

Karyopharm Therapeutics Inc.  
Form 10-Q  
December 20, 2013

**UNITED STATES**  
**SECURITIES AND EXCHANGE COMMISSION**

Washington, D.C. 20549

**FORM 10-Q**

(Mark One)

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

For the quarterly period ended September 30, 2013

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)

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

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

**2 Mercer Road**  
**Natick, MA**  
(Address of principal executive offices)

**01760**  
(Zip Code)

**(508) 975-4820**

(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, or a smaller reporting company. See the definitions of large accelerated filer, accelerated filer and smaller reporting 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

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 December 16, 2013, there were 29,749,593 shares of Common Stock, \$0.0001 par value per share, outstanding.

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## PART I FINANCIAL INFORMATION

## Item 1. Condensed Consolidated Financial Statements (Unaudited).

## Karyopharm Therapeutics Inc.

(A Development Stage Company)

## CONDENSED CONSOLIDATED BALANCE SHEETS

(unaudited)

(in thousands, except share and per share data)

	September 30, 2013	December 31, 2012
<b>Assets</b>		
Current assets:		
Cash and cash equivalents (NPM restricted December 31, 2012 \$12)	\$ 52,928	\$ 391
Prepaid expenses and other current assets (NPM restricted December 31, 2012 \$485)	658	563
Total current assets	53,586	954
Property and equipment, net	246	327
Other assets	2,072	30
Total assets	\$ 55,904	\$ 1,311
<b>Liabilities, convertible preferred stock and stockholders (deficit)</b>		
Current liabilities:		
Accounts payable (NPM restricted December 31, 2012 \$499)	\$ 1,749	\$ 1,076
Accrued liabilities (NPM restricted December 31, 2012 \$312)	1,920	764
Deferred revenue		66
Other liabilities	327	24
Total current liabilities	3,996	1,930
Commitments and contingencies		
Preferred stock subscription		8,980
Series A convertible preferred stock, \$0.0001 par value; Authorized-20,937,500; Issued and Outstanding - 20,937,500 shares at September 30, 2013 and 18,437,500 at December 31, 2012 (aggregate liquidation preference of \$20.9 million)	20,778	18,278
Series A-2 convertible preferred stock, \$0.0001 par value; Authorized, Issued and Outstanding-6,100,000 shares at September 30, 2013 and no shares at December 31, 2012 (aggregate liquidation preference of \$7.0 million)	6,980	
	3,000	

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Series A-3 convertible preferred stock, \$0.0001 par value Authorized, Issued and Outstanding-1,764,706 shares at September 30, 2013 and no shares at December 31, 2012 (aggregate liquidation preference of \$3.0 million)		
Series A-4 convertible preferred stock, \$0.0001 par value Authorized, Issued and Outstanding-1,538,461 shares at September 30, 2013 and no shares at December 31, 2012 (aggregate liquidation preference of \$2.0 million)	2,000	
Series B convertible preferred stock, \$0.0001 par value Authorized, issued and outstanding-24,100,000 shares at September 30, 2013 and no shares at December 31, 2012 (aggregate liquidation preference of \$48.2 million)	48,057	
Series B-1 convertible preferred stock, \$0.0001 par value Authorized 8,636,400, issued and outstanding 8,636,362 shares at September 30, 2013 and no shares at December 31, 2012 (aggregate liquidation preference of \$19.0 million)	18,877	
Special participation stock, \$0.0001 par value; Authorized, issued and outstanding-no shares at September 30, 2013 and 10,000 shares at December 31, 2012	99,692	27,258
Stockholders deficit		
Common stock, \$0.0001 par value; Authorized 83,500,000 shares at September 30, 2013 and 35,000,000 shares at December 31, 2012; Issued and Outstanding 2,591,333 shares at September 30, 2013 and 2,123,388 shares at December 31, 2012		
Additional paid-in capital	2,639	745
Deficit accumulated during the development stage	(50,423)	(28,622)
Total stockholders deficit	(47,784)	(27,877)
Total liabilities, convertible preferred stock and stockholders deficit	\$ 55,904	\$ 1,311

See accompanying notes to condensed consolidated financial statements.

