3931704**  
**(I.R.S. Employer**  
**Identification Number)**

**85 Wells Avenue, 2nd Floor**

**Newton, MA**  
**(Address of principal executive offices)**

**02459**  
**(Zip Code)**

**(617) 658-0600**

**(Registrant's telephone number, including area code)**

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

Indicate by check mark whether the registrant has submitted electronically 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 (§232.405 of this chapter) 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

As of May 4, 2018, there were 49,849,972 shares of Common Stock, \$0.0001 par value per share, outstanding.



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Karyopharm Therapeutics Inc.****CONDENSED CONSOLIDATED BALANCE SHEETS****(unaudited)****(in thousands, except share and per share amounts)**

	<b>March 31, 2018</b>	<b>December 31, 2017</b>
<b>Assets</b>		
Current assets:		
Cash and cash equivalents	\$ 37,499	\$ 68,997
Short-term investments	93,418	77,472
Prepaid expenses and other current assets	2,396	1,754
Restricted cash		200
Total current assets	133,313	148,423
Property and equipment, net	2,454	2,185
Long-term investments	10,314	29,396
Restricted cash	292	290
Total assets	\$ 146,373	\$ 180,294
<b>Liabilities and stockholders equity</b>		
Current liabilities:		
Accounts payable	\$ 4,949	\$ 5,665
Accrued expenses	21,545	21,445
Deferred revenue	19,729	21,921
Deferred rent	178	303
Other current liabilities	333	133
Total current liabilities	46,734	49,467
Deferred revenue, net of current portion	2,192	
Deferred rent, net of current portion	1,918	1,363
Total liabilities	50,844	50,830
Stockholders equity:		
Preferred stock, \$0.0001 par value; 5,000,000 shares authorized; none issued and outstanding		
	5	5

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Common stock, \$0.0001 par value; 100,000,000 shares authorized; 49,670,328 and 49,533,150 shares issued and outstanding at March 31, 2018 and December 31, 2017, respectively		
Additional paid-in capital	629,610	625,017
Accumulated other comprehensive loss	(286)	(217)
Accumulated deficit	(533,800)	(495,341)
<b>Total stockholders' equity</b>	<b>95,529</b>	<b>129,464</b>
<b>Total liabilities and stockholders' equity</b>	<b>\$ 146,373</b>	<b>\$ 180,294</b>

See accompanying notes to condensed consolidated financial statements.

Table of Contents**Karyopharm Therapeutics Inc.****CONDENSED CONSOLIDATED STATEMENTS OF OPERATIONS****(unaudited)****(in thousands, except share and per share amounts)**

	<b>Three Months Ended, March 31,</b>	
	<b>2018</b>	<b>2017</b>
License and other revenue	\$ 10,000	\$ 68
Operating expenses:		
Research and development	41,321	24,083
General and administrative	7,621	6,264
<b>Total operating expenses</b>	<b>48,942</b>	<b>30,347</b>
Loss from operations	(38,942)	(30,279)
Other income (expense):		
Interest income	509	400
Other expense	(14)	(15)
<b>Total other income, net</b>	<b>495</b>	<b>385</b>
Loss before income taxes	(38,447)	(29,894)
Provision for income taxes	(12)	(23)
<b>Net loss</b>	<b>\$ (38,459)</b>	<b>\$ (29,917)</b>
Net loss per share basic and diluted	\$ (0.78)	\$ (0.71)
Weighted-average number of common shares outstanding used in net loss per share basic and diluted	49,602,809	41,894,796

See accompanying notes to condensed consolidated financial statements.

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**Karyopharm Therapeutics Inc.**

**CONDENSED CONSOLIDATED STATEMENTS OF COMPREHENSIVE LOSS**

**(unaudited)**

**(in thousands)**

	<b>Three Months Ended March 31,</b>	
	<b>2018</b>	<b>2017</b>
Net loss	\$ (38,459)	\$ (29,917)
Comprehensive income (loss)		
Unrealized gain (loss) on investments	(108)	59
Foreign currency translation adjustments	39	11
Comprehensive loss	\$ (38,528)	\$ (29,847)

See accompanying notes to condensed consolidated financial statements.



Table of Contents**Karyopharm Therapeutics Inc.****CONDENSED CONSOLIDATED STATEMENTS OF CASH FLOWS****(unaudited)****(in thousands)**

	<b>Three Months Ended March 31,</b>	
	<b>2018</b>	<b>2017</b>
<b>Operating activities</b>		
Net loss	\$ (38,459)	\$ (29,917)
Adjustments to reconcile net loss to net cash used in operating activities:		
Depreciation and amortization	169	183
Net amortization of premiums and discounts on investments	160	267
Stock-based compensation expense	4,164	5,909
Changes in operating assets and liabilities:		
Prepaid expenses and other current assets	(638)	(61)
Accounts payable	(773)	(522)
Accrued expenses and other liabilities	295	(498)
Deferred rent	430	(69)
Net cash used in operating activities	(34,652)	(24,708)
<b>Investing activities</b>		
Purchases of property and equipment	(382)	
Proceeds from maturities of investments	27,602	25,624
Purchases of investments	(24,736)	(25,075)
Net cash provided by investing activities	2,484	549
<b>Financing activities</b>		
Proceeds from the exercise of stock options	429	57
Net cash provided by financing activities	429	57
Effect of exchange rate on cash	43	16
Net decrease in cash and cash equivalents	(31,696)	(24,086)
Cash, cash equivalents and restricted cash at beginning of period	69,487	50,142
Cash, cash equivalents and restricted cash at end of period	\$ 37,791	\$ 26,056
<b>Supplemental disclosure of non-cash activities</b>		
Purchases of property and equipment included in accounts payable	\$ 56	\$
Deferred financing costs included in accounts payable	\$	\$ 15

See accompanying notes to condensed consolidated financial statements.

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**Karyopharm Therapeutics Inc.**

**NOTES TO CONDENSED CONSOLIDATED FINANCIAL STATEMENTS**

(in thousands except share and per share data)

**1. Summary of Significant Accounting Policies**

*Basis of Presentation*

The accompanying unaudited condensed consolidated financial statements of Karyopharm Therapeutics Inc., a Delaware corporation (the Company), have been prepared in accordance with accounting principles generally accepted in the United States (GAAP) for interim financial reporting and as required by Regulation S-X, Rule 10-01. Accordingly, they do not include all of the information and footnotes required by GAAP for complete financial statements. In the opinion of management, all adjustments (including those which are normal and recurring) considered necessary for a fair presentation of the interim financial information have been included. When preparing financial statements in conformity with GAAP, the Company must make estimates and assumptions that affect the reported amounts of assets, liabilities, revenues, expenses and related disclosures at the date of the financial statements. Actual results could differ from those estimates. Additionally, operating results for the three months ended March 31, 2018 are not necessarily indicative of the results that may be expected for any other interim period or for the fiscal year ending December 31, 2018. For further information, refer to the financial statements and footnotes included in the Company's Annual Report on Form 10-K for the year ended December 31, 2017 as filed with the Securities and Exchange Commission (SEC) on March 15, 2018.

*Basis of Consolidation*

The condensed consolidated financial statements at March 31, 2018 include the accounts of (i) the Company, (ii) Karyopharm Securities Corp. (a wholly-owned Massachusetts corporation of the Company incorporated in December 2013), (iii) Karyopharm Europe GmbH (a wholly-owned German Limited Liability Company formed in August 2014) and (iv) Karyopharm Therapeutics (Bermuda) Ltd. (a wholly-owned Bermuda subsidiary of the Company formed in March 2015). All intercompany balances and transactions have been eliminated in consolidation.

*Revenue Recognition*

The Company adopted ASU 2014-09, *Revenue from Contracts with Customers* (ASC 606), as well as subsequent amendments, which were codified in ASC 606, on January 1, 2018, using the modified retrospective method for all contracts not completed as of the date of adoption. The reported results for the quarter ended March 31, 2018 reflect the application of ASC 606 while the reported results for 2017 were prepared under the guidance of ASC 605, *Revenue Recognition* (ASC 605), which is also referred to herein as legacy GAAP or the previous guidance. The adoption of ASC 606 did not have a material impact on the Company's consolidated financial position, results of operations, stockholder's equity or cash flows as of the adoption date, as no transition adjustment for any of the Company's contracts with customers was required.

ASC 606 applies to all contracts with customers, except for contracts that are within the scope of other standards, such as leases, insurance, collaboration arrangements and financial instruments. Under ASC 606, an entity recognizes revenue when its customer obtains control of promised goods or services, in an amount that reflects the consideration which the entity expects to receive in exchange for those goods or services. To determine revenue recognition for arrangements that an entity determines are within the scope of ASC 606, the entity performs the following five steps:

(i) identify the contract(s) with a customer; (ii) identify the performance obligations in the contract; (iii) determine the transaction price; (iv) allocate the transaction price to the performance obligations in the contract; and (v) recognize revenue when (or as) the entity satisfies a performance obligation. At contract inception, once the contract is determined to be within the scope of ASC 606, the Company assesses the goods or services promised within each contract and determines those that are performance obligations, and assesses whether each promised good or service is distinct. The Company then recognizes as revenue the amount of the transaction price that is allocated to the respective performance obligation when (or as) the performance obligation is satisfied.

The Company generates revenue from license or similar agreements with pharmaceutical companies for the development and commercialization of certain of its product candidates. Such agreements may include the transfer of intellectual property rights in the form of licenses, transfer of technological know-how, delivery of drug substances, research and development services, and participation on certain committees with the counterparty. Payments made by the customers may include non-refundable upfront fees, payments upon the exercise of customer options, payments based upon the achievement of defined milestones, and royalties on sales of product candidates if they are successfully approved and commercialized.

If the license to the Company's intellectual property is determined to be distinct from the other performance obligations identified in the arrangement, the Company recognizes the transaction price allocated to the license as revenue upon transfer of control of the license. The Company evaluates all other promised goods or services in the agreement to determine if they are distinct. If they are not distinct, they are combined with other promised goods or services to create a bundle of promised goods or services that is

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distinct. Optional future services where any additional consideration paid to the Company reflects their standalone selling prices do not provide the customer with a material right and, therefore, are not considered performance obligations. If optional future services are priced in a manner which provides the customer with a significant or incremental discount, they are material rights, and are accounted for as performance obligations.

The Company utilizes judgment to determine the transaction price. In connection therewith, the Company evaluates contingent milestones at contract inception to estimate the amount which is not probable of a material reversal to include in the transaction price using the most likely amount method. Milestone payments that are not within the control of the Company, such as regulatory approvals, are not considered probable of being achieved until those approvals are received and therefore the variable consideration is constrained. The transaction price is then allocated to each performance obligation on a relative stand-alone selling price basis, for which the Company recognizes revenue as or when the performance obligations under the contract are satisfied. At the end of each reporting period, the Company re-evaluates the probability of achieving development milestone payments which may not be subject to a material reversal and, if necessary, adjusts its estimate of the overall transaction price. Any such adjustments are recorded on a cumulative catch-up basis, which would affect license and other revenue, as well as earnings, in the period of adjustment.

The Company then determines whether the performance obligations or combined performance obligations are satisfied over time or at a point in time and, if over time, the appropriate method of measuring progress for purposes of recognizing revenue from non-refundable, upfront fees. The Company evaluates the measure of progress, as applicable, each reporting period and, if necessary, adjusts the measure of performance and related revenue recognition.

When consideration is received, or such consideration is unconditionally due, from a customer prior to transferring goods or services to the customer under the terms of a contract, a contract liability is recorded within deferred revenue. Contract liabilities within deferred revenue are recognized as revenue after control of the goods or services is transferred to the customer and all revenue recognition criteria have been met.

For arrangements that include sales-based royalties, including sales-based milestone payments, and the license is deemed to be the predominant item to which the royalties relate, the Company recognizes revenue at the later of when the related sales occur or when the performance obligation to which some or all of the royalty has been allocated has been satisfied (or partially satisfied).

## **2. Recent Accounting Pronouncements**

### *Recently Adopted Accounting Standards*

As detailed above, the Company adopted ASC 606 on January 1, 2018. Under the modified retrospective transition method, the Company applied ASC 606 to all contracts within scope as of January 1, 2018. Under the practical expedient concerning contract modifications contained in the transitional provisions of ASC 606, the Company has not retrospectively restated its contracts for modifications prior to the earliest period presented, and instead has reflected the aggregate effect of all modifications when identifying the satisfied and unsatisfied performance obligations, determining the transaction price and allocating the transaction price. Qualitatively, the effect of applying this practical expedient is not material to the periods presented in the consolidated financial statements. As more fully discussed in Note 3, Asset Purchase and License Agreements, only the Company's arrangement with Ono Pharmaceutical Co., Ltd. was determined to have unsatisfied performance obligations as of the adoption date. However, the pattern of revenue recognition was not affected and, therefore, no transition adjustment was recorded to the opening balance of accumulated deficit on January 1, 2018. All other agreements subject to transition, which only

included the Company's arrangement with Anivive Lifesciences Inc., were unaffected by the adoption of ASC 606 in all periods presented in the consolidated financial statements through application of the modified retrospective transition method.

In August 2016, the FASB issued ASU 2016-15, *Classification of Certain Cash Receipts and Cash Payments* ( ASU 2016-15 ). ASU 2016-15. This standard addresses eight specific cash flow issues with the objective of reducing the existing diversity in practice. The Company adopted ASU 2016-05 effective January 1, 2018 and the adoption did not have a material impact on the Company's statements of cash flows.

In October 2016, the FASB issued Accounting Standards Update ( ASU ) No. 2016-16, *Accounting for Income Taxes: Intra-Entity Asset Transfers of Assets Other than Inventory (Topic 740)*. Topic 740 eliminates the ability to defer the tax expense related to intra-entity asset transfers other than inventory. Under the new standard, entities should recognize the income tax consequences on an intra-entity transfer of an asset other than inventory when the transfer occurs. The Company adopted Topic 740 effective January 1, 2018 and the adoption did not have a material impact on the Company's financial position or results of operations.

In November 2016, the FASB issued ASU No. 2016-18, *Statement of Cash Flows (Topic 230): Restricted Cash*. The new standard requires that a statement of cash flows explain the change during the period in the total of cash, cash equivalents and amounts generally described as restricted cash or restricted cash equivalents. Therefore, amounts generally described as restricted cash and restricted cash equivalents should be included with cash and cash equivalents when reconciling the beginning-of-period and end-of-

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period total amounts shown on the statement of cash flows. The Company adopted this standard effective January 1, 2018 and reclassified restricted cash in the statements of cash flows to be included in the cash and cash equivalents balance. The standard resulted in the reclassification of \$292 and \$479 into the balance of cash, cash equivalents and restricted cash on the statement of cash flows for the periods ended March 31, 2018 and 2017, respectively.

In May 2017, the FASB issued ASU 2017-09, *Compensation-Stock Compensation (Topic 718)* ( ASU 2017-09 ) *Scope of Modification Accounting*. ASU 2017-09 provides clarification on when modification accounting should be used for changes to the terms or conditions of a share-based payment award. This ASU does not change the accounting for modifications but clarifies that modification accounting guidance should only be applied if there is a change to the value, vesting conditions, or award classification and would not be required if the changes are considered non-substantive. The Company adopted this standard effective January 1, 2018 and the adoption did not have a material impact on the Company's consolidated financial statements.

*Recently Issued Accounting Standards*

In February 2016, the FASB issued ASU No. 2016-02, *Leases (Topic 842)*. The new standard requires that all lessees recognize the assets and liabilities that arise from leases on the balance sheet and disclose qualitative and quantitative information about its leasing arrangements. The new standard will be effective for the Company on January 1, 2019. The Company is in process of evaluating this guidance and determining the potential impact on its consolidated financial statements; however, it anticipates that the new standard will result in the Company recording additional right of use assets and corresponding liabilities on its consolidated balance sheet.

**3. Asset Purchase and License Agreements****Biogen Asset Purchase Agreement**

On January 24, 2018, the Company entered into an Asset Purchase Agreement (the APA ) and Letter Agreement with Biogen MA Inc., a Massachusetts corporation and subsidiary of Biogen, Inc. ( Biogen ).

Under the terms of the APA and Letter Agreement, the Company sold Biogen exclusive worldwide rights to develop and commercialize the Company's oral Selective Inhibitor of Nuclear Export (SINE) compound KPT-350 and certain related assets with an initial focus in amyotrophic lateral sclerosis (ALS) (the Transfer of IP ), and also granted Biogen: (i) an exclusive worldwide license under certain of the Company's intellectual property to manufacture or have manufactured KPT-350 (the Manufacturing License ), (ii) a technology transfer package, consisting of information and the Company's know-how regarding the manufacture of KPT-350 (the Manufacturing Technology Transfer ), (iii) a right, at Biogen's request, to have the Company provide transition assistance regarding manufacturing and other matters (the Transition Assistance ), (iv) existing inventory of KPT-350 (the Inventory ), (v) an initial supply of KPT-350 (the Initial Supply ), and (vi) a right, at Biogen's request, to have the Company manufacture and supply the active pharmaceutical ingredient for an additional supply of KPT-350 (the Additional Supply ). In consideration for these rights, the Company received an upfront payment of \$10,000, and is eligible to receive additional payments of up to \$142,000 based on the achievement by Biogen of future specified development milestones, and up to \$65,000 based on the achievement by Biogen of future specified commercial milestones. The Company will also be eligible to receive tiered royalty payments that reach low double-digits based on future net sales until the later of the tenth anniversary of the first commercial sale of the applicable product and the expiration of specified patent protection for the applicable product, determined on a country-by-country basis.

The Company and Biogen have made customary representations and warranties and agreed to customary covenants in the APA, including covenants requiring Biogen to use commercially reasonable efforts to develop KPT-350 in

specified neurological indications, including ALS, in any of the United States, United Kingdom, France, Spain, Germany or Italy. The APA will continue in effect until the expiration of all royalty obligations, provided that the APA may be terminated earlier by Biogen, subject to the requirements that Biogen (i) negotiate in good faith with the Company regarding an assignment or license back to the Company of the purchased assets and (ii) not transfer or license the purchased assets to a third party unless such third party assumes Biogen's obligations to the Company under the APA.

The Company assessed this arrangement in accordance with ASC 606 and concluded that the contract counterparty, Biogen, is a customer. The Company identified the following material promises in the arrangement: the Transfer of IP and the Manufacturing License. The Company also identified other immaterial promises under the contract that were not deemed performance obligations. The Company further determined other promises for Additional Supply and Transition Assistance represented customer options, which would create an obligation for the Company if exercised by Biogen. Since either no additional or immaterial consideration is owed to the Company by Biogen upon exercise of the customer options for Additional Supply and Transition Assistance, the Company determined both are offered at significant and incremental discounts. Accordingly, they were assessed as material rights and, therefore, separate performance obligations in the arrangement.



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The Company then determined the Transfer of IP and the Manufacturing License were not distinct from one another and must be combined as a performance obligation (the Combined Performance Obligation). This is because Biogen requires the Manufacturing License to derive benefit from the Transfer of IP. Based on these determinations, as well as the considerations noted above with respect to the material rights for Additional Supply and Transition Assistance, the Company identified three distinct performance obligations at the inception of the contract: (i) the Combined Performance Obligation, (ii) the material right for Additional Supply, and (iii) the material right for Transition Assistance.

The Company further determined that the up-front payment of \$10,000 constituted the entirety of the consideration to be included in the transaction price at contract inception, which was allocated to the performance obligations based on their relative stand-alone selling prices. In connection therewith, the Company estimated the stand-alone selling price of the (i) Combined Performance Obligation, (ii) material right for Additional Supply, and (iii) material right for Transition Assistance, and determined the stand-alone selling price of the material rights for Additional Supply and Transition Assistance were insignificant based on various quantitative and qualitative considerations. Accordingly, the Company further determined the allocation of the transaction price to the material rights for Additional Supply and Transition Assistance was insignificant. Based on the estimates of the stand-alone selling prices for each of the performance obligations, the Company determined that substantially all the \$10,000 transaction price should be allocated to the Combined Performance Obligation. The Company believes that a change in the assumptions used to determine its best estimate of the stand-alone selling prices for the identified performance obligations would not have a significant effect on the allocation of the underlying transaction price to the performance obligations.

Upon execution of the Biogen Agreement, the transaction price included only the \$10,000 up-front payment owed to the Company. The Company may receive further payments upon the achievement of certain regulatory and sales milestones, as detailed above, as well as tiered royalty payments that reach low double-digits based on future net sales. The future regulatory milestones, which represent variable consideration, were evaluated under the most likely amount method, and were not included in the transaction price, because the amounts are fully constrained as of March 31, 2018. As part of its evaluation of the constraint, the Company considered numerous factors, including that receipt of such milestones is outside the control of the Company. Separately, any consideration related to sales-based milestones, as well as royalties on net sales upon commercialization by Biogen, will be recognized when the related sales occur, as they were determined to relate predominantly to the intellectual property and, therefore, have also been excluded from the transaction price in accordance with the sales-based royalty exception, as well as the Company's accounting policy. The Company will re-evaluate the transaction price in each reporting period, as uncertain events are resolved, or as other changes in circumstances occur.

During the quarter ended March 31, 2018, the Company recognized \$10,000 of revenue, as it had satisfied its promises under the Combined Performance Obligation by transferring the underlying promised goods at a point in time during the quarter ended March 31, 2018.

**Ono License Agreement**

Effective October 11, 2017 (the Effective Date), the Company entered into a license agreement (the License Agreement) with Ono Pharmaceutical Co., Ltd., a corporation organized and existing under the laws of Japan (Ono), pursuant to which the Company granted Ono exclusive rights to develop and commercialize, at its own cost, selinexor (KPT-330), the Company's lead, novel, oral SINE compound, as well as eltanexor (KPT-8602), the Company's second-generation oral SINE compound, for the diagnosis, treatment and/or prevention of all human oncology indications (the Field) in Japan, Republic of Korea, Republic of China (Taiwan) and Hong Kong, as well as in the ten Southeast Asian countries currently comprising the Association of Southeast Asian Nations (the Ono Territory) (the Exclusive License). Pursuant to the terms of the License Agreement, the Company received an upfront payment of

¥2.5 billion (US\$21,916 on the date received), and could receive up to ¥10.15 billion (approximately US\$90,500 at the exchange rate as of the Effective Date) in milestone payments if certain development goals are achieved and up to ¥9.0 billion (approximately US\$80,200 at the exchange rate as of the Effective Date) in milestone payments if certain sales milestones are achieved, as well as a low double-digit royalty based on future net sales of selinexor and eltanexor in the Ono Territory. In addition, upon Ono's election and the parties' full execution of a manufacturing technology transfer plan and satisfaction of other specified conditions (the Manufacturing Election), the Company will grant to Ono non-exclusive rights to manufacture selinexor, eltanexor and products containing such compounds in or outside of the Ono Territory solely for development and commercialization in the Field in the Ono Territory.

As part of the License Agreement, Ono will also have the right to participate in global clinical studies of selinexor and eltanexor, and will bear the cost and expense for patients enrolled in clinical studies in the Ono Territory. Ono is responsible for seeking regulatory and marketing approvals for selinexor and eltanexor in the Ono Territory, as well as any development of the products specifically necessary to obtain such approvals. Ono is also responsible for the commercialization of products containing selinexor or eltanexor in the Field in the Ono Territory at its own cost and expense.

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Subject to Ono's Manufacturing Election, the Company will furnish clinical supplies of drug substance to Ono for use in Ono's development efforts pursuant to a clinical supply agreement to be entered into by the Company and Ono, and Ono may elect to have the Company provide commercial supplies of drug product to Ono pursuant to a commercial supply agreement to be entered into by the Company and Ono, in each case the costs of which will be borne by Ono.

The License Agreement will continue in effect on a product-by-product, country-by-country basis until the later of the tenth anniversary of the first commercial sale of the applicable product in such country or the expiration of specified patent protection and regulatory exclusivity periods for the applicable product in such country. However, the License Agreement may be terminated earlier by (i) either party for breach of the License Agreement by the other party or in the event of the insolvency or bankruptcy of the other party, (ii) Ono on a product-by-product basis for certain safety reasons or on a product-by-product, country-by-country basis for any reason with 180 days' prior notice or (iii) the Company in the event Ono challenges or assists with a challenge to certain of the Company's patent rights.

The Company assessed this arrangement in accordance with ASC 606 and concluded that the contract counterparty, Ono, is a customer. The Company identified the following material promises under the contract: (i) Exclusive Licenses for selinexor and eltanexor, (ii) Initial Data Transfer for selinexor and eltanexor, which consisted of regulatory data compiled by the Company for the licensed compounds and products as of the Effective Date, (iii) Initial Clinical Supply for selinexor, which consisted of units of clinical supply for Ono to conduct its Phase I Trial, and (iv) an obligation to stand-ready to provide Initial Clinical Supply for eltanexor. The Company also identified several immaterial promises under the contract relating to information exchanges, and participation on operating committees and other working groups. Separately, the Company also identified certain customer options that would create an obligation for the Company if exercised by Ono, including the (i) Additional Data Transfer for selinexor and eltanexor, which would consist of the transfer of additional regulatory data compiled by the Company for the licensed compounds and products after the Effective Date, (ii) Additional Clinical Supply and Related Substance Supply for selinexor and eltanexor, which would consist of supplying Ono with units and substance of selinexor and eltanexor incremental to the Initial Clinical Supply for selinexor and the obligation to stand-ready to provide Initial Clinical Supply for eltanexor, as noted above, (iii) Manufacturing Technology Transfer and License for selinexor and eltanexor under Ono's Manufacturing Election, as detailed above, and (iv) Option for Backup Compound, which represents Ono's option to select a replacement compound in the event it elects to discontinue to development of either of the licensed compounds. Collectively, these options are referred to herein as the Transfer Option. The Transfer Options individually represent material rights, as they were offered at a significant and incremental discount. Therefore, they were further assessed as performance obligations under the License Agreement. The Company also identified certain other customer options that would create a manufacturing obligation for the Company if exercised by Ono, including commercial supply. This option is referred to herein as the Manufacturing Option. The Manufacturing Option does not represent a material right, as it is not offered at a significant and incremental discount.

In further evaluating the promises detailed above, the Company determined that the (i) Exclusive License, Initial Data Transfer, and Initial Clinical Supply for selinexor and (ii) Exclusive License, Initial Data Transfer, and obligation to stand-ready to provide Initial Clinical Supply of eltanexor were not distinct from one another, and must be combined as two separate performance obligations (the Combined License Obligation for selinexor and Combined License Obligation for eltanexor). This is because, for both selinexor and eltanexor, Ono requires the Initial Data Transfer and clinical supply to derive benefit from the Exclusive Licenses since the Company did not grant manufacturing licenses for selinexor and eltanexor at contract inception. The Company also determined that each of the Transfer Options represents a distinct performance obligation. Based on these determinations, the Company identified six distinct performance obligations at the inception of the License Agreement, including (i) the Combined License Obligation for selinexor, (ii) the Combined License Obligation for eltanexor, and the four components of the Transfer Options, including (iii) the material right for Additional Data Transfer, (iv) the material right for Additional Clinical Supply

and Related Substance Supply, (iv) the material right for Manufacturing Technology Transfer and License, and (vi) the material right for the Option for a Backup Compound.

The Company further determined the up-front payment of ¥2.5 billion (US\$21,916 on the date received) constituted the entirety of the consideration to be included in the transaction price at contract inception, which was allocated to the performance obligations based on the Company's best estimate of their relative stand-alone selling prices. The Company determined that substantially all of the value in the arrangement is through the Combined License Obligation for selinexor and Combined License Obligation for eltanexor. In connection therewith, the Company estimated the standalone selling price for each of the material rights within the Transfer Options, and determined such amounts were insignificant, and, therefore, immaterial for purposes of allocation. Accordingly, the Company allocated the ¥2.5 billion (US\$21,916 on the date received) upfront transaction price amongst the Combined License Obligations as follows: \$19,724 for selinexor and \$2,192 for eltanexor. The Company believes that a change in the assumptions used to determine its best estimate of the stand-alone selling prices for any of the identified performance obligations would not have a significant effect on the allocation of the underlying transaction price to the performance obligations.

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Upon execution of the Ono Agreement, the transaction price included only the ¥2.5 billion (US\$21,916 on the date received) up-front payment owed to the Company. As referenced above, the Company is eligible to receive additional payments of up to ¥10.15 billion based on the achievement by Ono of future specified development milestones and up to ¥9.0 billion based on the achievement by Ono of future specified commercial milestones, as well as a low double-digit royalty based on future net sales of selinexor and eltanexor in the Ono Territory. In addition, the Company could receive cost reimbursement in connection with its promise to stand-ready to provide Initial Clinical Supply for eltanexor in the future. The future regulatory milestones and cost reimbursement for providing Initial Clinical Supply of eltanexor, both of which represent variable consideration, were evaluated under the most likely amount method, and were not included in the transaction price, because the amounts were fully constrained as of March 31, 2018. As part of its evaluation of the constraint, the Company considered numerous factors, including that receipt of such amounts is outside the control of the Company. Separately, any consideration related to sales-based milestones, as well as royalties on net sales upon commercialization by Ono, will be recognized when the related sales occur, as they were determined to relate predominantly to the intellectual property granted to Ono and, therefore, have also been excluded from the transaction price in accordance with the sales-based royalty exception, as well as the Company's accounting policy. The Company will re-evaluate the transaction price in each reporting period, as uncertain events are resolved, or as other changes in circumstances occur.

To date, the Company recognized no revenue associated with this agreement. Revenue will be recognized for (i) the Combined License Obligation for selinexor once the Initial Clinical Supply is delivered, and (ii) the Combined License Obligation for eltanexor once the Company's promise to stand-ready to provide Initial Clinical Supply of eltanexor in the future is fulfilled, which are the only undelivered items in the Combined License Obligation for selinexor and Combined License Obligation for eltanexor, respectively. As of March 31, 2018, the ¥2.5 billion (US\$21,916 on the date received) upfront payment represents a contract liability, (i) US\$19,724 of which was included in deferred revenue and is classified as a current liability in the condensed consolidated balance sheet and (ii) \$2,192 of which was included in deferred revenue and is classified as a non-current liability in the condensed consolidated balance sheet. The Initial Clinical Supply of selinexor was fully delivered during the quarter ending June 30, 2018, and the transaction price allocated to the Combined License Obligation for selinexor, or US\$19,724, will be recognized in that period.

Given the determination that the license rights conveyed to Ono lacked standalone value from the initial clinical supply of product required for Ono to obtain benefit from the rights granted and the fact that no initial clinical supply had been provided to Ono as of December 31, 2017, the Company concluded that no revenue should be recognized under ASC 605. Arrangement consideration at the inception of the arrangement included the ¥2.5 billion (US\$21,916 on the date received) upfront payment. All other forms of consideration such as milestones and royalties, were considered contingent consideration, with no amount allocable to deliverables at the inception of the arrangement. The Company concluded the contingent consideration would be recognized when the underlying contingencies have been resolved, assuming all other revenue recognition criteria are met. As the accounting treatment for this agreement did not materially differ under ASC 605 and ASC 606, and no revenue was recognized under the Company's previous accounting policy through December 31, 2017, no transition adjustment was recorded to the opening balance of accumulated deficit as of January 1, 2018. Accordingly, the upfront payment of ¥2.5 billion (US\$21,916 on the date received), which again represents a contract liability, was also included in deferred revenue as of December 31, 2017.

**MMRF Research Agreement**

The Company is a party to a research agreement with the Multiple Myeloma Research Foundation (MMRF). Under this research agreement, the Company is obligated to make certain payments to MMRF, including if the Company out-licenses selinexor. The terms of this research agreement do not apply to eltanexor. In connection with the transactions contemplated under the Agreement, the Company paid to MMRF approximately ¥225 million

(US\$1,972) of the upfront cash payment from Ono in the year ended December 31, 2017, and it will be obligated to pay a percentage of any milestone payments from Ono and a mid-single-digit percentage of any royalty payments from Ono. Such payments are recorded within research and development expense in the Company's condensed consolidated statement of operations. The maximum aggregate amount the Company may be obligated to pay to MMRF under the research agreement is \$6,000.

### **Anivive License Agreement**

On April 28, 2017, the Company entered into a license agreement with Anivive Lifesciences, Inc. ( Anivive ), a biopharmaceutical company engaged in the research, development and commercialization of animal health medicines, pursuant to which the Company has granted Anivive an exclusive, worldwide license to develop and commercialize verdinexor (KPT-335) for the treatment of cancer in companion animals (the Anivive Agreement ) (the Exclusive License ). Pursuant to the terms of the Anivive Agreement, the Company received an upfront payment of \$1,000 and a payment of \$250 upon the completion of the technology transfer, which occurred during the year ended December 31, 2017. In addition, the Company is eligible to receive potential clinical, regulatory and commercial development milestone payments totaling up to \$43,250, as well as a low double-digit royalty based on Anivive's future net sales of verdinexor following commercialization. The potential future milestone payments are composed of \$5,750 based on achievement of clinical and regulatory milestone events and \$37,500 based on achievement of sales milestone events.

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The Company assessed this arrangement in accordance with ASC 606 and concluded that the contract counterparty, Anivive, is a customer. The Company identified the following material promises under the contract, the Exclusive License and the Technology Transfer, which consisted of regulatory data compiled by the Company for the licensed compound and product as of the Effective Date. The Company also identified the following immaterial promises under the contract that were not deemed performance obligations, including participating on a product advisory committee and sharing regulatory matter information. The Company further determined other promises for (i) transfer of additional technology in the future, if developed by the Company, and (ii) facilitating manufacturing and supply relationships with the Company's third-party contract manufacturers represented customer options, which would create an obligation for the Company if exercised by Anivive. Since either no additional or immaterial consideration is owed to the Company by Anivive upon exercise of the customer options noted, the Company determined both are offered at significant and incremental discounts. Accordingly, they were assessed as material rights and, therefore, separate performance obligations in the arrangement.

In further evaluating the promises detailed above, the Company determined that the Exclusive License and Technology Transfer were not distinct from one another and must be combined as a performance obligation (the Combined License Obligation). This is because Anivive requires the Technology Transfer to derive benefit from the Exclusive License. Based on these determinations, the Company identified three distinct performance obligations at the inception of the contract: (i) the Combined License Obligation, (ii) the material right for transfer of additional technology in the future, if developed by the Company, and (iii) the material right for facilitating manufacturing and supply relationships with the Company's third-party contract manufacturers.

The Company further determined that the up-front payment of \$1,000 upon contract execution, as well as the \$250 upon completion of the Technology Transfer, constituted the entirety of the consideration to be included in the transaction price as of the transition date, January 1, 2018, which was allocated to the performance obligations based on their relative stand-alone selling prices. In connection therewith, the Company estimated the stand-alone selling price of the (i) Combined License Obligation, (ii) material right for transfer of additional technology in the future, if developed by the Company, and (iii) the material right for facilitating manufacturing and supply relationships with the Company's third-party contract manufacturers, and determined the stand-alone selling price of the material rights noted were insignificant based on various qualitative considerations. Accordingly, the Company further determined the allocation of the upfront payment to the material rights noted was insignificant. Based on the estimates of the stand-alone selling prices for each of the performance obligations, the Company determined substantially all the \$1,250 transaction price should be allocated to the Combined License Obligation. The Company believes that a change in the assumptions used to determine its best estimate of the stand-alone selling prices for the identified performance obligations would not have a significant effect on the allocation of the underlying transaction price to the performance obligations.

As referenced above, the up-front payment of \$1,000 upon contract execution, as well as the \$250 upon completion of the Technology Transfer, constituted the entirety of the consideration to be included in the transaction price as of the transition date, January 1, 2018. The Company is also eligible to receive additional payments up to \$5,750 based on achievement of clinical and regulatory milestone events and up to \$37,500 based on achievement of sales milestone events, as well as a low double-digit royalty based on Anivive's future net sales of verdinexor following commercialization. The future regulatory milestones, which represent variable consideration, were evaluated under the most likely amount method, and were not included in the transaction price, because the amounts are fully constrained as of March 31, 2018. As part of its evaluation of the constraint, the Company considered numerous factors, including that receipt of such milestones is outside the control of the Company. Separately, any consideration related to sales-based milestones, as well as royalties on net sales upon commercialization by Anivive, will be recognized when the related sales occur, as they were determined to relate predominantly to the intellectual property granted to Anivive and, therefore, have also been excluded from the transaction price in accordance with the sales-based royalty

exception, as well as the Company's policy. The Company will re-evaluate the transaction price in each reporting period, as uncertain events are resolved, or as other changes in circumstances occur.

To date, the Company recognized \$1,250 of revenue associated with the Anivive Agreement. Revenue for the upfront payment and technology transfer milestone was recognized upon completion of the Technology Transfer in October 2017, as all promises under the Combined License Obligation had been fulfilled.

The Company reached similar conclusions when evaluating this agreement under its previous accounting policy, which was based on legacy guidance within ASC 605. When evaluating this agreement under ASC 605, the Company concluded that the licenses to verdinexor and technology transfer concerning the licensed product are essential to Anivive's intended use of the license to develop and commercialize the Licensed Compounds and represented a single unit of accounting. Other potential contractual obligations were evaluated and determined not to be deliverables at inception of the arrangement or were evaluated and determined to be immaterial to the arrangement and, therefore, not evaluated further in the Company's analysis. Arrangement consideration at the inception of the arrangement included the \$1,250 in upfront payments, which includes the milestone fee upon completion of the Technology Transfer. All other forms of consideration, such as milestones and royalties, were considered contingent consideration, with no amount allocable



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to deliverables at the inception of the arrangement. The Company concluded the contingent consideration would be recognized when the underlying contingencies have been resolved, assuming all other revenue recognition criteria are met. Given the single unit of accounting and that the Technology Transfer would be the last item to be delivered within the unit of accounting, the Company concluded that revenue would be recognized upon the completion of delivery of the technology transfer assuming all other general revenue recognition criteria would be met as of that date. As the accounting treatment for this agreement did not materially differ under ASC 605 and ASC 606, and the upfront payment and technology transfer fee, totaling \$1,250, was recognized as revenue during the year ended December 31, 2017 in accordance with the Company's previous accounting policy, and would have also been recognized during the year ended December 31, 2017 in accordance with the Company's accounting policy under ASC 606, no transition adjustment was recorded to the opening balance of accumulated deficit as of January 1, 2018.

**4. Fair Value of Financial Instruments**

Financial instruments, including cash, restricted cash, prepaid expenses and other current assets, accounts payable and accrued expenses are presented in the condensed consolidated financial statements at amounts that approximate fair value at March 31, 2018 and December 31, 2017.

The Company is required to disclose information on all assets and liabilities reported at fair value that enables an assessment of the inputs used in determining the reported fair values. The fair value hierarchy prioritizes valuation inputs based on the observable nature of those inputs. The fair value hierarchy applies only to the valuation inputs used in determining the reported fair value of the investments and is not a measure of the investment credit quality. The hierarchy defines three levels of valuation inputs:

Level 1 inputs Quoted prices in active markets for identical assets or liabilities

Level 2 inputs Inputs other than quoted prices included within Level 1 that are observable for the asset or liability, either directly or indirectly

Level 3 inputs Unobservable inputs that reflect the Company's own assumptions about the assumptions market participants would use in pricing the asset or liability

Items classified as Level 2 within the valuation hierarchy consist of commercial paper, corporate debt securities, U.S. government agency securities and certificates of deposit. The Company estimates the fair values of these marketable securities by taking into consideration valuations obtained from third-party pricing sources. These pricing sources utilize industry standard valuation models, including both income and market-based approaches, for which all significant inputs are observable, either directly or indirectly, to estimate fair value. These inputs include market pricing based on real-time trade data for the same or similar securities, issuer credit spreads, benchmark yields, and other observable inputs. The Company validates the prices provided by its third-party pricing sources by understanding the models used, obtaining market values from other pricing sources and analyzing pricing data in certain instances.

The following table presents information about the Company's financial assets that have been measured at fair value at March 31, 2018 and indicates the fair value hierarchy of the valuation inputs utilized to determine such fair value (in thousands):

Description	Total
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		<b>Quoted Prices in Active Markets (Level 1)</b>	<b>Significant Other Observable Inputs (Level 2)</b>	<b>Significant Unobservable Inputs (Level 3)</b>
<b>Financial assets</b>				
Cash equivalents:				
Money market funds	\$ 15,551	\$ 15,551	\$	\$
Investments:				
Current:				
Corporate debt securities	79,857		79,857	
Commercial paper	6,074		6,074	
U.S. government and agency securities	4,987		4,987	
Certificates of deposit	2,500		2,500	
Non-current:				
Corporate debt securities (one to two year maturity)	7,836		7,836	
U.S. government and agency securities	2,478		2,478	
	\$ 119,283	\$ 15,551	\$ 103,732	\$

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The following table presents information about the Company's financial assets that have been measured at fair value at December 31, 2017 and indicates the fair value hierarchy of the valuation inputs utilized to determine such fair value (in thousands):

Description	Total	Quoted Prices in Active Markets (Level 1)	Significant Other Observable Inputs (Level 2)	Significant Unobservable Inputs (Level 3)
<b>Financial assets</b>				
Cash equivalents:				
Money market funds	\$ 41,805	\$ 41,805	\$	\$
Investments:				
Current:				
Corporate debt securities	66,253		66,253	
Commercial paper	6,720		6,720	
Certificates of deposit	2,500		2,500	
U.S. government and agency securities	1,999		1,999	
Non-current:				
Corporate debt securities (one to two year maturity)	26,916		26,916	
U.S. government securities and agency securities	2,480		2,480	
	\$ 148,673	\$ 41,805	\$ 106,868	\$

**5. Investments**

The following table summarizes the Company's investments as of March 31, 2018 (in thousands):

	Amortized Cost	Gross Unrealized Gains	Gross Unrealized Loss	Fair Value
Current:				
Corporate debt securities	\$ 80,124	\$ 2	\$ (269)	\$ 79,857
Commercial paper	6,074			6,074
U.S. government and agency securities	4,989		(2)	4,987
Certificates of deposit	2,500			2,500
Non-current:				
Corporate debt securities (one to two year maturity)	7,907		(71)	7,836
U.S. government and agency securities	2,500		(22)	2,478
	\$ 104,094	\$ 2	\$ (364)	\$ 103,732

The following table summarizes the Company's investments as of December 31, 2017 (in thousands):

	Amortized Cost	Gross Unrealized Gains	Gross Unrealized Loss	Fair Value
Current:				
Corporate debt securities	\$ 66,384	\$	\$ (131)	\$ 66,253
Commercial paper	6,719	1		6,720
Certificates of deposit	2,500			2,500
U.S. government and agency securities	2,000		(1)	1,999
Non-current:				
Corporate debt securities (one to two year maturity)	27,018	2	(104)	26,916
U.S. government and agency securities	2,500		(20)	2,480
	\$ 107,121	\$ 3	\$ (256)	\$ 106,868

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At March 31, 2018 and December 31, 2017, the Company held 49 and 54 debt securities, respectively, that were in an unrealized loss position for less than one year. The aggregate fair value of debt securities in an unrealized loss position at March 31, 2018 and December 31, 2017 was \$91,549 and \$96,623, respectively. There were no individual securities that were in a significant unrealized loss position or that had been in an unrealized loss position for greater than one year as of March 31, 2018 or December 31, 2017.

The Company reviews investments for other-than-temporary impairment whenever the fair value of an investment is less than the amortized cost and evidence indicates that an investment's carrying amount is not recoverable within a reasonable period of time. Other-than-temporary impairments of investments are recognized in the condensed consolidated statements of operations if the Company has experienced a credit loss and has the intent to sell the investment or if it is more likely than not that the Company will be required to sell the investment before recovery of the amortized cost basis. Evidence considered in this assessment includes reasons for the impairment, compliance with the Company's investment policy, the severity and the duration of the impairment and changes in value subsequent to the end of the period.

**6. Property and Equipment, net**

Property and equipment, net consisted of the following (in thousands):

	Estimated Useful Life Years	March 31, 2018	December 31, 2017
Laboratory equipment	4	\$ 593	\$ 593
Furniture and fixtures	5	381	381
Office and computer equipment	3	378	378
Construction in process	N/A	438	
	Lesser of useful life		
Leasehold improvements	or lease term	3,391	3,391
		5,181	4,743
Less accumulated depreciation and amortization		(2,727)	(2,558)
		\$ 2,454	\$ 2,185

**7. Accrued Expenses**

Accrued expenses consisted of the following (in thousands):

	March 31, 2018	December 31, 2017
Research and development costs	\$ 16,978	\$ 16,198
Payroll and employee-related costs	2,518	3,982
Professional fees	1,764	972

Other	285	293
	\$ 21,545	\$ 21,445

### 8. Net Loss Per Share

Basic and diluted net loss per common share is calculated by dividing net loss by the weighted-average number of common shares outstanding during the period, without consideration for common stock equivalents. The Company's potentially dilutive shares, which include outstanding stock options and unvested restricted stock and restricted stock units, are considered to be common stock equivalents and are only included in the calculation of diluted net loss per share when their effect is dilutive.

The following potentially dilutive securities were excluded from the calculation of diluted net loss per share due to their anti-dilutive effect:

	<b>Three Months Ended March 31,</b>	
	<b>2018</b>	<b>2017</b>
Outstanding stock options	8,702,552	6,867,142
Unvested restricted stock units	228,100	462,250

**Table of Contents****9. Stock-based Compensation****Stock Options**

A summary of the Company's stock option activity and related information follows:

	Shares	Weighted-Average Exercise Price Per Share	Weighted-Average Remaining Contractual Term (years)	Aggregate Intrinsic Value (in thousands)
Outstanding at December 31, 2017	7,019,083	\$ 13.77	7.4	\$ 11,897
Granted	2,184,200	11.04		
Exercised	(132,178)	3.26		
Canceled	(368,553)	14.65		
Outstanding at March 31, 2018	8,702,552	\$ 13.21	7.8	\$ 31,741
Exercisable at March 31, 2018	4,038,071	\$ 15.51	6.1	\$ 17,903

Total stock-based compensation expense related to stock options for the three months ended March 31, 2018 and 2017 was \$3,918 and \$4,939, respectively.

As of March 31, 2018, there was \$33,656 of total unrecognized stock-based compensation expense related to stock options. The expense is expected to be recognized over a weighted-average period of 3.06 years.

**Restricted Stock Units**

A restricted stock unit ( RSU ) represents the right to receive one share of the Company's common stock upon vesting of the RSU. The fair value of each RSU is based on the closing price of the Company's common stock on the date of grant.

During the year ended December 31, 2017, the Company granted RSUs with service conditions that vest provided that the employee remains employed with the Company ( Time-Based RSUs ). The following is a summary of Time-Based RSU activity under the 2013 Stock Incentive Plan for the three months ended March 31, 2018:

	Number of Shares Underlying RSUs	Weighted-Average Grant Date Fair Value
Unvested at December 31, 2017	30,000	\$ 10.52
Granted		
Forfeited		
Vested	(5,000)	10.27

Unvested at March 31, 2018	25,000	\$	10.57
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The total stock-based compensation expense related to Time-Based RSUs for the three months ended March 31, 2018 and 2017 was \$39 and \$917, respectively. As of March 31, 2018, there was \$213 of unrecognized compensation costs related to unvested Time-Based RSUs, which are expected to be recognized over a weighted-average period of 1.4 years.

Separately, and during the year ended December 31, 2017, the Company granted performance-based RSUs, which vest upon the achievement of certain performance goals subject to the employee's continued employment ( Performance-Based RSUs ). The grant date fair value of the outstanding Performance-Based RSUs is \$2,400 as of March 31, 2018, and will be recognized on an accelerated attribution basis when the Performance-Based RSUs are deemed probable of achievement to the date the awards vest. During the three months ended March 31, 2018, the Company recognized \$137 of stock-based compensation expense related to the Performance-Based RSUs, as the performance goal related to certain Performance-Based RSUs was deemed probable of achievement as of March 31, 2018 and was achieved on April 28, 2018. However, as of March 31, 2018, the 203,100 outstanding awards were still unvested.



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**Table of Contents****Employee Stock Purchase Plan**

The Company has an Employee Stock Purchase Plan ( ESPP ) that permits eligible employees to enroll in six-month offering periods. Participants may purchase shares of the Company s common stock, through payroll deductions, at a price equal to 85% of the fair market value of the common stock on the first or last day of the applicable six-month offering period, whichever is lower. Purchase dates under the ESPP occur on or about May 1 and November 1 of each year. In 2013, the Company s stockholders approved the reservation of 242,424 shares of the Company s common stock for issuance under the ESPP, plus an annual increase to be added on the first day of each fiscal year, commencing on January 1, 2015 and ending on December 31, 2023, equal to the lesser of 484,848 shares of the Company s common stock, 1% of the number of outstanding shares on such date, or an amount determined by the board of directors.

For the three months ended March 31, 2018 and 2017, the Company recorded stock-based compensation expense related to the ESPP of \$70 and \$53, respectively. As of March 31, 2018, 433,511 shares of the Company s common stock remained available for issuance under the ESPP. As of March 31, 2018, there was \$23 of total unrecognized stock-based compensation expense related to the ESPP. The expense is expected to be recognized over a period of one month.

**10. Commitments and Contingencies**

In March 2014, the Company entered into an operating lease for approximately 29,933 square feet of office and research space in Newton, Massachusetts. The Company uses the leased premises as its corporate headquarters and for research and development purposes, as well as its commercial and administrative requirements. The lease was amended on December 31, 2014 by extending the term of the lease from November 30, 2021 to September 30, 2022. This amendment also provided for the expansion of the premises leased by the Company by approximately 16,234 square feet. The lease was amended again on February 28, 2018 by extending the term of the lease from September 30, 2022 to September 30, 2025. The amendment also provided for the expansion of the premises leased by the Company by approximately 15,976 square feet. The amendment from February 2018 also provided the Company with the right of first offer to lease between 20,000 and approximately 36,000 square feet of additional space.