**Karyopharm Therapeutics Inc.****(A Development Stage Company)****CONDENSED CONSOLIDATED STATEMENTS OF OPERATIONS****(unaudited)****(in thousands, except share and per share data)**

	Three months ended, September 30,		Nine Months ended September 30,		Period from December 22, 2008 (inception) to September 30, 2013
	2013	2012	2013	2012	
Contract and grant revenue	\$	\$ 34	\$ 366	\$ 601	\$ 1,245
Operating expenses:					
Research and development	7,738	2,997	18,763	10,429	43,146
General and administrative	1,583	672	3,405	1,824	8,337
Total operating expenses	9,321	3,669	22,168	12,253	51,483
Loss from operations	(9,321)	(3,635)	(21,802)	(11,652)	(50,238)
Other income (expense):					
Interest income			1	2	3
Interest expense					(188)
Net loss	\$ (9,321)	\$ (3,635)	\$ (21,801)	\$ (11,650)	\$ (50,423)
Net loss per share applicable to common stockholders basic and diluted	2,544,587	1,846,859	2,392,589	1,672,662	986,601
Weighted-average number of common shares used in net loss per share applicable to common stockholders basic and diluted	\$ (3.66)	\$ (1.97)	\$ (9.11)	\$ (6.96)	\$ (51.11)

See accompanying notes to condensed consolidated financial statements.

**Karyopharm Therapeutics Inc.****(A Development Stage Company)****CONDENSED CONSOLIDATED STATEMENTS OF CASH FLOWS****(unaudited)****(in thousands)**

	2013	Nine months ended September 30, 2012	Period from December 22, 2008 (Inception) to September 30, 2013
<b>Operating activities</b>			
Net loss	\$ (21,801)	\$ (11,650)	\$ (50,423)
Adjustments to reconcile net loss to net cash used in operating activities:			
Depreciation and amortization	106	92	312
Noncash consulting expense	88		788
Noncash interest expense on convertible notes			188
Stock-based compensation expense	1,769	329	2,492
Changes in operating assets and liabilities:			
Prepaid expenses and other current assets	(95)	124	(658)
Other assets	(2,042)		(2,072)
Accounts payable	673	(85)	1,749
Accrued expenses and other liabilities	1,156	(243)	1,944
Deferred revenue	(66)	(100)	
Net cash used in operating activities	(20,212)	(11,533)	(45,680)
<b>Investing activities</b>			
Purchases of property and equipment	(25)	(121)	(558)
Net cash used in investing activities	(25)	(121)	(558)
<b>Financing activities</b>			
Proceeds from issuance of common stock	340	9	362
Proceeds from the issuance of convertible notes			250
Proceeds from the issuance of preferred stock subscription		2,000	
Principal payments of convertible notes			(200)
Proceeds from sale of convertible preferred stock, net of issuance costs	72,434	5,000	98,754
Net cash provided by financing activities	72,774	7,009	99,166
Net Increase (decrease) in cash and cash equivalents	\$ 52,537	\$ (4,645)	\$ 52,928
Cash and cash equivalents at beginning of period	391	6512	
Cash and cash equivalents at end of period	\$ 52,928	\$ 1,867	\$ 52,928
<b>Supplemental disclosure of non-cash financing activity</b>			
Conversion of notes payable to preferred stock	\$	\$	\$ 750
Issuance of convertible notes in satisfaction of accrued expenses	\$	\$	\$ 700

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Issuance of preferred stock in satisfaction of preferred stock subscription	\$	13,980	\$	\$	13,980
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See accompanying notes to condensed consolidated financial statements.



**Karyopharm Therapeutics Inc.**

**(A development stage company)**

**NOTES TO CONDENSED CONSOLIDATED FINANCIAL STATEMENTS**

**1. Summary of significant accounting policies**

*Basis of presentation*

The accompanying unaudited condensed consolidated financial statements of 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 nine months ended September 30, 2013 are not necessarily indicative of the results that may be expected for any other interim period or for the fiscal year ending December 31, 2013. The condensed consolidated interim financial statements should be read in conjunction with the audited financial statements and notes thereto included in the Company s Prospectus filed with the SEC pursuant to Rule 424(b)(4) on November 7, 2013 (the Prospectus ).

In November 2013, the Company closed an initial public offering ( IPO ) of its common stock, which resulted in the sale of 6,800,000 shares of its common stock at a public offering price of \$16.00 per share. In December 2013, the Company issued 1,020,000 shares of common stock upon the exercise by the underwriters of their option to purchase additional shares at the public offering price. The Company received net proceeds from the IPO of approximately \$113.7 million, after deducting underwriting discounts and estimated expenses payable by the Company.

In connection with preparing for the IPO, the Company s Board of Directors and stockholders approved a one-for-3.3 reverse stock split of the Company s common stock. The reverse stock split became effective in October 2013. All share and per share amounts in the condensed consolidated interim financial statements and notes thereto have been retroactively adjusted for all periods presented to give effect to this reverse stock split, including reclassifying an amount equal to the reduction in par value of common stock to additional paid-in capital. In connection with the closing of the IPO, all of the Company s outstanding convertible preferred stock automatically converted to common stock in November 2013, resulting in an additional 19,114,241 shares of common stock of the Company becoming outstanding. The significant increase in common stock outstanding in November 2013 is expected to impact the year-over-year comparability of the Company s net loss per share calculations in future periods.