The Company evaluated the lease amendments and determined that the classification as an operating lease had not changed, and that the amendments did not constitute a new lease. As such, the unamortized balances of the existing deferred rent and tenant improvement allowances, along with the additions to deferred rent and tenant improvement allowances associated with the February 28, 2018 amendment, will be amortized over the term of that lease amendment. The Company is recording rent expense on a straight-line basis through the end of the lease term, inclusive of the period in which there are no scheduled rent payments. The Company has recorded deferred rent on the condensed consolidated balance sheets at March 31, 2018 and December 31, 2017, accordingly. The lease provided the Company with an allowance for improvements of \$1,616 which was incurred in the first quarter of 2015. The amended lease provided the Company with an allowance for improvements of up to \$731, of which \$438 was incurred in the first quarter of 2018. All improvements were deemed normal tenant improvements, were recorded as leasehold improvements and deferred rent and will be recorded as a reduction to rent expense ratably over the lease term. The Company evaluated the lease amendments and determined they did not constitute a new lease and the accounting treatment noted was appropriate. The Company has provided a security deposit in the form of a cash-collateralized letter of credit in the amount of \$400, which amount was reduced to \$200 in January 2018. The amount is classified as non-current restricted cash on the condensed consolidated balance sheet.

In November 2014, the Company signed a five-year operating lease agreement in Munich, Germany for approximately 3,681 square feet of office space. The lease is for the period February 2015 through January 2020. Pursuant to the lease agreement, the Company was obligated to make aggregate rent payments of 374 (approximately

US\$461) through January 31, 2020. The Company is recording rent expense on a straight-line basis through the end of the lease term, inclusive of the period in which there are no scheduled rent payments.

The Company recorded rent expense totaling \$373 and \$301 for the three months ended March 31, 2018 and 2017, respectively.

## **11. Equity**

### **Controlled Equity Offering Sales Agreement**

On December 7, 2015, the Company entered into a Controlled Equity Offering Sales Agreement (as amended from time to time, the Sales Agreement ) with Cantor Fitzgerald & Co., as sales agent ( Cantor ), pursuant to which the Company issued and sold through Cantor, shares of the Company s common stock (the Shares ) with an aggregate offering price of \$50,000. On November 7, 2016, the Company entered into an amendment to the Sales Agreement pursuant to which the Company issued and sold Shares with

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an additional aggregate offering price of \$50,000. On December 1, 2017, the Company entered into a second amendment to the Sales Agreement that provides that it may issue and sell Shares having an additional aggregate offering price of up to \$75,000.

Under the Sales Agreement, Cantor may sell the Shares by methods deemed to be an at-the-market offering as defined in Rule 415 promulgated under the Securities Act of 1933, as amended (the Securities Act ), including sales made directly on The Nasdaq Global Select Market, on any other existing trading market for the Shares or to or through a market maker. In addition, under the Sales Agreement, Cantor may sell the Shares by any other method permitted by law.

The Company is not obligated to make any sales of the Shares under the Sales Agreement. The Company or Cantor may suspend or terminate the offering of Shares upon notice to the other party and subject to other conditions. The Company will pay Cantor a commission of up to 3.0% of the gross proceeds from the sale of the Shares pursuant to the Sales Agreement and has agreed to provide Cantor with customary indemnification and contribution rights.

As of May 1, 2018, the Company had sold an aggregate of 9,172,159 Shares under the Sales Agreement, for net proceeds of approximately \$89,053. The Company sold no Shares under the Sales Agreement during the three months ended March 31, 2018.

**12. Subsequent Event**

On May 7, 2018, the Company completed a follow-on offering under its shelf registration statement on Form S-3 (File No. 333-222726) pursuant to which the Company issued an aggregate of 10,525,424 shares of common stock, which included the full exercise of the underwriters' option to purchase additional shares, at a public offering price of \$14.75 per share. The Company received aggregate net proceeds of approximately \$145,635 from the offering after deducting the underwriting discounts and commissions and other estimated offering expenses.

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

*You should read the following discussion and analysis of our financial condition and results of operations together with our financial statements and related notes appearing elsewhere in this quarterly report.*

### **FORWARD-LOOKING STATEMENTS**

This Quarterly Report on Form 10-Q, including the following discussion, contains forward-looking statements that involve substantial risks and uncertainties. All statements, other than statements of historical facts, contained in this Quarterly Report on Form 10-Q, including statements regarding possible achievement of discovery and development milestones, our future discovery and development efforts, our collaborations and partnering agreements with third parties, our strategy, our future operations, financial position and revenues, projected costs, prospects, plans and objectives of management, are forward looking statements. The words anticipate, believe, estimate, expect, intend, may, plan, predict, project, target, potential, will, would, could, should, continue and similar are used to identify forward-looking statements, although not all forward-looking statements contain these identifying words.

Forward-looking statements are not guarantees of future performance and our actual results could differ materially from the plans, intentions, expectations or results discussed in the forward-looking statements. Factors that could cause actual results to differ materially from those in the forward-looking statements include, but are not limited to, adverse results in our drug discovery and clinical development activities, decisions made by the U.S. Food and Drug Administration (FDA) and other regulatory authorities with respect to the development and commercialization of our drug candidates, our ability to raise additional capital to support our clinical development program and other operations, our ability to develop products of commercial value and to identify, discover and obtain rights to additional potential product candidates, our ability to obtain, maintain and enforce our intellectual property, the outcome of research and development activities and the fact that the preclinical and clinical testing of our compounds may not be predictive of the success of later clinical trials, our reliance on third-parties, competitive developments, the effect of current and future legislation and regulation and regulatory actions, as well as other risks described in this Quarterly Report on Form 10-Q, our Annual Report on Form 10-K for the year ended December 31, 2017 (2017 Form 10-K), as filed with the Securities and Exchange Commission (SEC), on March 15, 2018, and other filings with the SEC.

As a result of these and other factors, we may not actually achieve the plans, intentions, expectations or results disclosed in our forward-looking statements, and you should not place undue reliance on our forward-looking statements. Our forward-looking statements do not reflect the potential impact of any future acquisitions, mergers, dispositions, joint ventures or investments we may make. We do not assume any obligation to update any forward-looking statements, whether as a result of new information, future events or otherwise, except as required by law.

### **OVERVIEW**

We are a clinical-stage pharmaceutical company focused on the discovery, development and subsequent commercialization of novel, first-in-class drugs directed against nuclear transport and related targets for the treatment of cancer and other major diseases. Our scientific expertise is focused on understanding the regulation of intracellular communication between the nucleus and the cytoplasm. We have discovered and are developing wholly-owned, novel, small molecule **Selective Inhibitor of Nuclear Export (SINE)** compounds that inhibit the nuclear export protein exportin 1 (XPO1). These SINE compounds represent a new class of drug candidates with a novel mechanism of action that have the potential to treat a variety of diseases in areas of unmet medical need. Our SINE compounds were the first oral XPO1 inhibitors in clinical development.

Our focus is on seeking the regulatory approval and commercialization of our lead drug candidate, selinexor (KPT-330), as an oral agent in cancer indications with significant unmet clinical need, initially for hematologic malignancies. We then plan to seek additional approvals for the use of selinexor in combination therapies to expand the patient populations that are eligible for selinexor, as well as to move selinexor towards front-line cancer therapy. We are also advancing the clinical development of selinexor in multiple solid tumor indications. To date, over 2,400 patients have been treated with oral selinexor in company- and investigator-sponsored clinical trials in advanced hematologic malignancies and solid tumors. Clinical trials evaluating selinexor include the Phase 2b STORM (**S**elinexor **T**reatment **o**f **R**efractory **M**yeloma) study in multiple myeloma, the Phase 1b/2 STOMP (**S**elinexor and **B**ackbone **T**reatments **o**f **M**ultiple Myeloma **P**atients) study in combination with standard therapies in multiple myeloma, the Phase 2b SADAL (**S**elinexor **A**gainst **D**iffuse **A**ggressive **L**ymphoma) study in diffuse large B-cell lymphoma (DLBCL), the pivotal, randomized Phase 3 BOSTON (**B**ortezomib, **S**elinexor and **D**examethasone) study in multiple myeloma, and the Phase 2/3 SEAL (**S**elinexor in **A**dvanced **L**iposarcoma) study in liposarcoma.

We recently reported top-line data from the expanded cohort for the STORM study on April 30, 2018 and expect to provide top-line data from the SADAL study by the end of 2018, top-line data from the BOSTON study in 2019 and top-line data from the Phase 3

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portion of the SEAL study by the end of 2019. We are also establishing the commercial infrastructure to support a potential launch of selinexor in the United States and we intend to work with existing and potential partners to establish such commercial infrastructure outside the United States. To date, we have financed our operations principally through private placements of our preferred stock, proceeds from our initial public offering and follow-on offerings of common stock and cash generated from our business development activities.

As of March 31, 2018, we had an accumulated deficit of \$533.8 million. We had net losses of \$38.5 million and \$29.9 million for the three months ended March 31, 2018 and 2017, respectively. We have not generated any revenue to date from the sales of any drugs.

We expect to continue to incur significant expenses and increasing operating losses for the foreseeable future. The net losses we incur may fluctuate significantly from quarter to quarter. We anticipate that our expenses will increase substantially if and as we:

continue our research and preclinical and clinical development of our drug candidates;

initiate additional clinical trials for our drug candidates;

seek marketing approvals for any of our drug candidates that successfully complete clinical trials;

establish a sales, marketing and distribution infrastructure to commercialize any drugs for which we may obtain marketing approval;

maintain, expand and protect our intellectual property portfolio;

manufacture our drug candidates;

hire additional clinical, quality control and scientific personnel;

identify additional drug candidates;

acquire or in-license other drugs and technologies; and

add operational, financial and management information systems and personnel, including personnel to support our drug development, any future commercialization efforts and our other operations as a public company.

**CRITICAL ACCOUNTING POLICIES AND SIGNIFICANT JUDGMENTS AND ESTIMATES**

We believe that several accounting policies are important to understanding our historical and future performance. We refer to these policies as **critical** because these specific areas generally require us to make judgments and estimates about matters that are uncertain at the time we make the estimate, and different estimates **which also would have been reasonable** could have been used, which would have resulted in different financial results.

There were no changes to the critical accounting policies we identified in the 2017 Form 10-K, other than the adoption of ASU No. 2014-09, as described further in Note 1 to the Condensed Consolidated Financial Statements. It is important that the discussion of our operating results that follows be read in conjunction with the critical accounting policies disclosed in the 2017 Form 10-K.

**Table of Contents****RESULTS OF OPERATIONS****Comparison of the Three Months Ended March 31, 2018 and March 31, 2017**

	Three Months Ended March 31,		\$ Change	% Change
	2018 (in thousands)	2017		
License and other revenue	\$ 10,000	\$ 68	\$ 9,932	14,605.9%
Operating expenses:				
Research and development	41,321	24,083	17,238	71.6%
General and administrative	7,621	6,264	1,357	21.7%
Loss from operations	(38,942)	(30,279)	(8,663)	28.6%
Other income, net	495	385	110	28.6%
Loss before income taxes	(38,447)	(29,894)	(8,553)	28.6%
Provision for income taxes	(12)	(23)	11	(47.8)%
Net loss	\$ (38,459)	\$ (29,917)	\$ (8,542)	28.6%

*License and Other Revenue.* We recognized revenue pursuant to an Asset Purchase Agreement, or APA, with Biogen MA Inc., or Biogen, in 2018 and pursuant to a government grant in 2017. Revenue for the three months ended March 31, 2018 was \$10.0 million compared to \$0.1 million for the three months ended March 31, 2017. The increase in revenue during the three months ended March 31, 2018 was primarily the result of entering into the APA with Biogen in January 2018 and the satisfaction of the related revenue recognition criterion, which resulted in revenue of \$10.0 million.

*Research and Development Expense.* Research and development expense increased approximately \$17.2 million to \$41.3 million for the three months ended March 31, 2018 from approximately \$24.1 million for the three months ended March 31, 2017. The increase is primarily related to:

an increase of \$10.3 million in clinical trial costs, primarily related to the selinexor program;

an increase of \$2.2 million in consulting and professional expense;

an increase of \$1.8 million in personnel costs, primarily due to increased headcount and related onboarding costs;

an increase of \$1.6 million related to our obligation to pay a portion of upfront fees received from the APA with Biogen to a third party;



an increase of \$0.9 million in costs related to our focus on a New Drug Application (NDA), and discovery and travel costs; and

an increase of \$0.4 million in other costs.

We expect our research and development expenses to continue to increase for the full year 2018 compared with the prior year as we continue spending on our development programs and clinical trials, including the continued clinical development of selinexor in our lead indications with a focus on regulatory submissions for selinexor. We plan to submit a New Drug Application , or NDA, to the Food and Drug Administration, or FDA, during the second half of 2018, with a request for accelerated approval for selinexor as a new treatment for patients with penta-refractory multiple myeloma as a result of our positive outcome from the expanded cohort of the STORM study. We also plan to submit a Marketing Authorization Application to the European Medicines Agency in early 2019 with a request for conditional approval.

*General and Administrative Expense.* General and administrative expense increased approximately \$1.4 million to \$7.6 million for the three months ended March 31, 2018 from approximately \$6.3 million for the three months ended March 31, 2017. The increase is primarily related to:

an increase in consulting and professional costs of \$0.9 million;

an increase of \$0.2 million in occupancy costs; and

an increase of \$0.3 million in other costs.

We expect general and administrative expenses to increase in the future in support of our expanding operating and commercial activities.

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*Other Income, net.* Other income, net, increased approximately \$0.1 million to \$0.5 million for the three months ended March 31, 2018 from approximately \$0.4 million for the three months ended March 31, 2017. The increase is primarily due to increased investment returns resulting from a general increase in interest rates.

## **LIQUIDITY AND CAPITAL RESOURCES**

### **Sources of Liquidity**

To date, we have not generated any material revenues. We have financed our operations to date principally through private placements of our preferred stock, proceeds from public offerings of our common stock and cash generated from our business development activities.

As of March 31, 2018, we had \$141.2 million in cash, cash equivalents and short- and long-term investments compared to \$175.9 million in cash, cash equivalents and short- and long-term investments as of December 31, 2017.

In December 2015, we entered into a sales agreement (as amended from time to time, the Sales Agreement), relating to an at-the-market offering, pursuant to which we issued and sold shares of our common stock with an aggregate offering price of \$50.0 million. On November 7, 2016, we entered into an amendment to the Sales Agreement pursuant to which we issued and sold shares of our common stock with an additional aggregate offering price of \$50.0 million. On December 1, 2017, we entered into a second amendment to the Sales Agreement pursuant to which we may issue and sell shares of our common stock having an additional aggregate offering price of up to \$75.0 million on or after December 1, 2017. As of March 31, 2018, we had sold an aggregate of 9,172,159 shares pursuant to this at-the-market offering, for net proceeds of approximately \$89.1 million. There have been no sales pursuant to this at-the-market offering during 2018.

On May 7, 2018, we completed a follow-on offering under our shelf registration statement on Form S-3 (File No. 333-222726) pursuant to which we issued an aggregate of 10,525,424 shares of common stock, which included the full exercise of the underwriters' option to purchase additional shares, at a public offering price of \$14.75 per share. We received aggregate net proceeds of approximately \$145.6 million from the offering after deducting the underwriting discounts and commissions and other estimated offering expenses.

On October 11, 2017 (Effective Date), we entered into a license agreement (License Agreement), with Ono Pharmaceutical Co., Ltd., a corporation organized and existing under the laws of Japan (Ono), pursuant to which we granted Ono exclusive rights to develop and commercialize, at its own cost, selinexor and eltanexor for the diagnosis, treatment and/or prevention of all human oncology indications, or Field, in Japan, Republic of Korea, Republic of China (Taiwan) and Hong Kong as well as in the ten Southeast Asian countries currently comprising the Association of Southeast Asian Nations (Ono Territory). Pursuant to the terms of the License Agreement, we received an upfront payment of ¥2.5 billion (US\$21.9 million on the date received), and could receive up to ¥10.15 billion (US\$90.5 million at the exchange rate as of the Effective Date) in milestone payments if certain development goals are achieved and up to ¥9.0 billion (US\$80.2 million at the exchange rate as of the Effective Date) in milestone payments if certain sales milestones are achieved, as well as a low double-digit royalty based on future net sales of selinexor and eltanexor in the Ono Territory.

We are a party to a research agreement with the Multiple Myeloma Research Foundation (MMRF). Under this research agreement, we are obligated to make certain payments to MMRF, including payments in the event we out-license selinexor. The terms of this research agreement do not apply to eltanexor. In connection with the transactions contemplated under the License Agreement, we paid to MMRF approximately ¥225 million (approximately US\$2.0 million) of the upfront cash payment from Ono, and we are obligated to pay a percentage of

any milestone payments from Ono and a mid-single-digit percentage of any royalty payments from Ono. The maximum aggregate amount we may be obligated to pay to MMRF under the research agreement is \$6.0 million.

On January 24, 2018, we entered into an Asset Purchase Agreement (APA), with Biogen MA Inc., a Massachusetts corporation and subsidiary of Biogen, Inc. (Biogen), pursuant to which Biogen acquired exclusive worldwide rights to develop and commercialize our oral SINE compound KPT-350 and certain related assets with an initial focus in amyotrophic lateral sclerosis (ALS).

Under the terms of the APA, Biogen purchased KPT-350 and certain related assets and assumed certain related liabilities. We received a one-time upfront payment of \$10.0 million from Biogen and are eligible to receive additional payments of up to \$207.0 million based on the achievement by Biogen of future specified development and commercial milestones. We are also eligible to receive tiered royalty payments that reach low double digits based on future net sales until the later of the tenth anniversary of the first commercial sale of the applicable product and the expiration of specified patent protection for the applicable product, determined on a country-by-country basis.

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We expect that our cash, cash equivalents and short- and long-term investments as of March 31, 2018, totaling \$141.2 million, in addition to the \$145.6 million of net proceeds we raised in the public common stock offering in May 2018, will be sufficient to fund our current operating plans and capital expenditure requirements into the third quarter of 2019 while we are establishing the commercial infrastructure for a potential launch of selinexor in the United States. Our need for additional funds thereafter may be partially offset by: (i) cash generated from sales of drugs if selinexor receives accelerated approval and we successfully commercialize selinexor in the United States and (ii) from potential future payments related to collaboration or license arrangements we may seek to enter into as part of our strategy to commercialize selinexor outside the United States.

**Cash Flows**

The following table provides information regarding our cash flows:

	<b>Three Months Ended March 31,</b>	
	<b>2018</b>	<b>2017</b>
	<b>(in thousands)</b>	
Net cash used in operating activities	\$ (34,652)	\$ (24,708)
Net cash provided by investing activities	2,484	549
Net cash provided by financing activities	429	57
Effect of exchange rate changes	43	16
<b>Net increase (decrease) in cash and cash equivalents</b>	<b>\$ (31,696)</b>	<b>\$ (24,086)</b>

*Operating activities.* The net cash used in operating activities in both periods resulted primarily from our net losses adjusted for non-cash charges and changes in the components of working capital. The increase in cash used in operating activities during the three months ended March 31, 2018 compared to the three months ended March 31, 2017 was driven primarily by an increase in our net loss due to an increase in our operating expenses, as adjusted for stock-based compensation and offset by an increase of approximately \$9.9 million in revenue, which was primarily attributable to the upfront payment of \$10.0 million received from the Biogen.

*Investing activities.* The net cash provided by investing activities during the three months ended March 31, 2018 reflects an increase of \$2.0 million primarily related to the increase in proceeds from maturities of investments and a decrease of \$0.3 million in purchases of investments offset by an increase of \$0.4 million in purchases of property and equipment compared to the three months ended March 31, 2017.

*Financing activities.* The net cash provided by financing activities for the three months ended March 31, 2018 reflects an increase of \$0.4 million related to an increase in proceeds from the exercise of stock options compared to the three months ended March 31, 2017.

**Funding Requirements**

We expect our expenses to increase in connection with our ongoing activities, particularly as we continue the clinical trials of, and assuming positive results of our clinical trials and based on regulatory feedback, if and when we seek marketing approval for, selinexor and our other drug candidates. In addition, if we obtain marketing approval for any of our drug candidates, we expect to incur significant commercialization expenses related to drug sales, marketing, manufacturing and distribution to the extent that such sales, marketing, manufacturing and distribution are not the

responsibility of any collaborator that we may have at such time for any such drug. Furthermore, we expect to continue to incur additional costs associated with operating as a public company. Accordingly, we will need to obtain substantial additional funding in connection with our continuing operations. If we are unable to raise capital when needed or on attractive terms, we would be forced to delay, reduce or eliminate our research and development programs or future commercialization efforts.

We expect that our cash, cash equivalents and short- and long-term investments as of March 31, 2018, totaling \$141.2 million, in addition to the \$145.6 million of net proceeds we raised in the public common stock offering in May 2018, will be sufficient to fund our current operating and capital expenditure plans into the third quarter of 2019 while we are establishing the commercial infrastructure for a potential launch of selinexor in the United States. Our need for additional funds thereafter may be partially offset by: (i) cash generated from sales of drugs if selinexor receives accelerated approval and we successfully commercialize selinexor in the United States and (ii) from potential future payments related to collaboration or license arrangements we may seek to enter into as part of our strategy to commercialize selinexor outside the United States. However, our future capital requirements will depend on many factors, including:

the progress and results of our current and planned clinical trials of selinexor;

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the scope, progress, results and costs of drug discovery, preclinical development, laboratory testing and clinical trials for our other drug candidates;

the costs, timing and outcome of regulatory review of our drug candidates;

our ability to establish and maintain collaborations on favorable terms, if at all;

the success of any collaborations that we may enter into with third parties;

the extent to which we acquire or in-license other drugs and technologies;

the costs of future commercialization activities, including drug sales, marketing, manufacturing and distribution, for any of our drug candidates for which we receive marketing approval, to the extent that such sales, marketing, manufacturing and distribution are not the responsibility of any collaborator that we may have at such time;

the amount of revenue, if any, received from commercial sales of our drug candidates, should any of our drug candidates receive marketing approval; and

the costs of preparing, filing and prosecuting patent applications, maintaining and enforcing our intellectual property rights and defending intellectual property-related claims.

Identifying potential drug candidates and conducting preclinical studies and clinical trials is a time-consuming, expensive and uncertain process that takes years to complete, and we may never generate the necessary data or results required to obtain marketing approval and achieve drug sales. In addition, our drug candidates, if approved, may not achieve commercial success. Our commercial revenues, if any, will be derived from sales of drugs that may not be commercially available for several years, if at all. Accordingly, we will need to continue to rely on additional financing to achieve our business objectives. Adequate additional financing may not be available to us on acceptable terms, or at all. In addition, we may seek additional capital due to favorable market conditions or strategic considerations, even if we believe we have sufficient funds for our current or future operating plans.

***Contractual Obligations***

There have been no material changes to our contractual obligations described in Management's Discussion and Analysis of Financial Condition and Results of Operations in the 2017 Form 10-K.

**OFF-BALANCE SHEET ARRANGEMENTS**

We did not have during the periods presented, and we do not currently have, any off-balance sheet arrangements, as defined under SEC rules.

**Item 3. Quantitative and Qualitative Disclosures About Market Risk.**

We are exposed to market risk related to changes in interest rates. We had cash, cash equivalents, restricted cash and investments of \$141.5 million as of March 31, 2018. Our primary exposure to market risk is interest rate sensitivity, which is affected by changes in the general level of U.S. interest rates, particularly because all of our investments are in short-term securities. Due to the short-term duration of our investment portfolio and the low risk profile of our investments, an immediate 10% change in interest rates would not have a material effect on the fair market value of our investment portfolio.

We do not believe our cash, cash equivalents, restricted cash and investments have significant risk of default or illiquidity. While we believe our cash, cash equivalents and investments do not contain excessive risk, we cannot provide absolute assurance that in the future our investments will not be subject to adverse changes in securities at one or more financial institutions that are in excess of federally insured limits. Give the potential instability of financial institutions, we cannot provide assurance that we will not experience losses on these deposits.

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We are also exposed to market risk related to change in foreign currency exchange rates. We contract with contract research organizations and contract manufacturing organizations that are located in Canada and Europe, which are denominated in foreign currencies. We also contract with a number of clinical trial sites outside the United States, and our budgets for those studies are frequently denominated in foreign currencies. We are subject to fluctuations in foreign currency rates in connection with these agreements. We do not currently hedge our foreign currency exchange rate risk.

### **Item 4. Controls and Procedures.**

#### **Evaluation of Disclosure Controls and Procedures**

Our management, with the participation of our Chief Executive Officer (principal executive officer) and Executive Vice President, Chief Financial Officer and Treasurer (principal financial officer), evaluated the effectiveness of our disclosure controls and procedures as of March 31, 2018. The term disclosure controls and procedures, as defined in Rules 13a-15(e) and 15d-15(e) under the Securities Exchange Act of 1934, as amended (the Exchange Act), means controls and other procedures of a company that are designed to ensure that information required to be disclosed by a company in the reports that it files or submits under the Exchange Act is recorded, processed, summarized and reported, within the time periods specified in the SEC's rules and forms. Disclosure controls and procedures include, without limitation, controls and procedures designed to ensure that information required to be disclosed by a company in the reports that it files or submits under the Exchange Act is accumulated and communicated to the Company's management, including its principal executive and principal financial officers, as appropriate to allow timely decisions regarding required disclosure. Management recognizes that any controls and procedures, no matter how well designed and operated, can provide only reasonable assurance of achieving their objectives and management necessarily applies its judgment in evaluating the cost-benefit relationship of possible controls and procedures. Based on the evaluation of our disclosure controls and procedures as of March 31, 2018, our Chief Executive Officer and our Executive Vice President, Chief Financial Officer and Treasurer concluded that, as of such date, our disclosure controls and procedures were effective at the reasonable assurance level.

#### **Changes in Internal Control Over Financial Reporting**

No change in our internal control over financial reporting occurred during the fiscal quarter ended March 31, 2018 that has materially affected, or is reasonably likely to materially affect, the Company's internal control over financial reporting.



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**PART II OTHER INFORMATION**

**Item 1A. Risk Factors.**

*Careful consideration should be given to the following risk factors, in addition to the other information set forth in this Quarterly Report on Form 10-Q and in other documents that we file with the SEC, in evaluating the Company and our business. Investing in our common stock involves a high degree of risk. If any of the following risks and uncertainties actually occurs, our business, prospects, financial condition and results of operations could be materially and adversely affected. The risks described below are not intended to be exhaustive and are not the only risks facing the Company. New risk factors can emerge from time to time, and it is not possible to predict the impact that any factor or combination of factors may have on our business, prospects, financial condition and results of operations.*

**Risks Related to the Discovery, Development and Commercialization of Our Drug Candidates**

*We depend heavily on the success of our lead drug candidate selinexor (KPT-330), which is currently in clinical trials. Our clinical trials of selinexor may not be successful. If we are unable to commercialize selinexor or experience significant delays in doing so, our business will be materially harmed.*

We have invested a significant portion of our efforts and financial resources in the research and development of our lead drug candidate, selinexor. Our ability to generate revenues from the sale of drugs that treat cancer and other diseases in humans, which may not occur for several years, if ever, will depend heavily on the successful development, regulatory approval and eventual commercialization of selinexor.

We cannot commercialize drug candidates in the United States without first obtaining regulatory approval for the drug from the U.S. Food and Drug Administration, or FDA; similarly, we cannot commercialize drug candidates outside of the United States without obtaining regulatory approval from similar regulatory authorities outside of the United States. Even if selinexor or another drug candidate were to successfully obtain approval from the FDA and non-U.S. regulatory authorities, any approval might contain significant limitations related to use restrictions for specified age groups, warnings, precautions or contraindications, or may be subject to burdensome post-approval study or risk management requirements. If we are unable to obtain regulatory approval for selinexor in one or more jurisdictions, or any approval contains significant limitations, we may not be able to obtain sufficient funding or generate sufficient revenue to continue the development, marketing and/or commercialization of selinexor or any other drug candidate that we may discover, in-license, develop or acquire in the future. Furthermore, even if we obtain regulatory approval for selinexor, we will still need to develop a commercial organization, or collaborate with third parties, for the commercialization of selinexor, establish commercially viable pricing and obtain approval for adequate reimbursement from third-party and government payors. If we or our commercialization collaborators are unable to successfully commercialize selinexor, we may not be able to generate sufficient revenues to continue our business.

*The results of previous clinical trials may not be predictive of future results, and the results of our current and planned clinical trials may not satisfy the requirements of the FDA or non-U.S. regulatory authorities.*

We currently have no drugs approved for sale and we cannot guarantee that we will ever have marketable drugs. Clinical failure can occur at any stage of clinical development. Clinical trials may produce negative or inconclusive results, and we or any collaborators may decide, or regulators may require us, to conduct additional clinical trials or preclinical studies. We will be required to demonstrate with substantial evidence through well-controlled clinical trials that our drug candidates are safe and effective for use in a diverse population before we can seek regulatory approvals

for their commercial sale. Success in early-stage clinical trials does not mean that future larger registration clinical trials will be successful because drug candidates in later-stage clinical trials may fail to demonstrate sufficient safety and efficacy to the satisfaction of the FDA and non-U.S. regulatory authorities despite having progressed through early-stage clinical trials. Drug candidates that have shown promising results in early-stage clinical trials may still suffer significant setbacks in subsequent registration clinical trials. Additionally, the outcome of preclinical studies and early-stage clinical trials may not be predictive of the success of later-stage clinical trials, and interim results of a clinical trial are not necessarily indicative of final results. For example, we recently released top-line results from the expansion of our Selinexor Treatment of Refractory Myeloma (STORM) study. While we believe the results we have observed to date are positive, there can be no assurance that results that we believe to be positive will be viewed similarly by regulatory authorities or as sufficient to support a request for registration.

In addition, the design of a clinical trial can determine whether its results will support approval of a drug, and flaws in the design of a clinical trial may not become apparent until the clinical trial is well advanced. We may be unable to design and conduct a clinical trial to support regulatory approval. Further, if our drug candidates are found to be unsafe or lack efficacy, we will not be able to obtain regulatory approval for them and our business would be harmed. A number of companies in the pharmaceutical industry, including those with greater resources and experience than us, have suffered significant setbacks in advanced clinical trials, even after obtaining promising results in earlier clinical trials.

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In some instances, there can be significant variability in safety and/or efficacy results between different trials of the same drug candidate due to numerous factors, including changes in trial protocols, differences in size and type of the patient populations, adherence to the dosing regimen and other trial protocols and the rate of dropout among clinical trial participants. We do not know whether any Phase 2, Phase 3 or other clinical trials we may conduct will demonstrate consistent or adequate efficacy and safety sufficient to obtain regulatory approval to market our drug candidates.

Further, our drug candidates may not be approved even if they achieve their primary endpoints in Phase 3 clinical trials or other registration trials. The FDA or non-U.S. regulatory authorities may disagree with our trial design and our interpretation of data from preclinical studies and clinical trials. In addition, any of these regulatory authorities may change requirements for the approval of a drug candidate even after providing a positive opinion on, or otherwise reviewing and providing comments or advice on, a protocol for a clinical trial that has the potential to result in approval by the FDA or another regulatory authority. In addition, any of these regulatory authorities may also approve a drug candidate for fewer or more limited indications than we request or may grant approval contingent on the performance of costly post-marketing clinical trials. Furthermore, the FDA or other non-U.S. regulatory authorities may not approve the labeling claims that we believe would be necessary or desirable for the successful commercialization of our drug candidates.

To date, we have had several discussions with the FDA and non-U.S. regulatory authorities regarding the design of our later phase clinical trials for selinexor, including the BOSTON, STORM, SADAL and SEAL studies currently underway. We plan to seek regulatory approvals of selinexor in North America and Europe in each indication with respect to which such later phase clinical trial is being conducted and with respect to which we receive positive results that may support full or accelerated approval, as the case may be. We or our current or future partners may also seek such approvals in other geographies. We cannot be certain that we will commence additional later phase trials or complete ongoing later phase trials as anticipated. Before obtaining regulatory approvals for the commercial sale of any drug candidate for a target indication, we must demonstrate with substantial evidence gathered in preclinical studies and well-controlled clinical studies, and, with respect to approval in the United States, to the satisfaction of the FDA, that the drug candidate is safe and effective for use for that target indication. There is no assurance that the FDA or non-U.S. regulatory authorities would consider our current and planned later phase clinical trials to be sufficient to serve as the basis for filing for approval or to gain approval of selinexor for any indication. The FDA and non-U.S. regulatory authorities retain broad discretion in evaluating the results of our clinical trials and in determining whether the results demonstrate that selinexor is safe and effective. If we are required to conduct additional clinical trials of selinexor prior to approval, including additional earlier phase clinical trials that may be required prior to commencing any later phase clinical trials, or additional clinical trials following completion of our current and planned later phase clinical trials, we will need substantial additional funds, and there is no assurance that the results of any such additional clinical trials will be sufficient for approval.

The results to date in preclinical and early clinical studies conducted by us or our academic collaborators and in Phase 1 and Phase 2 clinical trials that we are currently conducting include the response of tumors to selinexor. We expect that in any later phase clinical trial where patients are randomized to receive either selinexor on the one hand, or standard of care, supportive care or placebo on the other hand, the primary endpoint will be either progression free survival, meaning the length of time on treatment until objective tumor progression, or overall survival, while the primary endpoint in any later phase clinical trial that is not similarly randomized may be different. For example, the primary endpoint of our Phase 2/3 SEAL study, the clinical trial of selinexor in patients with dedifferentiated liposarcoma, and a primary endpoint of our Phase 3 BOSTON study, the clinical trial of selinexor in combination with Velcade (bortezomib) and dexamethasone in patients with multiple myeloma, is progression free survival. We are in the early stages of collecting clinical data in humans relating to the impact of selinexor on overall survival and comparative clinical data between selinexor and supportive care. If selinexor does not demonstrate an overall survival

benefit, it will likely not be approved. In some instances, the FDA and other regulatory bodies have accepted overall response rate as a surrogate for a clinical benefit, and have granted regulatory approvals based on this or other surrogate endpoints. Overall response rate is defined as the portion of patients with tumor size reduction of a predefined amount for a minimum time period. For some types of cancer, we may use overall response rate as a primary endpoint, as we are doing in our SADAL study and our STORM study. These clinical trials will not be randomized against control arms and the primary endpoints of these trials are overall response rate. If selinexor does not demonstrate sufficient overall response rates in these indications, or any other indication for which a clinical trial has overall response rate as a primary endpoint, or if the FDA or non-U.S. regulatory authorities do not deem overall response rate a sufficient endpoint, or deem a positive overall response rate to be insufficient, it will likely not be approved for that indication based on the applicable study.

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*We are early in our development efforts with a limited number of drug candidates in human clinical development. If we are unable to successfully develop and commercialize our drug candidates or experience significant delays in doing so, our business will be materially harmed.*

We are early in our development efforts and have four drug candidates, selinexor, verdinexor, eltanexor and KPT-9274, in clinical development for treatment of human diseases. The success of these and any of our other drug candidates will depend on several factors, including the following:

successful completion of preclinical studies;

acceptance by the FDA of investigational new drug applications, or INDs, for our drug candidates prior to commencing clinical studies;

successful enrollment in, and completion of, clinical trials, including demonstration of a favorable risk-benefit ratio;

receipt of marketing approvals from applicable regulatory authorities;

establishing commercial manufacturing capabilities or making arrangements with third-party manufacturers;

obtaining and maintaining patent and trade secret protection and regulatory exclusivity for our drug candidates;

establishing sales, marketing, manufacturing and distribution capabilities to commercialize any drugs for which we may obtain marketing approval;

launching commercial sales of the drugs, if and when approved, whether alone or in collaboration with others;

acceptance of the drugs, if and when approved, by patients, the medical community and third-party payors;

effectively competing with other therapies;

obtaining and maintaining coverage and adequate reimbursement by third-party payors, including government payors, for any approved drugs;

maintaining an acceptable safety profile of the drugs following approval;

enforcing and defending intellectual property rights and claims; and

maintaining and growing an organization of scientists and business people, including collaborators, who can develop and commercialize our drug candidates.

If we do not achieve one or more of these factors in a timely manner or at all, we could experience significant delays or an inability to successfully commercialize our drug candidates, which would materially harm our business.

***Our approach to the discovery and development of drug candidates that target Exportin 1, or XPO1, is unproven, and we do not know whether we will be able to develop any drugs of commercial value. If selinexor is unsuccessful in proving that drug candidates targeting XPO1 have commercial value or experiences significant delays in doing so, our business may be materially harmed.***

Our SINE compounds inhibit the nuclear export protein XPO1. We believe that no currently approved cancer treatments are selectively targeting the restoration and increase in the levels of multiple tumor suppressor proteins in the nucleus. Despite promising results to date in preclinical studies of selinexor that we have conducted and in Phase 1 and Phase 2 clinical trials of selinexor conducted by us or our academic collaborators, we may not succeed in demonstrating safety and efficacy of SINE compounds in our current and future human clinical trials. Any drug candidates that we develop may not effectively prevent the exportation of tumor suppressor and/or growth regulatory proteins from the nucleus in humans with a particular form of cancer. If selinexor is unsuccessful in supporting the hypothesis that drug candidates targeting the regulation of intracellular transport of XPO1 have commercial value or experiences significant delays in doing so, our business may be materially harmed and we may not be able to generate sufficient revenues to continue our business.

***We may not be successful in our efforts to identify or discover additional potential drug candidates.***

Part of our strategy involves identifying and developing drug candidates to build a pipeline of novel drug candidates. Our drug discovery efforts may not be successful in identifying compounds that are useful in treating cancer or other diseases. Our research programs may initially show promise in identifying potential drug candidates, yet fail to yield drug candidates for clinical development for a number of reasons, including:

the research methodology used may not be successful in identifying potential drug candidates;

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potential drug candidates may, on further study, be shown to have harmful side effects or other characteristics that indicate that they are unlikely to be drugs that will receive marketing approval and/or achieve market acceptance; or

potential drug candidates may not be effective in treating their targeted diseases.

Research programs to identify new drug candidates require substantial technical, financial and human resources. We may choose to focus our efforts and resources on a potential drug candidate that ultimately proves to be unsuccessful.

If we are unable to identify suitable compounds for preclinical and clinical development, we will not be able to obtain revenues from sale of drugs in future periods, which likely would result in significant harm to our financial position and adversely impact our stock price.

***Clinical drug development is a lengthy and expensive process, with an uncertain outcome. If clinical trials of our drug candidates fail to demonstrate safety and efficacy to the satisfaction of regulatory authorities or do not otherwise produce positive results, we may incur additional costs or experience delays in completing, or ultimately be unable to complete, the development and commercialization of our drug candidates.***

Before obtaining marketing approval from regulatory authorities for the sale of our drug candidates, we must complete preclinical development and then conduct extensive clinical trials to demonstrate the safety and efficacy of our drug candidates in humans. Clinical testing is expensive, difficult to design and implement, can take many years to complete and is uncertain as to outcome. A failure of one or more clinical trials can occur at any stage of testing. The outcome of preclinical studies and early-stage clinical trials may not be predictive of the success of later clinical trials, and interim results of a clinical trial do not necessarily predict final results. For example, certain data from our Phase 1 and Phase 2 clinical trials of selinexor to date are based on unaudited data provided by our clinical trial investigators. An audit of this data may change the conclusions drawn from this unaudited data provided by our clinical trial investigators indicating less promising results than we currently anticipate. Moreover, preclinical and clinical data are often susceptible to varying interpretations and analyses, and many companies that believed their drug candidates performed satisfactorily in preclinical studies and clinical trials have nonetheless failed to obtain marketing approval of their drugs.

We may experience numerous unforeseen events during, or as a result of, clinical trials that could delay or prevent our ability to receive marketing approval or commercialize our drug candidates, including:

regulatory authorities or institutional review boards may not authorize us or our investigators to commence a clinical trial or conduct a clinical trial at a prospective trial site;

feedback from regulatory authorities that requires us to modify the design of our clinical trials;

we may have delays in reaching or fail to reach agreement on acceptable clinical trial contracts or clinical trial protocols with prospective trial sites or contract research organizations;

clinical trials of our drug candidates may produce negative or inconclusive results, and we may decide, or regulatory authorities may require us, to conduct additional clinical trials, suspend ongoing clinical trials or abandon drug development programs;

the number of patients required for clinical trials of our drug candidates may be larger than we anticipate, enrollment in these clinical trials may be slower than we anticipate or participants may drop out of these clinical trials at a higher rate than we anticipate;

our third-party contractors may fail to comply with regulatory requirements or meet their contractual obligations to us in a timely manner, or at all;

we or our investigators might have to suspend or terminate clinical trials of our drug candidates for various reasons, including non-compliance with regulatory requirements, a finding that our drug candidates have undesirable side effects or other unexpected characteristics, or a finding that the participants are being exposed to unacceptable health risks;

the cost of clinical trials of our drug candidates may be greater than we anticipate;

the supply or quality of our drug candidates or other materials necessary to conduct clinical trials of our drug candidates may be insufficient or inadequate;

regulators may revise the requirements for approving our drug candidates, or such requirements may not be as we anticipate; and

any partners and collaborators that help conduct clinical trials may face any of the above issues, and may conduct clinical trials in ways they view as advantageous to them but that are suboptimal for us.



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If we are required to conduct additional clinical trials or other testing of our drug candidates beyond those that we currently contemplate, if we are unable to successfully complete clinical trials of our drug candidates or other testing, if the results of these trials or tests are not positive or are only modestly positive or if there are safety concerns, we may:

be delayed in obtaining marketing approval for our drug candidates;

not obtain marketing approval at all;

obtain marketing approval in some countries and not in others;

obtain approval for indications or patient populations that are not as broad as intended or desired;

obtain approval with labeling that includes significant use or distribution restrictions or safety warnings, including boxed warnings;

be subject to additional post-marketing testing requirements; or

have the drug removed from the market after obtaining marketing approval.

Our drug development costs will also increase if we experience delays in testing or marketing approvals. We do not know whether clinical trials will begin as planned, will need to be restructured or will be completed on schedule, or at all. Significant clinical trial delays also could shorten any periods during which we may have the exclusive right to commercialize our drug candidates, allow our competitors to bring drugs to market before we do or impair our ability to successfully commercialize our drug candidates, which would harm our business and results of operations.

***If we experience delays or difficulties in the enrollment of patients in clinical trials, or we are otherwise delayed in our ability to conduct clinical trials, our receipt of necessary regulatory approvals could be delayed or prevented.***

We may not be able to initiate or continue clinical trials for our drug candidates if we are unable to locate and enroll a sufficient number of eligible patients to participate in these trials as required by the FDA or similar regulatory authorities outside of the United States. In addition, some of our competitors may have ongoing clinical trials for drug candidates that treat the same indications as our drug candidates, and patients who would otherwise be eligible for our clinical trials may instead enroll in clinical trials of our competitors' drug candidates.

Patient enrollment is affected by other factors, including:

severity of the disease under investigation;

availability and efficacy of approved drugs for the disease under investigation;

patient eligibility criteria for the study in question;

competing drugs in clinical development;

perceived risks and benefits of the drug candidate under study;

restrictions on our ability to conduct clinical trials, including full or partial clinical holds on ongoing or planned trials;

efforts to facilitate timely enrollment in clinical trials;

patient referral practices of physicians;

the ability to monitor patients adequately during and after treatment; and

proximity and availability of clinical trial sites for prospective patients.

In addition, patient enrollment may be affected by future regulatory actions, such as Form 483 observations or the partial clinical hold we were subject to previously. In February 2017, following the conclusion of a joint inspection conducted by the FDA and Danish Medicines Agency at our corporate headquarters, the FDA issued a Form 483 noting certain deficiencies in procedures and documentation that were identified in our selinexor development program. We implemented corrective actions, preventative actions and other initiatives directed at resolving the deficiencies identified in the Form 483 observations and provided the FDA with our responses to the Form 483 observations in February 2017.

In addition, in March 2017, the FDA notified us that it had placed the clinical trials under our IND for selinexor on partial clinical hold, which is an order by the FDA to delay or suspend part of a sponsor's clinical work requested under its IND as well as investigator-sponsored trials. The partial clinical hold was due to incomplete information in the existing version of the investigator's brochure, including an incomplete list of serious adverse events associated with selinexor, and not as a result of any new information

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regarding the safety profile of selinexor. The partial clinical holds on the clinical trials of selinexor were lifted by the FDA Division of Hematology Products (effective March 30, 2017), Division of Oncology Products 1 (effective April 5, 2017) and Division of Oncology Products 2 (effective March 31, 2017). However, if in the future we are delayed in addressing, or unable to address, any concerns of the FDA or other regulators, we could be delayed or prevented from enrolling patients in our clinical trials.

Our inability to enroll a sufficient number of patients for our clinical trials would result in significant delays or may require us to abandon one or more clinical trials altogether. Enrollment delays in our clinical trials may result in increased development costs for our drug candidates, which would cause the value of our company to decline and limit our ability to obtain additional financing.

***If serious adverse or unacceptable side effects are identified during the development of our drug candidates or we observe limited efficacy of our drug candidates, we may need to abandon or limit the development of one or more of our drug candidates.***

Four of our drug candidates are in clinical development for treatment of human diseases. Their risk of failure is high. It is impossible to predict when or if any of our drug candidates will prove effective or safe in humans or will receive marketing approval. If our drug candidates are associated with undesirable side effects or have characteristics that are unexpected, we may need to abandon their development or limit development to certain uses or subpopulations in which the undesirable side effects or other characteristics are less prevalent, less severe or more acceptable from a risk-benefit perspective. For example, we have modified our informed consent form and advised patients already enrolled in our clinical trials of the potential for worsening of pre-existing cataracts as a result of treatment with selinexor. Also, even though selinexor has generally been well-tolerated by patients in our clinical trials to date, in some cases there were adverse events, some of which were serious. The most common drug-related adverse events, or AEs, were gastrointestinal, such as nausea, anorexia, diarrhea and vomiting, and fatigue. These side effects were generally mild or moderate in severity. The most common AEs that were Grade 3 or Grade 4, meaning they were more than mild or moderate in severity, were thrombocytopenia, or low count of platelets in the blood, and neutropenia, or low neutrophil counts. A small percentage of patients have withdrawn from our clinical trials as a result of AEs. A small percentage of patients across our clinical trials have experienced serious adverse events, or SAEs, deemed by us and the clinical investigator to be related to selinexor. SAEs generally refer to AEs that result in death, are life threatening, require hospitalization or prolonging of hospitalization, or cause a significant and permanent disruption of normal life functions, congenital anomalies or birth defects, or require intervention to prevent such an outcome.

As a result of these AEs or further safety or toxicity issues that we may experience in our clinical trials in the future, we may not receive approval to market any drug candidates, which could prevent us from ever generating revenue from the sale of drugs or achieving profitability. Results of our trials could reveal an unacceptably high severity and prevalence of side effects. In such an event, our trials could be suspended or terminated and the FDA or comparable foreign regulatory authorities could order us to cease further development of or deny approval of our drug candidates for any or all targeted indications. Many compounds that initially showed promise in early-stage trials for treating cancer or other diseases have later been found to cause side effects that prevented further development of the compound.

***The FDA or non-U.S. regulatory authorities may disagree with our and/or our clinical trial investigators interpretation of data from clinical trials in determining if serious adverse or unacceptable side effects are drug-related.***

We, and our clinical trial investigators, currently determine if serious adverse or unacceptable side effects are drug-related. The FDA or non-U.S. regulatory authorities may disagree with our or our clinical trial investigators interpretation of data from clinical trials and the conclusion by us or our clinical trial investigators that a serious adverse effect or unacceptable side effect was not drug-related. The FDA or non-U.S. regulatory authorities may require more information, including additional preclinical or clinical data to support approval, which may cause us to incur additional expenses, delay or prevent the approval of one of our drug candidates, and/or delay or cause us to change our commercialization plans, or we may decide to abandon the development or commercialization of the drug candidate altogether.

***We may expend our limited resources to pursue a particular drug candidate or indication and fail to capitalize on drug candidates or indications that may be more profitable or for which there is a greater likelihood of success.***

Because we have limited financial and managerial resources, we focus on research programs and drug candidates that we identify for specific indications. As a result, we may forego or delay pursuit of opportunities with other drug candidates or for other indications that later prove to have greater commercial potential. Our resource allocation decisions may cause us to fail to capitalize on viable commercial drugs or profitable market opportunities. Our spending on current and future research and development programs and drug candidates for specific indications may not yield any commercially-viable drugs. If we do not accurately evaluate the commercial potential or target market for a particular drug candidate, we may relinquish valuable rights to that drug candidate through collaboration, licensing or other royalty arrangements in cases in which it would have been more advantageous for us to retain sole development and commercialization rights to such drug candidate.

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*Even if any of our drug candidates receives marketing approval, such drug may fail to achieve the degree of market acceptance by physicians, patients, third-party payors and others in the medical community necessary for commercial success.*

If any of our drug candidates receives marketing approval, it may nonetheless fail to gain sufficient market acceptance by physicians, patients, third-party payors and others in the medical community. For example, current cancer treatments like chemotherapy and radiation therapy are well-established in the medical community, and doctors may continue to rely on these treatments. If our drug candidates do not achieve an adequate level of acceptance, we may not generate significant revenues from sales of drugs and we may not become profitable. The degree of market acceptance of our drug candidates, if approved for commercial sale, will depend on a number of factors, including:

efficacy and potential advantages compared to alternative treatments;

the ability to offer our drugs for sale at competitive prices;

convenience and ease of administration compared to alternative treatments;

the willingness of the target patient population to try new therapies and of physicians to prescribe these therapies;

the strength of marketing and distribution support;

sufficient third-party coverage or reimbursement;

the prevalence and severity of any side effects;

any restrictions on the use of our drugs together with other medications; and

inability of certain types of patients to take our drugs.

*If, in the future, we are unable to establish sales and marketing capabilities or maintain current agreements or enter into additional agreements with third parties to sell and market our drug candidates, we may not be successful in commercializing our drug candidates if and when they are approved.*

We are in the early stages of establishing a sales and marketing infrastructure and our company has not previously sold or marketed pharmaceutical drugs. To achieve commercial success for any approved drug for which sales and marketing is not the responsibility of any strategic collaborator that we have or may have in the future, we must either develop a sales and marketing organization or outsource these functions to other third parties. In the future, we may choose to build a sales and marketing infrastructure to market or co-promote one or more of our drug candidates, if

and when they are approved, or enter into additional collaborations with respect to the sale and marketing of our drug candidates. We are currently establishing the commercial infrastructure to support a potential launch of selinexor in the United States, and we intend to work with existing and potential partners to establish such commercial infrastructure outside the United States.

There are risks involved with both establishing our own sales and marketing capabilities and entering into arrangements with third parties to perform these services. For example, recruiting and training a sales force is expensive and time-consuming and could delay any commercial launch of a drug candidate. If the commercial launch of a drug candidate for which we recruit a sales force and establish marketing capabilities is delayed or does not occur for any reason, we would have prematurely or unnecessarily incurred these commercialization expenses. This may be costly, and our investment would be lost if we cannot retain or reposition our sales and marketing personnel.

Factors that may inhibit our efforts to commercialize our drugs on our own include:

our inability to recruit and retain adequate numbers of effective sales and marketing personnel;

the inability of sales personnel to obtain access to physicians or persuade adequate numbers of physicians to prescribe any future drugs;

the lack of complementary drugs to be offered by sales personnel, which may put us at a competitive disadvantage relative to companies with more extensive drug lines;

unforeseen costs and expenses associated with creating an independent sales and marketing organization;  
and

inability to obtain sufficient coverage and reimbursement from third-party payors and governmental agencies.

Entering into arrangements with third parties to perform sales and marketing services may result in lower revenues from the sale of drug or the profitability of these revenues to us than if we were to market and sell any drugs that we develop ourselves. In addition, we may not be successful in maintaining current arrangements or entering into additional arrangements with third parties to sell and market our drug candidates or may be unable to do so on terms that are favorable to us. We likely will have little control over such third parties, and any of them may fail to devote the necessary resources and attention to sell and market our drugs effectively. If we do not establish sales and marketing capabilities successfully, either on our own or in collaboration with third parties, we will not be successful in commercializing our drug candidates.

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***We may not receive royalty or milestone revenue under our license agreements for several years, or at all.***

Our license agreements provide for payments on achievement of development and/or commercialization milestones and for royalties on product sales. However, because none of our drug candidates have been approved for commercial sale, our drug candidates are at early stages of development and drug development entails a high risk of failure, we may never realize any material portion of the milestone revenue provided in our license agreements and we do not expect to receive any royalty revenue for several years, if at all.

***We face substantial competition, which may result in others discovering, developing or commercializing drugs before or more successfully than we do.***

The discovery, development and commercialization of new drugs is highly competitive. We face competition with respect to our current drug candidates, and will face competition with respect to any drug candidates that we may seek to discover and develop or commercialize in the future, from major pharmaceutical companies, specialty pharmaceutical companies and biotechnology companies worldwide. There are a number of major pharmaceutical, specialty pharmaceutical and biotechnology companies that currently market and sell drugs or are pursuing the development of drugs for the treatment of cancer and the other disease indications for which we are developing our drug candidates, although we believe that to date, none of these competitive drugs and therapies currently in development are based on scientific approaches that are the same as our approach. Potential competitors also include academic institutions and governmental agencies and public and private research institutions.

We are initially focused on developing our current drug candidates for the treatment of cancer. There are a variety of available therapies marketed for cancer. In many cases, cancer drugs are administered in combination to enhance efficacy. Some of these drugs are branded and subject to patent protection, and others are available on a generic basis. Many of these approved drugs are well-established therapies and are widely accepted by physicians, patients and third-party payors. Insurers and other third-party payors may also encourage the use of generic drugs. We expect that if our drug candidates are approved, they will be priced at a significant premium over competitive generic drugs. This may make it difficult for us to achieve our business strategy of using our drug candidates in combination with existing therapies or replacing existing therapies with our drug candidates.

Our competitors may develop drugs that are more effective, safer, more convenient or less costly than any that we are developing or that would render our drug candidates obsolete or non-competitive. Our competitors may also obtain marketing approval from the FDA or other regulatory authorities for their drugs 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 or preventing us from entering into a particular indication at all.

Many of our competitors have significantly greater financial resources and expertise in research and development, manufacturing, preclinical studies, conducting clinical trials, obtaining regulatory approvals and marketing approved drugs than we do. Mergers and acquisitions in the pharmaceutical and biotechnology industries may result in even more resources being concentrated among a smaller number of our competitors. Smaller and other early-stage companies may also prove to be significant competitors, particularly through collaborative arrangements with large and established companies. These third parties compete with us in recruiting and retaining qualified scientific and management personnel, establishing clinical trial sites and patient registration for clinical trials, as well as in acquiring technologies complementary to, or that may be necessary for, our programs.

***Even if we are able to commercialize any drug candidates, the drugs may not receive coverage or may become subject to unfavorable pricing regulations, third-party reimbursement practices or healthcare reform initiatives, all of which would harm our business.***

The legislation and regulations that govern marketing approvals, pricing and reimbursement for new drug products vary widely from country to country. Some countries require approval of the sale price of a drug before it can be marketed. In many countries, the pricing review period begins after marketing or drug licensing approval is granted. In some foreign markets, prescription pharmaceutical pricing remains subject to continuing governmental control even after initial approval is granted. In the United States, approval and reimbursement decisions are not linked directly, but there is increasing scrutiny from the Congress and regulatory authorities of the pricing of pharmaceutical products. As a result, we might obtain marketing approval for a drug in a particular country, but then be subject to price regulations that delay our commercial launch of the drug, possibly for lengthy time periods, and negatively impact the revenues we are able to generate from the sale of the drug in that country. Adverse pricing limitations may hinder our ability to recoup our investment in one or more drug candidates, even if our drug candidates obtain marketing approval.



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Significant uncertainty exists as to the coverage and reimbursement status of our product candidates for which we seek regulatory approval. Our ability to commercialize any drugs successfully will depend, in part, on the extent to which reimbursement for these drugs and related treatments will be available from government health administration authorities, private health insurers and other organizations. Government authorities and third-party payors, such as private health insurers and health maintenance organizations, decide which medications they will pay for and establish reimbursement levels. Obtaining and maintaining adequate reimbursement for our product candidates, if approved, may be difficult. Moreover, the process for determining whether a third-party payor will provide coverage for a product may be separate from the process for setting the price of a product or for establishing the reimbursement rate that such a payor will pay for the product. Further, one payor's determination to provide coverage for a product does not assure that other payors will also provide coverage and reimbursement for our products, if they are approved, by third-party payors.

A primary trend in the healthcare industry in the United States and elsewhere is cost containment. Government authorities and third-party payors have attempted to control costs by limiting coverage and the amount of reimbursement for particular medications. Increasingly, third-party payors are requiring that drug companies provide them with predetermined discounts from list prices and are challenging the prices charged for medical products. Third-party payors may also seek, with respect to an approved product, additional clinical evidence that goes beyond the data required to obtain marketing approval. They may require such evidence to demonstrate clinical benefits and value in specific patient populations or they may call for costly pharmaceutical studies to justify coverage and reimbursement or the level of reimbursement relative to other therapies before covering our products. Accordingly, we cannot be sure that reimbursement will be available for any drug that we commercialize and, if reimbursement is available, we cannot be sure as to the level of reimbursement and whether it will be adequate. Coverage and reimbursement may impact the demand for, or the price of, any drug candidate for which we obtain marketing approval. If reimbursement is not available or is available only at limited levels, we may not be able to successfully commercialize any drug candidate for which we obtain marketing approval.

There may be significant delays in obtaining reimbursement for newly-approved drugs, and coverage may be more limited than the indications for which the drug is approved by the FDA or comparable regulatory authorities outside of the United States. Moreover, eligibility for reimbursement does not imply that any drug will be paid for in all cases or at a rate that covers our costs, including research, development, manufacture, sale and distribution. Interim reimbursement levels for new drugs, if applicable, may also not be sufficient to cover our costs and may not be made permanent. Reimbursement rates may vary according to the use of the drug and the clinical setting in which it is used, may be based on reimbursement levels already set for lower cost drugs and may be incorporated into existing payments for other services. Net prices for drugs may be reduced by mandatory discounts or rebates required by government healthcare programs or private payors and by any future relaxation of laws that presently restrict imports of drugs from countries where they may be sold at lower prices than in the United States. Third-party payors often rely upon Medicare coverage policy and payment limitations in setting their own reimbursement policies. Our inability to promptly obtain coverage and profitable payment rates from both government-funded and private payors for any approved drugs that we develop could have a material adverse effect on our operating results, our ability to raise capital needed to commercialize drugs and our overall financial condition.

***Product liability lawsuits against us could cause us to incur substantial liabilities and to limit commercialization of any drugs that we may develop.***

We face an inherent risk of product liability exposure related to the testing of our drug candidates in human clinical trials and will face an even greater risk if we commercially sell any drugs that we may develop. If we cannot successfully defend ourselves against claims that our drug candidates or drugs caused injuries, we will incur substantial liabilities. Regardless of merit or eventual outcome, liability claims may result in:

decreased demand for any drug candidates or drugs that we may develop;

injury to our reputation and significant negative media attention;

withdrawal of clinical trial participants;

significant costs to defend the related litigation;

substantial monetary awards to trial participants or patients;

loss of revenue;

reduced resources of our management to pursue our business strategy; and

the inability to commercialize any drugs that we may develop.

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We currently hold clinical trial liability insurance coverage, but that coverage may not be adequate to cover any and all liabilities that we may incur. We would need to increase our insurance coverage when we begin the commercialization of our drug candidates, if ever. Insurance coverage is increasingly expensive. We may not be able to maintain insurance coverage at a reasonable cost or in an amount adequate to satisfy any liability that may arise.

### ***The business that we conduct outside the United States may be adversely affected by international risk and uncertainties.***

Although our operations are based in the United States, we conduct business outside the United States and expect to continue to do so in the future. For instance, many of the sites at which our clinical trials are being conducted are located outside the United States. In addition, we plan to seek approvals to sell our products in foreign countries. Any business that we conduct outside the United States will be subject to additional risks that may materially adversely affect our ability to conduct business in international markets, including:

potentially reduced protection for intellectual property rights;

the potential for so-called parallel importing, which is what happens when a local seller, faced with high or higher local prices, opts to import goods from a foreign market (with low or lower prices) rather than buying them locally;

unexpected changes in tariffs, trade barriers and regulatory requirements;

economic weakness, including inflation, volatility in currency exchange rates or political instability in particular foreign economies and markets;

workforce uncertainty in countries where labor unrest is more common than in the United States;

production shortages resulting from any events affecting a product candidate and/or finished drug product supply or manufacturing capabilities abroad;

business interruptions resulting from geo-political actions, including war and terrorism, or natural disasters, including earthquakes, hurricanes, typhoons, floods and fires; and

failure to comply with Office of Foreign Asset Control rules and regulations and the Foreign Corrupt Practices Act, or FCPA.

### **Risks Related to Our Financial Position and Need for Additional Capital**

***We have incurred significant losses since inception. We expect to incur losses for the foreseeable future and may never achieve or maintain profitability.***

## Edgar Filing: Karyopharm Therapeutics Inc. - Form 10-Q

Since inception, we have incurred significant operating losses. Our net loss was \$38.5 million for the three months ended March 31, 2018. As of March 31, 2018, we had an accumulated deficit of \$533.8 million. We have not generated any revenue to date from sales of any drugs and have financed our operations to date principally through private placements of our preferred stock, proceeds from our initial public offering and follow-on offerings of common stock and cash generated from our business development activities. We have devoted substantially all of our efforts to research and development. Our lead drug candidate, oral selinexor, as well as verdinexor, eltanexor and KPT-9274, are in clinical development. As a result, we expect that it will be several years, if ever, before we have a drug candidate ready for commercialization for the treatment of human disease. We expect to continue to incur significant expenses and increasing operating losses for the foreseeable future. The net losses we incur may fluctuate significantly from quarter to quarter. We anticipate that our expenses will increase substantially if and as we:

continue our research and preclinical and clinical development of our drug candidates;

initiate additional clinical trials for our drug candidates;

seek marketing approvals for any of our drug candidates that successfully complete clinical trials;

establish a sales, marketing and distribution infrastructure to commercialize any drugs for which we may obtain marketing approval;

maintain, expand and protect our intellectual property portfolio;

manufacture our drug candidates;

hire additional clinical, quality control and scientific personnel;

identify additional drug candidates;

acquire or in-license other drugs and technologies; and

add operational, financial and management information systems and personnel, including personnel to support our drug development, any future commercialization efforts and our other operations as a public company.

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To become and remain profitable, we must develop and eventually commercialize a drug or drugs with significant market potential, either on our own or with a collaborator. This will require us to be successful in a range of challenging activities, including completing preclinical studies and clinical trials of our drug candidates, obtaining marketing approval for these drug candidates, manufacturing, marketing and selling those drugs for which we may obtain marketing approval and establishing and managing any collaborations for the development, marketing and/or commercialization of our drug candidates. We may never succeed in these activities and, even if we do, may never generate revenues that are significant or large enough to achieve profitability. If we do achieve profitability, we may not be able to sustain or increase profitability on a quarterly or annual basis. Our failure to become and remain profitable would decrease the value of the company and could impair our ability to raise capital, maintain our research and development efforts, expand our business and/or continue our operations. A decline in the value of our company could also cause our stockholders to lose all or part of their investment.

***The nature and length of our operating history may make it difficult for stockholders to evaluate the success of our business to date and to assess our future viability.***

We were incorporated in 2008 and commenced operations in 2009. Our operations to date have been limited to organizing and staffing our company, business planning, raising capital, developing our platform, identifying potential drug candidates and conducting preclinical studies and early-phase and later-phase clinical trials of our drug candidates. Our lead drug candidate is currently in multiple Phase 2 and Phase 3 clinical trials and all of our other drug candidates for the treatment of human disease are in early clinical development. We have not yet demonstrated our ability to successfully complete any late-phase clinical trials in humans, including large-scale clinical trials, obtain marketing approvals, manufacture a commercial scale drug, or arrange for a third party to do so on our behalf, or conduct sales and marketing activities necessary for successful drug commercialization. Typically, it takes about six to ten years to develop one new drug from the time it is in Phase 1 clinical trials to when it is commercially available for treating patients. Consequently, any predictions stockholders make about our future success or viability may not be as accurate as they could be if we had a longer operating history.

In addition, as a business with a short operating history, we may encounter unforeseen expenses, difficulties, complications, delays and other known and unknown factors. We will need to transition from a company with a research focus to a company capable of supporting commercial activities. We may not be successful in such a transition.

As we continue to build our business, we expect our financial condition and operating results may fluctuate significantly from quarter to quarter and year to year due to a variety of factors, many of which are beyond our control. Accordingly, stockholders should not rely upon the results of any particular quarterly or annual periods as indications of future operating performance.

***We will need substantial additional funding. If we are unable to raise capital when needed, we would be forced to delay, reduce or eliminate our research and drug development programs or commercialization efforts.***

We expect our expenses to increase in connection with our ongoing activities, particularly as we continue the clinical trials of, and seek marketing approval for, selinexor and our other drug candidates. In addition, if we obtain marketing approval for any of our drug candidates, we expect to incur significant commercialization expenses related to drug sales, marketing, manufacturing and distribution to the extent that such sales, marketing, manufacturing and distribution are not the responsibility of any collaborator that we may have at such time for any such drug. Furthermore, we will continue to incur additional costs associated with operating as a public company. Accordingly, we will need to obtain substantial additional funding in connection with our continuing operations. If we are unable to raise capital when needed or on attractive terms, we would be forced to delay, reduce or eliminate our research and

drug development programs or commercialization efforts.

We expect that our existing cash, cash equivalents and investments will enable us to fund our current operating and capital expenditure plans into the third quarter of 2019 while we are establishing the commercial infrastructure for a potential launch of selinexor in the United States. Our future capital requirements will depend on many factors, including:

the progress and results of our current and planned clinical trials of selinexor;

the scope, progress, results and costs of drug discovery, preclinical development, laboratory testing and clinical trials for our other drug candidates;

the costs, timing and outcome of regulatory review of our drug candidates;

our ability to establish and maintain collaborations on favorable terms, if at all;

the success of any collaborations that we may enter into with third parties;

the extent to which we acquire or in-license other drugs and technologies;

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the costs of future commercialization activities, including drug sales, marketing, manufacturing and distribution, for any of our drug candidates for which we receive marketing approval, to the extent that such sales, marketing, manufacturing and distribution are not the responsibility of any collaborator that we may have at such time;

the amount of revenue, if any, received from commercial sales of our drug candidates, should any of our drug candidates receive marketing approval; and

the costs of preparing, filing and prosecuting patent applications, maintaining and enforcing our intellectual property rights and defending intellectual property-related claims.

Identifying potential drug candidates and conducting preclinical studies and clinical trials is a time-consuming, expensive and uncertain process that takes years to complete, and we may never generate the necessary data or results required to obtain marketing approval and achieve drug sales. In addition, our drug candidates, if approved, may not achieve commercial success. Our commercial revenues, if any, will be derived from sales of drugs that we do not expect to be commercially available for at least one, or possibly many years, if at all. Accordingly, we will need to continue to rely on additional financing to achieve our business objectives. Adequate additional financing may not be available to us on acceptable terms, or at all. In addition, we may seek additional capital due to favorable market conditions or strategic considerations, even if we believe we have sufficient funds for our current or future operating plans.

***Raising additional capital may cause dilution to our stockholders, restrict our operations or require us to relinquish rights to our drug candidates.***

Until such time, if ever, as we can generate substantial revenues from the sale of drugs, we expect to finance our cash needs through a combination of equity offerings, debt financings, collaborations, strategic alliances and/or licensing arrangements. We do not have any committed external source of funds. To the extent that we raise additional capital through the sale of equity or convertible debt securities, the ownership interests of stockholders will be diluted, and the terms of these securities may include liquidation or other preferences that adversely affect the rights of common stockholders. Debt financing, if available, may involve agreements that include covenants limiting or restricting our ability to take specific actions, such as incurring additional debt, making capital expenditures or declaring dividends.

If we raise funds through further collaborations, strategic alliances or licensing arrangements with third parties, we may have to relinquish valuable rights to our future revenue streams, research programs or drug candidates or to grant licenses on terms that may not be favorable to us. If we are unable to raise additional funds through equity or debt financings when needed, we may be required to delay, limit, reduce or terminate our research and drug development or commercialization efforts or grant rights to develop and market drug candidates that we would otherwise prefer to develop and market ourselves.

***Unstable market and economic conditions may have serious adverse consequences on our business, financial condition and stock price.***

Global credit and financial markets have experienced extreme disruptions over some of the past several years. Such disruptions have resulted, and could in the future result, in diminished liquidity and credit availability, declines in consumer confidence, declines in economic growth, increases in unemployment rates and uncertainty about economic stability. There can be no assurance that any deterioration in credit and financial markets and confidence in economic conditions will not occur. Our general business strategy may be compromised by economic downturns, a volatile

business environment and unpredictable and unstable market conditions. If the equity and credit markets deteriorate, it may make any necessary equity or debt financing more difficult to secure, more costly or more dilutive. Failure to secure any necessary financing in a timely manner and on favorable terms could harm our growth strategy, financial performance and stock price and could require us to delay or abandon plans with respect to our business, including clinical development plans. In addition, there is a risk that one or more of our current service providers, manufacturers or other third parties with which we conduct business may not survive difficult economic times, which could directly affect our ability to attain our operating goals on schedule and on budget.

#### **Risks Related to Our Dependence on Third Parties**

*We depend on third parties for certain aspects of the development, marketing and/or commercialization of our drug candidates and plan to enter into additional collaborations. If those collaborations are not successful, we may not be able to capitalize on the market potential of these drug candidates.*

We intend to maintain our existing collaborations and will continue to seek additional third-party collaborators for certain aspects of the development, marketing and/or commercialization of our drug candidates. For example, we have entered into a collaboration with Ono Pharmaceutical Co., Ltd., and plan to continue to seek



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to enter into additional collaborations, for marketing and commercialization of selinexor for other geographies outside the United States. In addition, we intend to seek one or more collaborators to aid in the further development, marketing and/or commercialization of our other SINE compounds for indications outside of oncology. Our likely collaborators for any collaboration arrangements include large and mid-size pharmaceutical companies, regional and national pharmaceutical companies and biotechnology companies. In connection with any such arrangements with third parties, we will likely have limited control over the amount and timing of resources that our collaborators dedicate to the development, marketing and/or commercialization of our drug candidates. Our ability to generate revenues from these arrangements will depend on our collaborators' abilities to successfully perform the functions assigned to them in these arrangements.

Collaborations involving our drug candidates pose the following risks to us:

collaborators have significant discretion in determining the efforts and resources that they will apply to these collaborations;

collaborators may not pursue development, marketing and/or commercialization of our drug candidates or may elect not to continue or renew development, marketing or commercialization programs based on clinical trial results, changes in the collaborator's strategic focus or available funding or external factors such as an acquisition that diverts resources or creates competing priorities;

collaborators may delay clinical trials, provide insufficient funding for a clinical trial program, stop a clinical trial or abandon a drug candidate, repeat or conduct new clinical trials or require a new formulation of a drug candidate for clinical testing;

collaborators could independently develop, or develop with third parties, drugs that compete directly or indirectly with our drugs or drug candidates if the collaborators believe that competitive drugs are more likely to be successfully developed or can be commercialized under terms that are more economically attractive than ours;

a collaborator with marketing and distribution rights to one or more drugs may not commit sufficient resources to the marketing and distribution of such drug or drugs;

collaborators may not properly maintain or defend our intellectual property rights or may use our proprietary information in such a way as to invite litigation that could jeopardize or invalidate our proprietary information or expose us to potential litigation;

collaborators may infringe the intellectual property rights of third parties, which may expose us to litigation and potential liability;

disputes may arise between the collaborators and us that result in the delay or termination of the research, development or commercialization of our drugs or drug candidates or that result in costly litigation or arbitration that diverts management's attention and resources of the company;

we may lose certain valuable rights under circumstances identified in any collaboration arrangement that we enter into, such as if we undergo a change of control;

collaborations may be terminated and, if terminated, may result in a need for additional capital to pursue further development, marketing and/or commercialization of the applicable drug candidates;

collaborators may learn about our discoveries and use this knowledge to compete with us in the future; and

the number and type of our collaborations could adversely affect our attractiveness to collaborators or acquirers.

Collaboration agreements may not lead to development or commercialization of drug candidates in the most efficient manner, or at all. If our collaborations do not result in the successful development and commercialization of products or if one of our collaborators terminates its agreement with us, we may not receive any future milestone or royalty payments under the collaboration. If we do not receive the funding we expect under these agreements, our development of our product candidates could be delayed and we may need additional resources to develop product candidates. All of the risks relating to product development, regulatory approval and commercialization described in this Quarterly Report on Form 10-Q also apply to the activities of our collaborators.

***If we are not able to maintain our existing collaborations or establish additional collaborations as we currently plan, we may have to alter our development and commercialization plans.***

Our drug development programs and the potential commercialization of our drug candidates will require substantial additional cash to fund expenses. As noted above, we expect to maintain our existing collaborations and collaborate with additional pharmaceutical and biotechnology companies for the development and/or commercialization of our drug candidates.

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We face significant competition in seeking appropriate collaborators. Whether we reach a definitive agreement for a collaboration will depend, among other things, upon our assessment of the collaborator's resources and expertise, the terms and conditions of the proposed collaboration and the proposed collaborator's evaluation of a number of factors. Those factors may include the design or results of clinical trials, the likelihood of approval by the FDA or similar regulatory authorities outside of the United States, the potential market for the subject drug candidate, the costs and complexities of manufacturing and delivering such drug candidate to patients, the potential of competing drugs, the existence of uncertainty with respect to our ownership of intellectual property, which can exist if there is a challenge to such ownership without regard to the merits of the challenge, and industry and market conditions generally. The collaborator may also consider alternative drug candidates or technologies for similar indications that may be available to collaborate on and whether such a collaboration could be more attractive than the one with us for our drug candidate.

We may also be restricted under then-existing collaboration agreements from entering into future agreements on certain terms with potential collaborators.

Collaborations are complex and time-consuming to negotiate and document. In addition, there have been a significant number of recent business combinations among large pharmaceutical companies that have resulted in a reduced number of potential future collaborators.

We may not be able to negotiate collaborations on a timely basis, on acceptable terms, or at all. If we are unable to do so, we may have to curtail the development of such drug candidate, reduce or delay its development program or one or more of our other development programs, delay its potential commercialization or reduce the scope of any sales or marketing activities, or increase our expenditures and undertake development or commercialization activities at our own expense. If we elect to increase our expenditures to fund development or commercialization activities on our own, we may need to obtain additional capital, which may not be available to us on acceptable terms, or at all. If we do not have sufficient funds, we may not be able to further develop our drug candidates or bring them to market and generate revenue from sales of drugs.

***We rely on some third parties as we conduct our clinical trials and some aspects of our research and preclinical studies, and those third parties may not perform satisfactorily, including failing to meet deadlines for the completion of such trials, research or testing.***

We rely on some third parties, such as contract research organizations, clinical data management organizations, medical institutions and clinical investigators, as we conduct our clinical trials. We currently rely and expect to continue to rely on third parties to conduct some aspects of our research and preclinical studies. Any of these third parties may terminate their engagements with us at any time. If we need to enter into alternative arrangements, it would delay our drug development activities.

Our reliance on these third parties for research and development activities will reduce our control over these activities but will not relieve us of our responsibilities. For example, we will remain responsible for ensuring that each of our clinical trials is conducted in accordance with the general investigational plan and protocols for the trial. Moreover, the FDA requires us to comply with standards, commonly referred to as Good Clinical Practices, for conducting, recording and reporting the results of clinical trials to assure that data and reported results are credible and accurate and that the rights, integrity and confidentiality of trial participants are protected. The European Medicines Agency, or EMA, also requires us to comply with comparable standards. We also are required to register ongoing clinical trials and post the results of completed clinical trials on a government-sponsored database, ClinicalTrials.gov, within certain timeframes. Failure to do so can result in fines, adverse publicity and civil and criminal sanctions.

Furthermore, these third parties may also have relationships with other entities, some of which may be our competitors. If these third parties do not successfully carry out their contractual duties, meet expected deadlines or conduct our clinical trials in accordance with regulatory requirements or our stated protocols, we will not be able to obtain, or may be delayed in obtaining, marketing approvals for our drug candidates and will not be able to, or may be delayed in our efforts to, successfully commercialize our drug candidates.

We also expect to rely on other third parties to store and distribute drug supplies for our clinical trials. Any performance failure on the part of such third parties could delay clinical development or marketing approval of our drug candidates or commercialization of our drugs, producing additional losses and depriving us of potential revenue from sales of drugs.

***We rely on third parties to conduct investigator-sponsored clinical trials of selinexor and our other drug candidates. Any failure by a third party to meet its obligations with respect to the clinical development of our drug candidates may delay or impair our ability to obtain regulatory approval for selinexor and our other drug candidates.***

We rely on academic and private non-academic institutions to conduct and sponsor clinical trials relating to selinexor and our other drug candidates. We do not control the design or conduct of the investigator-sponsored trials, and it is possible that the FDA or

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non-U.S. regulatory authorities will not view these investigator-sponsored trials as providing adequate support for future clinical trials, whether controlled by us or third parties, for any one or more reasons, including elements of the design or execution of the trials or safety concerns or other trial results.

Such arrangements will provide us certain information rights with respect to the investigator-sponsored trials, including access to and the ability to use and reference the data, including for our own regulatory filings, resulting from the investigator-sponsored trials. However, we do not have control over the timing and reporting of the data from investigator-sponsored trials, nor do we own the data from the investigator-sponsored trials. If we are unable to confirm or replicate the results from the investigator-sponsored trials or if negative results are obtained, we would likely be further delayed or prevented from advancing further clinical development of our drug candidates. Further, if investigators or institutions breach their obligations with respect to the clinical development of our drug candidates, or if the data proves to be inadequate compared to the first-hand knowledge we might have gained had the investigator-sponsored trials been sponsored and conducted by us, then our ability to design and conduct any future clinical trials ourselves may be adversely affected.

Additionally, the FDA or non-U.S. regulatory authorities may disagree with the sufficiency of our right of reference to the preclinical, manufacturing or clinical data generated by these investigator-sponsored trials, or our interpretation of preclinical, manufacturing or clinical data from these investigator-sponsored trials. If so, the FDA or other non-U.S. regulatory authorities may require us to obtain and submit additional preclinical, manufacturing, or clinical data before we may initiate our planned trials and/or may not accept such additional data as adequate to initiate our planned trials.

***We contract with third parties for the manufacture of our drug candidates for preclinical studies and clinical trials and expect to continue to do so for clinical trials and ultimately for commercialization. This reliance on third parties increases the risk that we will not have sufficient quantities of our drug candidates or drugs or such quantities at an acceptable cost, which could delay, prevent or impair our development or commercialization efforts.***

We do not have any manufacturing facilities or personnel. We currently rely, and expect to continue to rely, on third-party manufacturers for the manufacture of our drug candidates for preclinical studies and clinical trials under the guidance of members of our organization. We have engaged third-party manufacturers for drug substance and drug product services. We do not have a long term supply agreement with any of these third-party manufacturers, and we purchase our required drug supplies on a purchase order basis.

We expect to rely on third-party manufacturers or third-party collaborators for the manufacture of our drug candidates for clinical trials and ultimately for commercial supply of any of these drug candidates for which we or any of our collaborators obtain marketing approval. We may be unable to establish any agreements with third-party manufacturers or to do so on acceptable terms. Even if we are able to establish agreements with third-party manufacturers, reliance on third-party manufacturers entails additional risks, including:

reliance on the third party for regulatory compliance and quality assurance;

the possible breach of the manufacturing agreement by the third party;

the possible failure of the third party to manufacture our drug candidate according to our schedule, or at all, including if the third-party manufacturer gives greater priority to the supply of other drugs over our drug candidates, or otherwise does not satisfactorily perform according to the terms of the manufacturing agreement;

the possible misappropriation or disclosure by the third party or others of our proprietary information, including our trade secrets and know-how; and

the possible termination or nonrenewal of the agreement by the third party at a time that is costly or inconvenient for us.

Third-party manufacturers may not be able to comply with current Good Manufacturing Practices, or cGMP, regulations or similar regulatory requirements outside of the United States. As with all drug manufacturing, our failure, or the failure of our third-party manufacturers, to comply with applicable regulations could result in sanctions being imposed on us, including fines, injunctions, civil penalties, delays, suspension or withdrawal of approvals, license revocation, seizures or recalls of drug candidates or drugs, operating restrictions and criminal prosecutions, any of which could significantly and adversely affect supplies of our drugs and harm our business and results of operations.

Any drugs that we may develop may compete with other drug candidates and drugs for access to manufacturing facilities. There are a limited number of manufacturers that operate under cGMP regulations and that might be capable of manufacturing for us.

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Any performance failure on the part of our existing or future manufacturers could delay clinical development or marketing approval. If our current contract manufacturers cannot perform as agreed, we may be required to replace those manufacturers. Although we believe that there are several potential alternative manufacturers who could manufacture our drug candidates, we may incur added costs and delays in identifying and qualifying any such replacement.

Our current and anticipated future dependence upon others for the manufacture of our drug candidates or drugs may adversely affect our future profit margins and our ability to commercialize any drugs that receive marketing approval on a timely and competitive basis.

## **Risks Related to Our Intellectual Property**

*If we are unable to obtain and maintain patent protection for our drug candidates and other discoveries, or if the scope of the patent protection obtained is not sufficiently broad, our competitors could develop and commercialize drugs and other discoveries similar or identical to ours, and our ability to successfully commercialize our drug candidates and other discoveries may be adversely affected.*

Our success depends in large part on our ability to obtain and maintain patent protection in the United States and other countries with respect to our proprietary drug candidates and other discoveries. We seek to protect our proprietary position by filing patent applications in the United States and abroad related to our novel drug candidates and other discoveries that are important to our business. To date, 44 patents have issued that relate to XPO1 inhibitors, including composition of matter patents for selinexor, verdinexor and eltanexor in the United States, and their use in targeted therapeutics. In addition, two patents have issued that relate to our PAK4/NAMPT inhibitor, KPT-9274, including a composition of matter patent in the United States and its use in targeted therapeutics. We cannot be certain that any other patents will issue with claims that cover any of our key drug candidates or other discoveries or drug candidates.

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 or in a timely manner. 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.

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. 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 drug candidates or other discoveries, or which effectively prevent others from commercializing competitive drugs and discoveries. 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.

The laws of foreign countries may not protect our rights to the same extent as the laws of the United States. For example, in some foreign jurisdictions, our ability to secure patents based on our filings in the United States may depend, in part, on our ability to timely obtain assignment of rights to the invention from the employees and consultants who invented the technology. 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. Therefore, we cannot be certain that we were the first to make the inventions claimed in our patents or pending patent applications, or that we were the first to file for patent protection of such inventions.

Assuming the other requirements for patentability are met, prior to March 2013, in the United States, the first to invent the claimed invention was entitled to the patent, while outside of the United States, the first to file a patent application is entitled to the patent. In March 2013, the United States transitioned to a first-inventor-to-file system in which, assuming the other requirements for patentability are met, the first inventor to file a patent application is entitled to the patent. We may be subject to a third-party preissuance submission of prior art to the U.S. Patent and Trademark Office, or become involved in opposition, derivation, revocation, reexamination, or post-grant or *inter partes* review or interference proceedings challenging our patent rights or the patent rights of others. An adverse determination in any such submission, proceeding or litigation could reduce the scope of, or invalidate, our patent rights, allow third parties to commercialize our discoveries or drugs and compete directly with us, without payment to us, or result in our inability to manufacture or commercialize drugs without infringing third-party patent rights.

Even if our 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 patents by developing similar or alternative discoveries or drugs in a non-infringing manner.



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The issuance of a patent is not conclusive as to its inventorship, scope, validity or enforceability, and our 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 in patent claims being narrowed, invalidated or held unenforceable, which could limit our ability to stop others from using or commercializing similar or identical discoveries and drugs, or limit the duration of the patent protection of our discoveries and drug candidates. Given the amount of time required for the development, testing and regulatory review of new drug candidates, patents protecting such candidates might expire before or shortly after such candidates are commercialized. As a result, our patent portfolio may not provide us with sufficient rights to exclude others from commercializing drugs similar or identical to ours.

***We may become involved in lawsuits to protect or enforce our patents and other intellectual property rights, which could be expensive, time-consuming and unsuccessful.***

Competitors or commercial supply companies or others may infringe our patents and other intellectual property rights. For example, we are aware of a third party selling a version of our lead product candidate for research purposes, which may infringe our intellectual property rights. To counter such infringement, we may advise such companies of our intellectual property rights, including, in some cases, intellectual property rights that provide protection for our lead product candidates, and demand that they stop infringing those rights. Such demand may provide such companies the opportunity to challenge the validity of certain of our intellectual property rights, or the opportunity to seek a finding that their activities do not infringe our intellectual property rights. We may also be required to file infringement actions, which can be expensive and time-consuming. In an infringement proceeding, a defendant may assert and a court may agree with a defendant that a patent of ours is invalid or unenforceable, or may refuse to stop the other party from using the intellectual property at issue. An adverse result in any litigation could put one or more of our patents at risk of being invalidated or interpreted narrowly. Furthermore, because of the substantial amount of discovery required in connection with intellectual property litigation, there is a risk that some of our confidential information could be compromised by disclosure during this type of litigation.

***Third parties may initiate legal proceedings alleging that we are infringing their intellectual property rights, the outcome of which would be uncertain and could have a material adverse effect on the success of our business.***

Our commercial success depends upon our ability and the ability of any current and future collaborators to develop, manufacture, market and sell our drug candidates and use our proprietary technologies without infringing the proprietary rights of third parties. We may become party to, or threatened with, future adversarial proceedings or litigation regarding intellectual property rights with respect to our drug candidates and technology, including interference proceedings before the U.S. Patent and Trademark Office. Third parties may assert infringement claims against us based on existing patents or patents that may be granted in the future. No litigation asserting such infringement claims is currently pending against us, and we have not been found by a court of competent jurisdiction to have infringed a third party's intellectual property rights. If we are found to infringe, or think there is a risk we may be found to infringe, a third party's intellectual property rights, we could be required or choose to obtain a license from such third party to continue developing and marketing our drug candidates and using our technology. However, we may not be able to obtain any required license on commercially reasonable terms, or at all. Even if we were able to obtain a license, it could be non-exclusive, thereby giving our competitors access to the same intellectual property licensed to us. We could be forced, including by court order, to cease commercializing the infringing intellectual property or drug or to cease using the infringing technology. In addition, we could be found liable for monetary damages. A finding of infringement could prevent us from commercializing our drug candidates or force us to cease some of our business operations, which could materially harm our business. Claims that we have misappropriated the confidential information or trade secrets of third parties could have a similar negative impact on our business.

*We may be subject to claims that our employees have wrongfully used or disclosed alleged trade secrets of their former employers.*

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 we or these employees have used or disclosed intellectual property, including trade secrets or other proprietary information, of any such employee's former employer. Although we have no knowledge of any such claims being alleged to date, if such claims were to arise, litigation may be necessary to defend against any such claims. If we fail in 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 defending against such claims, litigation could result in substantial costs and be a distraction to management.

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***Intellectual property litigation could cause us to spend substantial resources and distract our personnel from their normal responsibilities.***

Even if resolved in our favor, litigation or other legal proceedings relating to intellectual property claims may cause us to incur significant expenses, and could distract our technical and management personnel from their normal responsibilities. In addition, there could be public announcements of the results of hearings, motions or other interim proceedings or developments and if securities analysts or investors perceive these results to be negative, it could have a material adverse effect on the price of our common stock. Such litigation or proceedings could substantially increase our operating losses and reduce the resources available for development activities or any future sales, marketing or distribution activities. We may not have sufficient financial or other resources to adequately conduct such litigation or proceedings. Some of our competitors may be able to sustain the costs of such litigation or proceedings more effectively than we can because of their greater financial resources. Uncertainties resulting from the initiation and continuation of patent litigation or other proceedings could have a material adverse effect on our ability to compete in the marketplace.

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

Periodic maintenance fees, renewal fees, annuity fees and various other governmental fees on patents and/or applications will be due to the United States Patent and Trademark Office, or USPTO, and various foreign patent offices at various points over the lifetime of the patents and/or applications. We have systems in place to remind us to pay these fees, and we rely on our outside counsel to pay these fees when due. Additionally, the USPTO and various foreign patent offices require compliance with a number of procedural, documentary, fee payment and other similar provisions during the patent application process. We employ reputable law firms and other professionals to help us comply with such provisions, and in many cases, an inadvertent lapse can be cured by payment of a late fee or by other means in accordance with rules applicable to the particular jurisdiction. However, there are situations in which non-compliance 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. If such an event were to occur, it could have a material adverse effect on our business.

***If we do not successfully extend the term of patents covering our drug candidates under the Hatch-Waxman Amendments and similar foreign legislation, our business may be materially harmed.***

Depending upon the timing, duration and conditions of FDA marketing approval, if any, of our drug candidates, one or more of our U.S. patents may be eligible for patent term extension under the Drug Price Competition and Patent Term Restoration Act of 1984, referred to as the Hatch-Waxman Amendments. The Hatch-Waxman Amendments permit a patent term extension of up to five years for one patent covering an approved product as compensation for effective patent term lost during product development and the FDA regulatory review process. However, we may not receive an extension if we fail to apply within applicable deadlines, fail to apply prior to expiration of relevant patents or otherwise fail to satisfy applicable requirements. Moreover, the length of the extension could be less than we request. The total patent term, including the extension period, may not exceed 14 years following FDA approval. Accordingly, the length of the extension, or the ability to even obtain an extension, depends on many factors.

In the United States, only a single patent can be extended for each qualifying FDA approval, and any patent can be extended only once and only for a single product. Laws governing analogous patent term extensions in foreign jurisdictions vary widely, as do laws governing the ability to obtain multiple patents from a single patent family. Because both selinexor and verdinexor are protected by a single family of patents and applications, we may not be

able to secure patent term extensions for both of these drug candidates in all jurisdictions where these drug candidates are approved, if ever.

If we are unable to obtain a patent term extension for a drug candidate or the term of any such extension is less than we request, the period during which we can enforce our patent rights for that drug candidate, if any, in that jurisdiction will be shortened and our competitors may obtain approval to market competing products sooner. As a result, our revenue could be materially reduced.

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

In addition to seeking patents for our drug candidates and other discoveries, we also rely on trade secrets, including unpatented know-how, technology and other proprietary information, to maintain our competitive position. We seek to protect these trade secrets, in part, by entering into non-disclosure and confidentiality agreements with parties who have access to them, such as our employees, outside scientific collaborators, contract research organizations, contract manufacturers, consultants, advisors and other third parties. We also enter into confidentiality and invention or patent assignment agreements with our employees and consultants. Despite these efforts, any of these parties may breach the agreements and disclose our proprietary information, including our trade secrets, and we may not be able to obtain adequate remedies for such breaches. To the extent that we are unable to timely enter into confidentiality and invention or patent assignment agreements with our employees and consultants, our ability to protect our business through trade

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secrets and patents may be harmed. 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 of 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 from using that technology or information to compete with us. If any of our trade secrets were to be disclosed to or independently developed by a competitor, our competitive position would be harmed. To the extent inventions are made by a third party under an agreement that does not grant us an assignment of their rights in inventions, we may choose or be required to obtain a license.

***Not all of our trademarks are registered. Failure to secure those registrations could adversely affect our business.***

As of May 1, 2018, four of our trademarks are registered in the United States. We also have eleven pending intent-to-use applications in the United States, some of which have been allowed, meaning that we can perfect our registrations when we have commenced use in commerce. Outside the United States, we have registrations in the European Union for five trademarks (potential drug names for selinexor), pending applications for those same five marks and a pending application for a sixth. Applications for the same six trademarks were filed in 15 other jurisdictions, some of which have also proceeded to registration. If we do not secure registrations for our trademarks, we may encounter more difficulty in enforcing them against third parties than we otherwise would, which could adversely affect our business. During trademark registration proceedings in the United States and foreign jurisdictions, we may receive rejections. We are given an opportunity to respond to those rejections, but we may not be able to overcome such rejections. In addition, in the USPTO and in comparable agencies in many foreign jurisdictions, third parties are given an opportunity to oppose pending trademark applications and to seek to cancel registered trademarks. Opposition or cancellation proceedings may be filed against our trademarks, and our trademarks may not survive such proceedings.

In addition, any proprietary name we propose to use with our key drug candidates in the United States must be approved by the FDA, regardless of whether we have registered it, or applied to register it, as a trademark. The FDA typically conducts a review of proposed drug names, including an evaluation of potential for confusion with other drug names. If the FDA objects to any of our proposed proprietary drug names for any of our drug candidates, if approved, we may be required to expend significant additional resources in an effort to identify a suitable proprietary drug name that would qualify under applicable trademark laws, not infringe the existing rights of third parties and be acceptable to the FDA.

**Risks Related to Regulatory Approval and Marketing of Our Product Candidates and Other Legal Compliance Matters**

***Even if we complete the necessary preclinical studies and clinical trials, the marketing approval process is expensive, time-consuming and uncertain and may prevent us from obtaining approvals for the commercialization of some or all of our drug candidates. As a result, we cannot predict when or if we or any of our collaborators will obtain marketing approval to commercialize a drug candidate.***

The research, testing, manufacturing, labeling, approval, selling, marketing, promotion and distribution of drugs are subject to extensive regulation by the FDA and comparable foreign regulatory authorities, whose laws and regulations may differ from country to country. We are not permitted to market our drug candidates in the United States or in other countries until we or any of our collaborators receive approval of a New Drug Application, or NDA, from the FDA or marketing approval from applicable regulatory authorities outside of the United States. Our drug candidates are in early stages of development and are subject to the risks of failure inherent in drug development. We have not submitted an application for or received marketing approval for any of our drug candidates in the United States or in

any other jurisdiction. We have limited experience in conducting and managing the clinical trials necessary to obtain marketing approvals, including FDA approval of an NDA.

The process of obtaining marketing approvals, both in the United States and abroad, is a lengthy, expensive and uncertain process. It may take many years, if approval is obtained at all, and can vary substantially based upon a variety of factors, including the type, complexity and novelty of the drug candidates involved.

In addition, changes in marketing approval policies during the development period, changes in or the enactment or promulgation of additional statutes, regulations or guidance or changes in regulatory review for each submitted drug application, may cause delays in the approval or rejection of an application. Regulatory authorities have substantial discretion in the approval process and may refuse to accept any application or may decide that our data are insufficient for approval and require additional preclinical studies, clinical trials or other studies and testing. In addition, varying interpretations of the data obtained from preclinical studies and clinical trials could delay, limit or prevent marketing approval of a drug candidate. Any marketing approval we or any of our collaborators ultimately obtain may be limited or subject to restrictions or post-approval commitments that render the approved drug not commercially viable.

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Any delay in obtaining or failure to obtain required approvals could materially adversely affect our ability or that of any of our collaborators to generate revenue from the particular drug candidate, which likely would result in significant harm to our financial position and adversely impact our stock price.

***Our failure to obtain marketing approval in foreign jurisdictions would prevent our product candidates from being marketed abroad, and any approval we are granted for our product candidates in the United States would not assure approval of product candidates in foreign jurisdictions.***

In order to market and sell our drugs in the European Union and many other jurisdictions, we and our current or future collaborators must obtain separate marketing approvals and comply with numerous and varying regulatory requirements. The approval procedure varies among countries and can involve additional testing. The time required to obtain approval may differ substantially from that required to obtain FDA approval. The marketing approval process outside of the United States generally includes all of the risks associated with obtaining FDA approval. In addition, in many countries outside of the United States, it is required that the drug be approved for reimbursement before the drug can be approved for sale in that country. We and our collaborators may not obtain approvals from regulatory authorities outside of the United States on a timely basis, if at all. Approval by the FDA does not ensure approval by regulatory authorities in other countries or jurisdictions, and approval by one regulatory authority outside of the United States does not ensure approval by regulatory authorities in other countries or jurisdictions or by the FDA.

Additionally, on June 23, 2016, the electorate in the United Kingdom voted in favor of leaving the European Union, commonly referred to as Brexit. On March 29, 2017, the country formally notified the European Union of its intention to withdraw pursuant to Article 50 of the Lisbon Treaty. Since a significant proportion of the regulatory framework in the United Kingdom is derived from European Union directives and regulations, the referendum could materially impact the regulatory regime with respect to the approval of our product candidates in the United Kingdom or the European Union. Any delay in obtaining, or an inability to obtain, any marketing approvals, as a result of Brexit or otherwise, would prevent us from commercializing our product candidates in the United Kingdom and/or the European Union and restrict our ability to generate revenue and achieve and sustain profitability. If any of these outcomes occur, we may be forced to restrict or delay efforts to seek regulatory approval in the United Kingdom and/or European Union for our product candidates, which could significantly and materially harm our business.

***We may seek approval from the FDA or comparable non-U.S. regulatory authorities to use accelerated development pathways for our product candidates, including for selinexor in multiple myeloma and diffuse large B-cell lymphoma. If we are not able to use such pathways, we may be required to conduct additional clinical trials beyond those that we contemplate and that would increase the expense of obtaining, and delay the receipt of, necessary marketing approvals, if we receive them at all. In addition, even if we are able to use an accelerated approval pathway, it may not lead to expedited approval of our product candidates, or approval at all.***

Under the Federal Food, Drug and Cosmetic Act, or FDCA, and implementing regulations, the FDA may grant accelerated approval to a product candidate to treat a serious or life-threatening condition that provides meaningful therapeutic benefit over available therapies, upon a determination that the product has an effect on a surrogate endpoint or intermediate clinical endpoint that is reasonably likely to predict clinical benefit. The FDA considers a clinical benefit to be a positive therapeutic effect that is clinically meaningful in the context of a given disease, such as irreversible morbidity or mortality. For the purposes of accelerated approval, a surrogate endpoint is a marker, such as a laboratory measurement, radiographic image, physical sign, or other measure that is thought to predict clinical benefit, but is not itself a measure of clinical benefit. An intermediate clinical endpoint is a clinical endpoint that can be measured earlier than an effect on irreversible morbidity or mortality that is reasonably likely to predict an effect on irreversible morbidity or mortality or other clinical benefit measurement of a therapeutic effect that is considered reasonably likely to predict the clinical benefit of a drug. The accelerated approval pathway may be used in cases in

which the advantage of a new drug over available therapy may not be a direct therapeutic advantage, but is a clinically important improvement from a patient and public health perspective.

Prior to seeking such accelerated approval, we will continue to seek feedback from the FDA and otherwise evaluate our ability to seek and receive such accelerated approval. We intend to use the data from our expanded STORM study to support a request that the FDA consider granting accelerated approval for selinexor in penta-refractory multiple myeloma. The FDA has reiterated to us in its feedback that accelerated approval is available only for drugs that provide a meaningful therapeutic benefit over existing treatments at the time of consideration of the application for accelerated approval. Any experimental or approved therapies showing activity in patients with penta-refractory multiple myeloma that may exist at the time the FDA acts on any request we may make for accelerated approval could cause the FDA to deny our request. In addition, the FDA has indicated that additional therapies may receive full approval in multiple myeloma prior to the submission of an NDA by us, which could mean that, at the time the FDA takes action on our accelerated approval submission, treatment of



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the penta-refractory group is no longer considered an unmet medical need or a patient population that has exhausted available therapies. The FDA has recommended that we plan for regular approval based on a randomized trial for the evaluation of safety and efficacy of selinexor for the treatment of multiple myeloma, and has previously indicated to us its preference for studies that isolate the effects of individual drugs. Although we believe that the STORM study design and the expansion in the penta-refractory patient group present an opportunity for us to request that the FDA grant accelerated approval, there can be no assurance that the FDA will grant such approval, whether on an accelerated basis, or at all.

Similarly, assuming positive results from our SADAL study and remaining unmet medical need, we intend to use the data from the study to support a request that the FDA consider granting accelerated approval for selinexor in relapsed and/or refractory diffuse large B-cell lymphoma, or DLBCL. While the FDA agreed that the current trial design and indication appear appropriate for accelerated approval, they reiterated to us in their feedback that the availability of accelerated approval will depend on the trial results and available therapies at the time of regulatory action. Although we believe that our SADAL study presents an opportunity for us to request that the FDA grant accelerated approval for selinexor in relapsed and/or refractory DLBCL if data from our SADAL study support such an application, there can be no assurance that the FDA will grant such approval, whether on an accelerated basis, or at all.

There can also be no assurance that the FDA will agree with our surrogate endpoints or intermediate clinical endpoints, or that we will decide to pursue or submit an NDA for accelerated approval or any other form of expedited development, review or approval. Similarly, there can be no assurance that, after feedback from FDA, we will continue to pursue or apply for accelerated approval or any other form of expedited development, review or approval, even if we initially decide to do so. Furthermore, if we decide to submit an application for accelerated approval or under another expedited regulatory designation, there can be no assurance that such submission or application will be accepted or that any expedited development, review or approval will be granted on a timely basis, or at all.

Moreover, for drugs granted accelerated approval, the FDA typically requires post-marketing confirmatory trials to evaluate the anticipated effect on irreversible morbidity or mortality or other clinical benefit. These confirmatory trials must be completed with due diligence. The FDA may withdraw approval of a product candidate approved under the accelerated approval pathway if, for example, the trial required to verify the predicted clinical benefit of our product candidate fails to verify such benefit or does not demonstrate sufficient clinical benefit to justify the risks associated with the drug. The FDA may also withdraw approval if other evidence demonstrates that our product candidate is not shown to be safe or effective under the conditions of use, we fail to conduct any required post approval trial of our product candidate with due diligence or we disseminate false or misleading promotional materials relating to our product candidate. Similar risks to those described above are also applicable to any application that we may submit to the EMA to support conditional approval of selinexor to treat penta-refractory multiple myeloma, relapsed/refractory diffuse large B-cell lymphoma, or any other cancer indication. A failure to obtain accelerated approval or any other form of expedited development, review or approval for our product candidates, or withdrawal of a product candidate, would result in a longer time period for commercialization of such product candidate, could increase the cost of development of such product candidate and could harm our competitive position in the marketplace.

***A fast track designation, grant of priority review status or breakthrough therapy status by the FDA is not assured and, in any event, may not actually lead to a faster development or regulatory review or approval process and, moreover, would not assure FDA approval of our product candidates.***

We may be eligible for fast track designation, priority review or breakthrough therapy status for product candidates that we develop. If a product is intended for the treatment of a serious or life-threatening disease or condition and the product demonstrates the potential to address unmet medical needs for this disease or condition, the product sponsor may apply for FDA fast track designation. If a product offers major advances in treatment, the product sponsor may

apply for FDA priority review status. Additionally, a product candidate may be designated as a breakthrough therapy if it is intended, either alone or in combination with one or more other drugs, to treat a serious or life-threatening disease or condition and preliminary clinical evidence indicates that the product may demonstrate substantial improvement over existing therapies on one or more clinically significant endpoints. The FDA has broad discretion whether or not to grant these designations, so even if we believe a particular product candidate is eligible for such designation or status, the FDA could decide not to grant it. Moreover, even if we do receive such a designation, we may not experience a faster development process, review or approval compared to conventional FDA procedures and there is no assurance that our product candidate will be approved by the FDA.

In April 2018, the FDA granted fast track designation to selinexor for the treatment of patients with multiple myeloma who have received at least three prior lines of therapy that include regimens comprised of an alkylating agent, a glucocorticoid, Velcade® (bortezomib), Kyprolis® (carfilzomib), Revlimid® (lenalidomide), Pomalyst® (pomalidomide) and Darzalex® (daratumumab). In addition, a patient's disease must be refractory to at least one proteasome inhibitor (Velcade or Kyprolis), one immunomodulatory agent (Revlimid or Pomalyst), glucocorticoids and to Darzalex, as well as to the most recent therapy. However, even with this fast

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track designation, we may not experience a faster development process, review or approval compared to conventional FDA procedures and there is no assurance that selinexor will be approved by the FDA. The FDA may withdraw fast track designation if it believes that the designation is no longer supported by data from our clinical development program.

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

Regulatory authorities in some jurisdictions, including the United States and Europe, may designate drugs and biologics for relatively small patient populations as orphan drugs. Under the Orphan Drug Act, the FDA may designate a product as an orphan drug if it is a drug or biologic intended to treat a rare disease or condition, which is generally defined as a patient population of fewer than 200,000 individuals annually in the United States.

Generally, if a product with an orphan drug designation subsequently receives the first marketing approval for the indication for which it has such designation, the product is entitled to a period of marketing exclusivity, which precludes the EMA or the FDA from approving another marketing application for the same product for that time period. The applicable period is seven years in the United States and ten years in Europe. The European exclusivity period can be reduced to six years if a product no longer meets the criteria for orphan drug designation or if the product is sufficiently profitable so that market exclusivity is no longer justified. Orphan drug exclusivity may be lost if the FDA or EMA determines that the request for designation was materially defective or if the manufacturer is unable to assure sufficient quantity of the product to meet the needs of patients with the rare disease or condition.

Even if we obtain orphan drug exclusivity from the FDA for a product, as we have for selinexor in acute myeloid leukemia, DLBCL and multiple myeloma, that exclusivity may not effectively protect the product from competition because different products can be approved for the same condition. Even after an orphan drug is approved, the FDA can subsequently approve a different product for the same condition if the FDA concludes that the later product is clinically superior in that it is shown to be safer, more effective or makes a major contribution to patient care.

On August 3, 2017, Congress passed the FDA Reauthorization Act of 2017, or FDARA. FDARA, among other things, codified the FDA's pre-existing regulatory interpretation, to require that a drug sponsor demonstrate the clinical superiority of an orphan drug that is otherwise the same as a previously approved drug for the same rare disease in order to receive orphan drug exclusivity. The new legislation reverses prior precedent holding that the Orphan Drug Act unambiguously requires that the FDA recognize the orphan exclusivity period regardless of a showing of clinical superiority. The FDA may further reevaluate the Orphan Drug Act and its regulations and policies. We do not know if, when, or how the FDA may change the orphan drug regulations and policies in the future, and it is uncertain how any changes might affect our business. Depending on what changes the FDA may make to its orphan drug regulations and policies, our business could be adversely impacted.

### ***Even if we or any of our collaborators obtain marketing approvals for our drug candidates, the terms of approvals and ongoing regulation of our drugs may limit how we, or they, manufacture and market our drugs, which could materially impair our ability to generate revenue.***

Once marketing approval has been granted, an approved drug and its manufacturer and marketer are subject to ongoing review and extensive regulation. We and our collaborators must therefore comply with requirements concerning advertising and promotion for any of our drug candidates for which we or they obtain marketing approval. Promotional communications with respect to prescription drugs are subject to a variety of legal and regulatory restrictions and must be consistent with the information in the drug's approved labeling. Thus, we and our collaborators may not be able to promote any drugs we develop for indications or uses for which they are not approved.

In addition, manufacturers of approved drugs and those manufacturers' facilities are required to comply with extensive FDA requirements, including ensuring that quality control and manufacturing procedures conform to cGMPs, which include requirements relating to quality control and quality assurance as well as the corresponding maintenance of records and documentation and reporting requirements. We, our contract manufacturers, our collaborators and their contract manufacturers could be subject to periodic unannounced inspections by the FDA to monitor and ensure compliance with cGMPs.

Accordingly, assuming we or our current or future collaborators receive marketing approval for one or more of our drug candidates, we, and our collaborators, and our and their contract manufacturers will continue to expend time, money and effort in all areas of regulatory compliance, including manufacturing, production, product surveillance and quality control.

If we and our collaborators are not able to comply with post-approval regulatory requirements, we and our collaborators could have the marketing approvals for our drugs withdrawn by regulatory authorities, and our or our collaborators' ability to market any future drugs could be limited, which could adversely affect our ability to achieve or sustain profitability. Further, the cost of compliance with post-approval regulations may have a negative effect on our operating results and financial condition.

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***Any of our drug candidates for which we or our collaborators obtain marketing approval in the future could be subject to post-marketing restrictions or withdrawal from the market, and we and our collaborators may be subject to substantial penalties if we, or they, fail to comply with regulatory requirements or if we, or they, experience unanticipated problems with our drugs following approval.***

Any of our drug candidates for which we or our collaborators obtain marketing approval in the future, as well as the manufacturing processes, post-approval studies and measures, labeling, advertising and promotional activities for such drug, among other things, will be subject to continual requirements of and review by the FDA and other regulatory authorities. These requirements include submissions of safety and other post-marketing information and reports, registration and listing requirements, requirements relating to manufacturing, quality control, quality assurance and corresponding maintenance of records and documents, requirements regarding the distribution of samples to physicians and recordkeeping. Even if marketing approval of a drug candidate is granted, the approval may be subject to limitations on the indicated uses for which the drug may be marketed or to the conditions of approval, including the requirement to implement a Risk Evaluation and Mitigation Strategy, which could include requirements for a restricted distribution system.

The FDA may also impose requirements for costly post-marketing studies or clinical trials and surveillance to monitor the safety or efficacy of a drug. The FDA and other agencies, including the Department of Justice, or the DOJ, closely regulate and monitor the post-approval marketing and promotion of drugs to ensure that they are manufactured, marketed and distributed 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 or our collaborators do not market any of our drug candidates for which we, or they, receive marketing approval for only their approved indications, we, or they, may be subject to warnings or enforcement action for off-label marketing. Violation of the FDCA and other statutes, including the False Claims Act, relating to the promotion and advertising of prescription drugs may lead to investigations or allegations of violations of federal and state health care fraud and abuse laws and state consumer protection laws.

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

litigation involving patients taking our drug;

restrictions on such drugs, manufacturers or manufacturing processes;

restrictions on the labeling or marketing of a drug;

restrictions on drug distribution or use;

requirements to conduct post-marketing studies or clinical trials;

warning letters or untitled letters;

withdrawal of the drugs from the market;

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

recall of drugs;

finest, restitution or disgorgement of profits or revenues;

suspension or withdrawal of marketing approvals;

damage to relationships with any potential collaborators;

unfavorable press coverage and damage to our reputation;

refusal to permit the import or export of drugs;

drug seizure; or

injunctions or the imposition of civil or criminal penalties.

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***Under the Cures Act and the Trump Administration's regulatory reform initiatives, the FDA's policies, regulations and guidance may be revised or revoked and that could prevent, limit or delay regulatory approval of our product candidates, which would impact our ability to generate revenue.***

In December 2016, the 21st Century Cures Act, or Cures Act, was signed into law. The Cures Act, among other things, is intended to modernize the regulation of drugs and spur innovation, but its ultimate implementation is unclear. If we are slow or unable to adapt to changes in existing requirements or the adoption of new requirements or policies, or if we are not able to maintain regulatory compliance, we may lose any marketing approval that we may have obtained and we may not achieve or sustain profitability, which would adversely affect our business, prospects, financial condition and results of operations.

We also cannot predict the likelihood, nature or extent of government regulation that may arise from future legislation or administrative or executive action, either in the United States or abroad. For example, certain policies of the Trump Administration may impact our business and industry. Namely, the Trump Administration has taken several executive actions, including the issuance of a number of executive orders, that could impose significant burdens on, or otherwise materially delay, the FDA's ability to engage in routine regulatory and oversight activities such as implementing statutes through rulemaking, issuance of guidance, and review and approval of marketing applications. An under-resourced FDA could result in delays in the FDA's responsiveness or in its ability to review submissions or applications, issue regulations or guidance, or implement or enforce regulatory requirements in a timely fashion or at all. In January 2017, President Trump issued an executive order, applicable to all executive agencies including the FDA, which requires that for each notice of proposed rulemaking or final regulation to be issued in fiscal year 2017, the agency shall identify at least two existing regulations to be repealed, unless prohibited by law. These requirements are referred to as the "two-for-one" provisions. This executive order includes a budget neutrality provision that requires the total incremental cost of all new regulations in the 2017 fiscal year, including repealed regulations, to be no greater than zero, except in limited circumstances. For fiscal years 2018 and beyond, the executive order requires agencies to identify regulations to offset any incremental cost of a new regulation and approximate the total costs or savings associated with each new regulation or repealed regulation. In interim guidance issued by the Office of Information and Regulatory Affairs within OMB in February 2017, the administration indicates that the "two-for-one" provisions may apply not only to agency regulations, but also to significant agency guidance documents. In addition, on February 24, 2017, President Trump issued an executive order directing each affected agency to designate an agency official as a "Regulatory Reform Officer" and establish a "Regulatory Reform Task Force" to implement the two-for-one provisions and other previously issued executive orders relating to the review of federal regulations. It is difficult to predict how these various requirements will be implemented, and the extent to which they will impact the FDA's ability to exercise its regulatory authority. If these executive actions impose constraints on the FDA's ability to engage in oversight and implementation activities in the normal course, our business may be negatively impacted.

***Current and future legislation may increase the difficulty and cost for us and any collaborators to obtain marketing approval and commercialize our drug candidates and affect the prices we, or they, may obtain.***

In the United States and some foreign jurisdictions, there have been a number of legislative and regulatory changes and proposed changes regarding the healthcare system that could, among other things, prevent or delay marketing approval of our drug candidates, restrict or regulate post-approval activities and affect our ability, or the ability of any collaborators, to profitably sell any drugs for which we, or they, obtain marketing approval. We expect that current laws, 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, or any collaborators, may receive for any approved drugs.

Among the provisions of the Patient Protection and Affordable Care Act, or ACA, of potential importance to our business and our drug candidates are the following:

an annual, non-deductible fee on any entity that manufactures or imports specified branded prescription drugs and biologic agents;

an increase in the statutory minimum rebates a manufacturer must pay under the Medicaid Drug Rebate Program;

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

a new Medicare Part D coverage gap discount program, in which manufacturers must agree to offer 50% (and 70% starting January 1, 2019) point-of-sale discounts off negotiated prices to eligible beneficiaries during their coverage gap period, as a condition for a manufacturer's outpatient drugs to be covered under Medicare Part D;

extension of manufacturers' Medicaid rebate liability;

expansion of eligibility criteria for Medicaid programs;

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



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new requirements to report certain financial arrangements with physicians and teaching hospitals;

a new requirement to annually report drug samples that manufacturers and distributors provide to physicians; and

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

Other legislative changes have been proposed and adopted since the ACA was enacted. These changes include the Budget Control Act of 2011, which, among other things, led to aggregate reductions to Medicare payments to providers of up to 2% per fiscal year that started in April 2013 and, due to subsequent legislative amendments, will stay in effect through 2027 unless additional Congressional action is taken, and the American Taxpayer Relief Act of 2012, which, among other things, reduced Medicare payments to several types of providers and increased the statute of limitations period for the government to recover overpayments to providers from three to five years. These new laws may result in additional reductions in Medicare and other healthcare funding and otherwise affect the prices we may obtain for any of our product candidates for which we may obtain regulatory approval or the frequency with which any such product candidate is prescribed or used. Further, there have been several recent U.S. congressional inquiries and proposed state and federal legislation designed to, among other things, bring more transparency to drug pricing, review the relationship between pricing and manufacturer patient programs, reduce the costs of drugs under Medicare and reform government program reimbursement methodologies for drug products.

We expect that these healthcare reforms, as well as other healthcare reform measures that may be adopted in the future, may result in additional reductions in Medicare and other healthcare funding, more rigorous coverage criteria, new payment methodologies and additional downward pressure on the price that we receive for any approved product and/or the level of reimbursement physicians receive for administering any approved product we might bring to market. Reductions in reimbursement levels may negatively impact the prices we receive or the frequency with which our products are prescribed or administered. Any reduction in reimbursement from Medicare or other government programs may result in a similar reduction in payments from private payors.

Since enactment of the ACA, there have been numerous legal challenges and Congressional actions to repeal and replace provisions of the law. For example, with the December 2017 enactment of the Tax Cuts and Jobs Act of 2017, Congress repealed the individual mandate. The repeal of this provision, which requires most Americans to carry a minimal level of health insurance, will become effective in 2019. According to the Congressional Budget Office, the repeal of the individual mandate will cause 13 million fewer Americans to be insured in 2027 and premiums in insurance markets may rise. Additionally, on January 22, 2018, President Trump signed a continuing resolution on appropriations for fiscal year 2018 that delayed the implementation of certain ACA-mandated fees, including the so-called Cadillac tax on certain high cost employer-sponsored insurance plans, the annual fee imposed on certain health insurance providers based on market share, and the medical device excise tax on non-exempt medical devices. Further, the Bipartisan Budget Act of 2018, among other things, amends the ACA, effective January 1, 2019, to increase from 50 percent to 70 percent the point-of-sale discount that is owed by pharmaceutical manufacturers who participate in Medicare Part D and to close the coverage gap in most Medicare drug plans, commonly referred to as the donut hole. Further, each chamber of the Congress has put forth multiple bills designed to repeal or repeal and replace portions of the ACA. Although none of these measures has been enacted by Congress to date, Congress may consider other legislation to repeal and replace elements of the ACA. The Congress will likely consider other legislation to replace elements of the ACA during the next Congressional session.

The Trump Administration has also taken executive actions to undermine or delay implementation 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. In October 2017, the President signed a second executive order allowing for the use of association health plans and short-term health insurance, which may provide fewer health benefits than the plans sold through the ACA exchanges. At the same time, the Trump Administration announced that it will discontinue the payment of cost-sharing reduction, or CSR, payments to insurance companies until Congress approves the appropriation of funds for such CSR payments. The loss of the CSR payments is expected to increase premiums on certain policies issued by qualified health plans under the ACA. A bipartisan bill to appropriate funds for CSR payments was introduced in the Senate, but the future of that bill is uncertain.

We will continue to evaluate the effect that the ACA and its possible repeal and replacement could have on our business. It is possible that repeal and replacement initiatives, if enacted into law, could ultimately result in fewer individuals having health insurance coverage or in individuals having insurance coverage with less generous benefits. While the timing and scope of any potential future legislation to repeal and replace ACA provisions is uncertain in many respects, it is also possible that some of the ACA provisions that generally are not favorable for the research-based pharmaceutical industry could also be repealed along with ACA coverage expansion provisions. Accordingly, such reforms, if enacted, could have an adverse effect on anticipated revenue from product candidates that we may successfully develop and for which we may obtain marketing approval and may affect our overall financial condition and ability to develop commercialize product candidates.

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Further, there have been several recent U.S. congressional inquiries and proposed and enacted federal and state legislation designed to, among other things, bring more transparency to drug pricing, review the relationship between pricing and manufacturer patient programs, reduce the costs of drugs under Medicare and reform government program reimbursement methodologies for drug products. At the federal level, the Trump administration's budget proposal for fiscal year 2019 contains further drug price control measures that could be enacted during the 2019 budget process or in other future legislation, including, for example, measures to permit Medicare Part D plans to negotiate the price of certain drugs under Medicare Part B, to allow some states to negotiate drug prices under Medicaid, and to eliminate cost sharing for generic drugs for low-income patients. While any proposed measures will require authorization through additional legislation to become effective, Congress and the Trump administration have each indicated that it will continue to seek new legislative and/or administrative measures to control drug costs. At the state level, individual states are increasingly aggressive in passing legislation and implementing regulations designed to control pharmaceutical and biological product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain product access and marketing cost disclosure and transparency measures, and, in some cases, designed to encourage importation from other countries and bulk purchasing. In addition, regional health care authorities and individual hospitals are increasingly using bidding procedures to determine what pharmaceutical products and which suppliers will be included in their prescription drug and other health care programs. These measures could reduce the ultimate demand for our products, once approved, or put pressure on our product pricing.

Moreover, legislative and regulatory proposals have also been made to expand post-approval requirements and restrict sales and promotional activities for pharmaceutical drugs. We cannot be sure whether additional legislative changes will be enacted, or whether the FDA regulations, guidance or interpretations will be changed, or what the impact of such changes on the marketing approvals of our drug candidates, if any, may be. In addition, increased scrutiny by the Congress of the FDA's approval process may significantly delay or prevent marketing approval, as well as subject us and any collaborators to more stringent drug labeling and post-marketing testing and other requirements.

***Our relationships with healthcare providers and physicians and third-party payors will be subject to applicable anti-kickback, fraud and abuse and other healthcare laws and regulations, which could expose us to criminal sanctions, civil penalties, contractual damages, reputational harm and diminished profits and future earnings.***

Healthcare providers, physicians and third party payors will play a primary role in the recommendation and prescription of any drugs for which we obtain marketing approval. Our future arrangements with third party payors, healthcare providers and physicians may expose us to broadly applicable fraud and abuse and other healthcare laws and regulations that may constrain the business or financial arrangements and relationships through which we market, sell and distribute any drugs for which we obtain marketing approval. These include the following:

**Anti-Kickback Statute** the federal healthcare anti-kickback statute prohibits, among other things, persons from knowingly and willfully soliciting, offering, receiving or providing remuneration, directly or indirectly, in cash or in kind, to induce or reward, or in return for, either the referral of an individual for, or the purchase, order or recommendation or arranging of, any good or service, for which payment may be made under a federal healthcare program such as Medicare and Medicaid;

**False Claims Act** the federal False Claims Act imposes criminal and civil penalties, including through civil whistleblower or qui tam actions, against individuals or entities for, among other things, knowingly presenting, or causing to be presented false or fraudulent claims for payment by a federal healthcare program or making a false statement or record material to payment of a false claim or avoiding, decreasing or

concealing an obligation to pay money to the federal government, with potential liability including mandatory treble damages and significant per-claim penalties, currently set at \$5,500 to \$11,000 per false claim;

**HIPAA** the federal Health Insurance Portability and Accountability Act of 1996, or HIPAA, imposes criminal and civil liability for executing a scheme to defraud any healthcare benefit program or making false statements relating to healthcare matters, and, as amended by the Health Information Technology for Economic and Clinical Health Act and its implementing regulations, also imposes obligations, including mandatory contractual terms and technical safeguards, with respect to maintaining the privacy, security and transmission of individually identifiable health information;

**Transparency Requirements** federal laws require applicable manufacturers of covered drugs to report payments and other transfers of value to physicians and teaching hospitals; and

**Analogous State and Foreign Laws** analogous state and foreign fraud and abuse laws and regulations, such as state anti-kickback and false claims laws, can apply to sales or marketing arrangements and claims involving healthcare items or services and are generally broad and are enforced by many different federal and state agencies as well as through private actions.

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Some state laws require pharmaceutical companies to comply with the pharmaceutical industry's voluntary compliance guidelines and the relevant compliance guidance promulgated by the federal government and require drug manufacturers to report information related to payments and other transfers of value to physicians and other healthcare providers or marketing expenditures. State and foreign laws also govern the privacy and security of health information in some circumstances, many of which differ from each other in significant ways and often are not pre-empted by HIPAA, thus complicating compliance efforts.

Efforts to ensure that our business arrangements with third parties will comply with applicable healthcare laws and regulations will involve substantial costs. It is possible that governmental authorities will conclude that our business practices may not comply with current or future statutes, regulations or case law involving applicable fraud and abuse or other healthcare laws and regulations. If our operations are found to be in violation of any of these laws or any other governmental regulations that may apply to us, we may be subject to significant civil, criminal and administrative penalties, damages, fines, imprisonment, exclusion of drugs from government funded healthcare programs, such as Medicare and Medicaid, and the curtailment or restructuring of our operations. If any of the physicians or other healthcare providers or entities with whom we expect to do business is found to be not in compliance with applicable laws, they may be subject to criminal, civil or administrative sanctions, including exclusions from government funded healthcare programs.

The provision of benefits or advantages to physicians to induce or encourage the prescription, recommendation, endorsement, purchase, supply, order or use of medicinal products is also prohibited in the European Union. The provision of benefits or advantages to physicians is governed by the national anti-bribery laws of European Union Member States, such as the UK Bribery Act 2010. Infringement of these laws could result in substantial fines and imprisonment.

Payments made to physicians in certain European Union Member States must be publicly disclosed. Moreover, agreements with physicians often must be the subject of prior notification and approval by the physician's employer, his or her competent professional organization and/or the regulatory authorities of the individual European Union Member States. These requirements are provided in the national laws, industry codes or professional codes of conduct, applicable in the European Union Member States. Failure to comply with these requirements could result in reputational risk, public reprimands, administrative penalties, fines or imprisonment.

The collection and use of personal health data of individuals in the European Union is governed by strict data protection laws. The Data Protection Directive imposes several requirements relating to the consent of the individuals to whom the personal data relates, the information provided to the individuals, notification of data processing obligations to the competent national data protection authorities and the security and confidentiality of the personal data. The Data Protection Directive also imposes strict rules on the transfer of personal data out of the European Union to the United States. Failure to comply with the requirements of the Data Protection Directive and the related national data protection laws of the European Union Member States may result in fines and other administrative penalties. In addition to existing laws, from May 25, 2018, the stricter General Data Protection Regulation will replace the current Data Protection Directive. The regulation introduces new obligations with respect to European Union data and substantial fines for breaches of the data protection rules. It will increase our responsibility and potential liability in relation to personal data that we process and we will be required to put in place additional mechanisms ensuring compliance with the new European Union data protection rules. This may be onerous and adversely affect our business, financial condition, results of operations and prospects.

***Our employees may engage in misconduct or other improper activities, including non-compliance with regulatory standards and requirements, which could cause significant liability for us and harm our reputation.***

We are exposed to the risk of employee fraud or other misconduct, including intentional failures to comply with FDA regulations or similar regulations of comparable foreign regulatory authorities, provide accurate information to the FDA or comparable foreign regulatory authorities, comply with manufacturing standards we have established, comply with federal and state healthcare fraud and abuse laws and regulations and similar laws and regulations established and enforced by comparable foreign regulatory authorities, report financial information or data accurately or disclose unauthorized activities to us. Employee misconduct could also involve the improper use of information obtained in the course of clinical trials, which could result in regulatory sanctions and serious harm to our reputation. It is not always possible to identify and deter employee misconduct, and the precautions we take to detect and prevent this activity may not be effective in controlling unknown or unmanaged risks or losses or in protecting us from governmental investigations or other actions or lawsuits stemming from a failure to be in compliance with such laws, standards or regulations. If any such actions are instituted against us, and we are not successful in defending ourselves or asserting our rights, those actions could have a significant impact on our business and results of operations, including the imposition of significant fines or other sanctions.

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***If we fail to comply with environmental, health and safety laws and regulations, we could become subject to fines or penalties or incur costs that could have a material adverse effect on our business.***

We are subject to numerous environmental, health and safety laws and regulations, including those governing laboratory procedures and the handling, use, storage, treatment and disposal of hazardous materials and wastes. Our operations involve the use of hazardous and flammable materials, including chemicals and biological and radioactive materials. Our operations also produce hazardous waste products. We generally contract with third parties for the disposal of these materials and wastes. We cannot eliminate the risk of contamination or injury from these materials. In the event of contamination or injury resulting from our use of hazardous materials, we could be held liable for any resulting damages, and any liability could exceed our resources. We also could incur significant costs associated with civil or criminal fines and penalties.

Although we maintain workers' compensation insurance to cover us for costs and expenses we may incur due to injuries to our employees resulting from the use of hazardous materials, this insurance may not provide adequate coverage against potential liabilities. We do not maintain insurance for environmental liability or toxic tort claims that may be asserted against us in connection with our storage or disposal of biological, hazardous or radioactive materials.

In addition, we may incur substantial costs in order to comply with current or future environmental, health and safety laws and regulations. These current or future laws and regulations may impair our research, development or commercialization efforts. Failure to comply with these laws and regulations also may result in substantial fines, penalties or other sanctions.

***Laws and regulations governing any international operations we may have in the future may preclude us from developing, manufacturing and selling certain drug candidates outside of the United States and require us to develop and implement costly compliance programs.***

We are subject to numerous laws and regulations in each jurisdiction outside the United States in which we operate. The creation, implementation and maintenance of international business practices compliance programs is costly and such programs are difficult to enforce, particularly where reliance on third parties is required.

The FCPA prohibits any U.S. individual or business from paying, offering, authorizing payment or offering of anything of value, directly or indirectly, to any foreign official, political party or candidate for the purpose of influencing any act or decision of the foreign entity in order to assist the individual or business in obtaining or retaining business. The FCPA also obligates companies whose securities are listed in the United States to comply with certain accounting provisions requiring the company to maintain books and records that accurately and fairly reflect all transactions of the corporation, including international subsidiaries, and to devise and maintain an adequate system of internal accounting controls for international operations. The anti-bribery provisions of the FCPA are enforced primarily by the DOJ. The Securities and Exchange Commission, or SEC, is involved with enforcement of the books and records provisions of the FCPA.

Compliance with the FCPA is expensive and difficult, particularly in countries in which corruption is a recognized problem. In addition, the FCPA presents particular challenges in the pharmaceutical industry, because, in many countries, hospitals are operated by the government, and doctors and other hospital employees are considered foreign officials. Certain payments to hospitals in connection with clinical trials and other work have been deemed to be improper payments to government officials and have led to FCPA enforcement actions.

Various laws, regulations and executive orders also restrict the use and dissemination outside of the United States, or the sharing with certain non-U.S. nationals, of information classified for national security purposes, as well as certain

products and technical data relating to those products. Our expansion outside of the United States, has required, and will continue to require, us to dedicate additional resources to comply with these laws, and these laws may preclude us from developing, manufacturing, or selling certain drugs and drug candidates outside of the United States, which could limit our growth potential and increase our development costs. The failure to comply with laws governing international business practices may result in substantial penalties, including suspension or debarment from government contracting. Violation of the FCPA can result in significant civil and criminal penalties. Indictment alone under the FCPA can lead to suspension of the right to do business with the U.S. government until the pending claims are resolved. Conviction of a violation of the FCPA can result in long-term disqualification as a government contractor. The termination of a government contract or relationship as a result of our failure to satisfy any of our obligations under laws governing international business practices would have a negative impact on our operations and harm our reputation and ability to procure government contracts. The SEC also may suspend or bar issuers from trading securities on U.S. exchanges for violations of the FCPA's accounting provisions.



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***Governments outside of the United States tend to impose strict price controls, which may adversely affect our revenues from the sales of drugs, if any.***

In some countries, including the countries of the European Union, the pricing of prescription pharmaceuticals is subject to governmental control. In these countries, pricing negotiations with governmental authorities can take considerable time after the receipt of marketing approval for a drug. To obtain reimbursement or pricing approval in some countries, we or our existing and future collaborators may be required to conduct a clinical trial that compares the cost-effectiveness of our drug to other available therapies. If reimbursement of our drugs is unavailable or limited in scope or amount, or if pricing is set at unsatisfactory levels, our business could be materially harmed.

## **Risks Related to Employee Matters and Managing Growth**

***Our future success depends on our ability to retain our Chief Executive Officer, our President and Chief Scientific Officer and other key executives and to attract, retain and motivate qualified personnel.***

We are highly dependent on Michael Kauffman, M.D., Ph.D., our Chief Executive Officer, and Sharon Shacham, Ph.D., M.B.A., our President and Chief Scientific Officer, as well as the other principal members of our management and scientific teams. Although we have entered into formal employment agreements with Drs. Kauffman and Shacham, these agreements do not prevent them from terminating their employment with us at any time. We do not maintain key person insurance for any of our executives or other employees. The loss of the services of any of our key employees could impede the achievement of our research, development, commercialization and other business objectives.

Recruiting and retaining qualified scientific, clinical, manufacturing and sales and marketing personnel will also be critical to our success. We may not be able to attract and retain these personnel on acceptable terms given the competition among numerous pharmaceutical and biotechnology companies for similar personnel. We also experience competition for the hiring of scientific and clinical personnel from universities and research institutions. In addition, we rely on consultants and advisors, including scientific and clinical advisors, to assist us in formulating our research and development and commercialization strategy. Our consultants and advisors may be employed by employers other than us and may have commitments under consulting or advisory contracts with other entities that may limit their availability to us.

***Drs. Kauffman and Shacham are married to each other. The separation or divorce of the couple in the future could adversely affect our business.***

Dr. Kauffman, our Chief Executive Officer and member of our board of directors, and Dr. Shacham, our President and Chief Scientific Officer, are married to each other. They are two of our executive officers and are a vital part of our operations. If they were to become separated or divorced or could otherwise not amicably work with each other, one or both of them may decide to cease his or her employment with us or it could negatively impact our working environment. Alternatively, their work performance may not be satisfactory if they become preoccupied with issues relating to their personal situation. In these cases, our business could be materially harmed.

***We expect to expand our development, regulatory and future sales and marketing capabilities, and as a result, we may encounter difficulties in managing our growth, which could disrupt our operations.***

We expect to experience significant growth in the number of our employees and the scope of our operations, particularly in the areas of drug development, regulatory affairs and sales and marketing. To manage our anticipated future growth, we must continue to implement and improve our managerial, operational and financial systems, expand

our facilities and continue to recruit and train additional qualified personnel. Due to our limited financial resources and the limited experience of our management team in managing a company with such anticipated growth, we may not be able to effectively manage the expansion of our operations or recruit and train additional qualified personnel. The physical expansion of our operations may lead to significant costs and may divert our management and business development resources. Any inability to manage growth could delay the execution of our business plans or disrupt our operations.

***Our business and operations may be materially adversely affected in the event of computer system failures or security breaches, and the costs and consequences of implementing data protection measures could be significant.***

Despite the implementation of security measures, our internal computer systems, and those of our contract research organizations and other third parties on which we rely, are vulnerable to damage from computer viruses, unauthorized access, cyber attacks, natural disasters, fire, terrorism, war and telecommunication and electrical

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failures. If such an event were to occur and cause interruptions in our operations, it could result in a material disruption of our drug development programs. For example, the loss of clinical trial data from ongoing or planned clinical trials could result in delays in our regulatory approval efforts and significantly increase our costs to recover or reproduce the data. To the extent that any disruption or security breach results in a loss of or damage to our data or applications, or inappropriate disclosure of confidential or proprietary information, we could incur liability, our reputation could be damaged, and the further development of our drug candidates could be delayed. We may also be vulnerable to cyber attacks by hackers, or other malfeasance. This type of breach of our cybersecurity may compromise our confidential information and/or our financial information and adversely affect our business or result in legal proceedings. In addition, the cost and operational consequences of implementing further data protection measures could be significant. Moreover, because the techniques used to obtain unauthorized access, disable or degrade service or sabotage systems change frequently and often are not recognized until launched against a target, we may be unable to anticipate these techniques or to implement adequate security measures.

### **Risks Related to Our Common Stock**

*Our executive officers, directors and principal stockholders maintain the ability to control all matters submitted to stockholders for approval.*

As of March 31, 2018, our executive officers, directors and a small number of stockholders own more than a majority of our outstanding common stock. As a result, if these stockholders were to choose to act together, they would be able to control all matters submitted to our stockholders for approval, as well as our management and affairs. For example, these persons, if they choose to act together, would control the election of directors and approval of any merger, consolidation or sale of all or substantially all of our assets. This concentration of voting power could delay or prevent an acquisition of our company on terms that other stockholders may desire.

*Provisions in our corporate charter documents and under Delaware law could make an acquisition of us, which may be beneficial to our stockholders, more difficult and may prevent attempts by our stockholders to replace or remove our current management.*

Provisions in our corporate charter and our bylaws may discourage, delay or prevent a merger, acquisition or other change in control of us that stockholders may consider favorable, including transactions in which stockholders might otherwise receive a premium for their shares. These provisions could also limit the price that investors might be willing to pay in the future for shares of our common stock, thereby depressing the market price of our common stock. In addition, because our board of directors is responsible for appointing the members of our management team, these provisions may frustrate or prevent any attempts by our stockholders to replace or remove our current management by making it more difficult for stockholders to replace members of our board of directors. Among other things, these provisions:

establish a classified board of directors such that not all members of the board are elected at one time;

allow the authorized number of our directors to be changed only by resolution of our board of directors;

limit the manner in which stockholders can remove directors from the board;

establish advance notice requirements for stockholder proposals that can be acted on at stockholder meetings and nominations to our board of directors;

require that stockholder actions must be effected at a duly called stockholder meeting and prohibit actions by our stockholders by written consent;

limit who may call stockholder meetings;

authorize our board of directors to issue preferred stock without stockholder approval, which could be used to institute a poison pill that would work to dilute the stock ownership of a potential hostile acquirer, effectively preventing acquisitions that have not been approved by our board of directors; and

require the approval of the holders of at least 75% of the votes that all our stockholders would be entitled to cast to amend or repeal certain provisions of our charter or bylaws.

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Moreover, because we are incorporated in Delaware, we are governed by the provisions of Section 203 of the Delaware General Corporation Law, which prohibits a person who owns in excess of 15% of our outstanding voting stock from merging or combining with us for a period of three years after the date of the transaction in which the person acquired in excess of 15% of our outstanding voting stock, unless the merger or combination is approved in a prescribed manner.

***An active trading market for our common stock may not be sustained.***

Although our common stock is listed on The Nasdaq Global Select Market, an active trading market for our shares may not be sustained. If an active market for our common stock does not continue, it may be difficult for you to sell shares of our common stock without depressing the market price for the shares, or at all. An inactive trading market for our common stock may also impair our ability to raise capital to continue to fund our operations by selling shares and may impair our ability to acquire other companies or technologies by using our shares as consideration.

***If securities analysts do not continue to publish research or reports about our business or if they publish negative evaluations of our stock, the price of our stock could decline.***

The trading market for our common stock relies in part on the research and reports that industry or financial analysts publish about us or our business. There can be no assurance that analysts will provide favorable coverage or continue to cover us. If one or more of the analysts covering our business downgrade their evaluations of our stock, the price of our stock could decline. If one or more of these analysts cease to cover our stock, we could lose visibility in the market for our stock, which in turn could cause our stock price to decline.

***The price of our common stock has been and may be volatile in the future and fluctuate substantially.***

Our stock price has been and is likely to be volatile and may fluctuate substantially. For example, since January 1, 2015, our common stock has traded at prices per share as high as \$38.47 and as low as \$4.83. On May 4, 2018, the closing sale price of our common stock on The Nasdaq Global Select Market was \$16.48 per share. The stock market in general and the market for pharmaceutical and biotechnology companies in particular have experienced extreme volatility that has often been unrelated to the operating performance of particular companies. The market price for our common stock may be influenced by many factors, including:

the success of competitive drugs or technologies;

results of clinical trials of our drug candidates or those of our competitors;

regulatory or legal developments in the United States and other countries;

developments or disputes concerning patent applications, issued patents or other proprietary rights;

the recruitment or departure of key personnel;

the level of expenses related to any of our drug candidates or clinical development programs;

the results of our efforts to discover, develop, acquire or in-license additional drug candidates or drugs;

actual or anticipated changes in estimates as to financial results, development timelines or recommendations by securities analysts;

variations in our financial results or those of companies that are perceived to be similar to us;

changes in the structure of healthcare payment systems;

market conditions in the pharmaceutical and biotechnology sectors;

general economic, industry and market conditions; and

the other factors described in this Risk Factors section.

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### ***We could be subject to securities class action litigation.***

In the past, securities class action litigation has often been brought against a company following a decline in the market price of its securities. This risk is especially relevant for us because pharmaceutical companies have experienced significant stock price volatility in recent years. If we face such litigation, it could result in substantial costs and a diversion of management's attention and our resources, which could harm our business.

### ***We have broad discretion in the use of our cash and cash equivalents and may not use them effectively.***

Our management has broad discretion to use our cash and cash equivalents to fund our operations and could spend these funds in ways that do not improve our results of operations or enhance the value of our common stock. The failure by our management to apply these funds effectively could result in financial losses that could have a material adverse effect on our business, cause the price of our common stock to decline and delay the development of our drug candidates. Pending their use to fund our operations, we may invest our cash and cash equivalents in a manner that does not produce income or that loses value.

### ***We are an emerging growth company, and the reduced disclosure requirements applicable to emerging growth companies may make our common stock less attractive to investors.***

We are an emerging growth company, as defined in the Jumpstart Our Business Startups Act of 2012, or the JOBS Act, and may remain an emerging growth company through 2018. For so long as we remain an emerging growth company, we are permitted and intend to rely on exemptions from certain disclosure requirements that are applicable to other public companies that are not emerging growth companies. These exemptions include not being required to comply with the auditor attestation requirements of Section 404 of the Sarbanes-Oxley Act of 2002, or Section 404, not being required to comply with any requirement that may be adopted by the Public Company Accounting Oversight Board regarding mandatory audit firm rotation or a supplement to the auditor's report providing additional information about the audit and the financial statements, reduced disclosure obligations regarding executive compensation and exemptions from the requirements of holding a nonbinding advisory vote on executive compensation and shareholder approval of any golden parachute payments not previously approved. We cannot predict whether investors will find our common stock less attractive if we rely on these exemptions. If some investors find our common stock less attractive as a result, there may be a less active trading market for our common stock and our stock price may be more volatile.

In addition, the JOBS Act provides that an emerging growth company can take advantage of an extended transition period for complying with new or revised accounting standards. This allows an emerging growth company to delay the adoption of certain accounting standards until those standards would otherwise apply to private companies. We have irrevocably elected not to avail ourselves of this exemption from new or revised accounting standards and, therefore, we will be subject to the same new or revised accounting standards as other public companies that are not emerging growth companies.

### ***We will continue to incur increased costs as a result of operating as a public company, and our management will need to continue to devote substantial time to compliance initiatives and corporate governance practices.***

As a public company, and particularly after we are no longer an emerging growth company, we will incur significant legal, accounting and other expenses. In addition, the Sarbanes-Oxley Act of 2002 and rules subsequently implemented by the SEC and Nasdaq have imposed various requirements on public companies, including establishment and maintenance of effective disclosure and financial controls and corporate governance practices. Our management and other personnel will need to continue to devote a substantial amount of time to these compliance

initiatives. Moreover, these rules and regulations will increase our legal and financial compliance costs and will make some activities more time-consuming and costly.

We cannot predict with certainty the amount of additional costs we may incur to continue to operate as a public company, nor can we predict the timing of such costs. In addition, the rules and regulations applicable to public companies are often subject to varying interpretations, in many cases due to their lack of specificity, and, as a result, their application in practice may evolve over time as new guidance is provided by regulatory and governing bodies which could result in continuing uncertainty regarding compliance matters and higher costs necessitated by ongoing revisions to disclosure and governance practices.

Pursuant to Section 404, we are required to furnish a report by our management on our internal control over financial reporting. However, while we remain an emerging growth company, we are not required to include an attestation report on internal control over financial reporting issued by our independent registered public accounting firm. To achieve compliance with Section 404 within the prescribed period, we are engaged in a process to document and evaluate our internal control over financial reporting, which is both costly and challenging. In this regard, we will need to continue to dedicate internal resources, potentially engage outside consultants and adopt a detailed work plan to assess and document the adequacy of internal control over financial reporting, continue steps to improve control processes as appropriate, validate through testing that controls are functioning as documented and implement a



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continuous reporting and improvement process for internal control over financial reporting. There is a risk that neither we nor our independent registered public accounting firm will be able to conclude within the prescribed timeframe that our internal control over financial reporting is effective as required by Section 404. This could result in an adverse reaction in the financial markets due to a loss of confidence in the reliability of our financial statements. In addition, if we identify one or more material weaknesses, it could result in an adverse reaction in the financial markets due to a loss of confidence in the reliability of our financial statements.

***Because we do not anticipate paying any cash dividends on our capital stock in the foreseeable future, capital appreciation, if any, of our common stock will be the sole source of gain for our stockholders.***

We have never declared or paid cash dividends on our capital stock. We currently intend to retain all of our future earnings, if any, to finance the growth and development of our business. In addition, the terms of any future debt agreements may preclude us from paying dividends. As a result, capital appreciation, if any, of our common stock will be the sole source of gain for our stockholders for the foreseeable future.

***A significant portion of our total outstanding shares are restricted from immediate resale but may be sold into the market in the near future, which could cause the market price of our common stock to drop significantly, even if our business is doing well.***

Sales of a substantial number of shares of our common stock in the public market could occur at any time. These sales, or the perception in the market that the holders of a large number of shares intend to sell shares, could reduce the market price of our common stock. We had 49,670,328 shares outstanding as of March 31, 2018. Of such shares, at least 10.3 million shares are eligible for sale in the public market under Rule 144 of the Securities Act of 1933, as amended, or the Securities Act, subject to the volume limitations and other conditions of Rule 144. The holders of these shares may at any time decide to sell their shares in the public market.

Moreover, holders of an aggregate of at least 10.5 million shares of our common stock as of March 31, 2018 have rights, subject to some conditions, to require us to file registration statements covering their shares or to include their shares in registration statements that we may file for ourselves or other stockholders. We have also registered all shares of common stock that we may issue under our equity compensation plans. As a result, these shares can be freely sold in the public market upon issuance, subject to volume limitations applicable to affiliates, to the extent applicable.

***Our ability to use our net operating loss carryforwards and tax credit carryforwards to offset future taxable income may be subject to certain limitations.***

Under the provisions of the Internal Revenue Code of 1986, as amended, or the Code, our net operating loss and tax credit carryforwards are subject to review and possible adjustment by the Internal Revenue Service (and state tax authorities under relevant state tax rules). In addition, as a result of the Tax Cuts and Jobs Act of 2017, for U.S. federal income tax purposes, the use of net operating loss carryforwards arising in taxable years beginning after December 31, 2017 is limited to 80% of our taxable income in any future taxable year, although such losses may be carried forward indefinitely. It is uncertain how various states will respond to the newly enacted federal tax law. Furthermore, the use of net operating loss and tax credit carryforwards may become subject to an annual limitation under Sections 382 and 383 of the Code, respectively, and similar state provisions in the event of certain cumulative changes in the ownership interest of significant shareholders in excess of 50 percent over a three-year period. This could limit the amount of tax attributes that can be utilized annually to offset future taxable income or tax liabilities. The amount of the annual limitation is determined based on the value of a company immediately prior to the ownership change. Subsequent ownership changes may further affect the limitation in future years. Our company has

completed several financings since its inception which resulted in an ownership change under Sections 382 and 383 of the Code. In addition, future changes in our stock ownership, some of which are outside of our control, could result in ownership changes in the future. For these reasons, we may not be able to use some or all of our net operating loss and tax credit carryforwards, even if we attain profitability.

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

The Tax Cuts and Jobs Act of 2017 enacted in December 2017, or the Tax Act, significantly revises the Internal Revenue Code of 1986, as amended. The newly enacted federal income tax law, among other things, contains significant changes to corporate taxation, including reduction of the corporate tax rate from a top marginal rate of 34% to a flat rate of 21%, limitation of the tax deduction for net interest expense to 30% of adjusted earnings (except for certain small businesses), limitation of the deduction for net operating losses to 80% of current year taxable income and elimination of net operating loss carrybacks, in each case, for losses arising in taxable years beginning after December 31, 2017 (though any such net operating losses may be carried forward indefinitely), one time taxation of offshore earnings at reduced rates regardless of whether they are repatriated, elimination of U.S. tax on foreign earnings (subject to certain important exceptions), immediate deductions for certain new investments instead of deductions

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for depreciation expense over time, and modifying or repealing many business deductions and credits. Notwithstanding the reduction in the corporate income tax rate, the overall impact of the new federal tax law is uncertain and our business and financial condition could be adversely affected. In addition, it is uncertain how various states will respond to the newly enacted federal tax law.

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Exhibit Number	Description of Exhibit	Incorporated by Reference			Provided Herewith
		Form	File Number	Date of Filing Exhibit Number	
10.1	<u>Asset Purchase Agreement, dated January 24, 2018, by and between Biogen MA Inc. and the Registrant.</u>				X
10.2	<u>Third Amendment to Lease, dated February 28, 2018, by and between the Registrant and AG-JCM Wells Avenue Property Owner, LLC.</u>				X
10.3	<u>Form of Nonstatutory Stock Option Agreement for Inducement Grants.</u>				X
31.1	<u>Certification of principal executive officer pursuant to Rule 13a-14(a)/15d-14(a) of the Securities Exchange Act of 1934, as amended.</u>				X
31.2	<u>Certification of principal financial officer pursuant to Rule 13a-14(a)/15d-14(a) of the Securities Exchange Act of 1934, as amended.</u>				X
32.1	<u>Certification of principal executive officer pursuant to 18 U.S.C. §1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002.</u>				X
32.2	<u>Certification of principal financial officer pursuant to 18 U.S.C. §1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002.</u>				X
101.INS	Instance Document				X
101.SCH	Scheme Document				X
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101.CAL	Calculation Linkbase Document	X
101.DEF	Definition Linkbase Document	X
101.LAB	Labels Linkbase Document	X
101.PRE	Presentation Linkbase Document	X

Confidential treatment has been requested for certain portions which are omitted in the copy of the exhibit electronically filed with the Commission. The omitted information has been filed separately with the Commission pursuant to the Company's application for confidential treatment.  
Indicates a compensatory arrangement.

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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.

**KARYOPHARM THERAPEUTICS INC.**

Date: May 10, 2018

By: /s/ MICHAEL KAUFFMAN  
Michael Kauffman, M.D., Ph.D.  
*Chief Executive Officer*  
*(Principal executive officer)*

Date: May 10, 2018

By: /s/ MICHAEL F. FALVEY  
Michael F. Falvey  
*Executive Vice President,*  
*Chief Financial Officer and Treasurer*  
*(Principal financial and accounting officer)*