The consolidated financial statements include the accounts of Karyopharm Therapeutics Inc. (a Delaware corporation) and the accounts of NPM Pharma Inc. ( NPM , a Canadian corporation), which was a variable interest entity requiring consolidation. In August 2013, the Company purchased for nominal consideration from the other shareholder the 50% not owned by the Company. As a result NPM is a wholly owned

subsidiary of the Company as of this date.

NPM was formed in December 2011 and was 50% owned by the Company until it became a wholly-owned subsidiary in August 2013. NPM was established to procure research and development services in connection with clinical pharmaceutical studies with Canadian vendors on the Company's behalf. Total NPM assets and liabilities as of December 31, 2012 are reflected on the Company's balance sheet. As of December 31, 2012, all assets of NPM are restricted to use to settle obligations of NPM. Liabilities of NPM are non-recourse to the Company.

#### *Subsequent Events*

The Company considers events or transactions that occur after the balance sheet date but prior to the issuance of the financial statements to provide additional evidence relative to certain estimates or to identify matters that require additional disclosure. The Company has completed an evaluation of all subsequent events through the date of the filing of this Form 10-Q.

## **2. Fair value of financial instruments**

The Company's financial instruments consist principally of cash and cash equivalents, accounts payable and accrued liabilities. Fair value measurements are classified and disclosed in one of the following three categories:

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

Financial instruments measured at fair value are classified below based on the three fair value hierarchy tiers described above:

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	Total	Quoted prices in active markets (Level 1)	Significant other observable inputs (Level 2)	Significant unobservable inputs (Level 3)
<b>December 31, 2012</b>				
Money market funds, included in cash equivalents	\$ 2	\$	\$ 2	\$
<b>September 30, 2013</b>				
Money market funds, included in cash equivalents	\$ 52,901	\$	\$ 52,901	\$

The Company measures cash equivalents at fair value on a recurring basis. The fair value of cash equivalents is determined based on Level 2 inputs. The carrying values of cash and cash equivalents, accounts payable and accrued expenses approximate their fair values due to the short maturity of these instruments.

### 3. Property and equipment

Property and equipment, net, consist of the following:

	Estimated Useful Life Years	September 30, 2013	December 31, 2012
Laboratory equipment	4	\$ 314	\$ 314
Furniture and fixtures	5	90	90
Office and computer equipment	3	85	85
Leasehold improvements	Lease term	69	44
		558	533
Less accumulated depreciation and amortization		(312)	(206)
Property and equipment, net		\$ 246	\$ 327

### 4. Accrued liabilities

Accrued liabilities consisted of the following:

	September 30, 2013	December 31, 2012
Payroll and employee-related costs	\$ 643	\$ 302
Research and development costs	621	333
Professional fees	486	
Other	170	129
	\$ 1,920	\$ 764

### 5. Net loss per common share

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Basic net loss per common share is calculated by dividing net loss applicable to common stockholders by the weighted-average number of common shares outstanding during the period, without consideration for common stock equivalents or unvested restricted stock. Diluted net loss per share is computed by dividing the net loss applicable to common stockholders by the weighted average number of common share equivalents outstanding for the period determined using the treasury-stock method. For purposes of this calculation, convertible preferred stock and stock options 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 amounts in the table below were excluded from the calculation of diluted weighted-average shares outstanding due to their anti-dilutive effect:

	Three Months ended September 30,		Nine Months ended September 30,		Period from December 22, 2008 (inception) to September 30, 2013
	2013	2012	2013	2012	
Convertible preferred stock	19,114,241	4,829,544	19,114,241	4,829,544	19,114,241
Special Participation Stock		10,000		10,000	
Outstanding stock options	1,775,593	551,128	1,775,593	551,128	1,775,593
Unvested restricted stock	224,019	761,875	224,019	761,875	224,019

## 6. Stockholders' Equity

In July 2013, the Company issued and sold an aggregate of 8,636,362 shares of its series B-1 convertible preferred stock at a purchase price per share of \$2.20, for an aggregate purchase price of \$18,999,996.

In August 2013, the Company issued (i) an aggregate of 6,100,000 shares of its series A-2 preferred stock at a purchase price per share of \$1.15, for an aggregate purchase price of \$7,015,000, (ii) an aggregate of 1,764,706 shares of its series A-3 preferred stock at a purchase price per share of \$1.70, for an aggregate purchase price of \$3,000,000, and (iii) an aggregate of 1,538,461 shares of its series A-4 preferred stock, at a purchase price per share of \$1.30, for an aggregate purchase price of \$1,999,999.

In September 2013, the Company issued and sold an aggregate of 12,500,000 shares of its series B preferred stock at a purchase price per share of \$2.00, for an aggregate purchase price of \$25,000,000.

## 7. Stock-based compensation

During 2010, the Company established the 2010 Stock Incentive Plan (the "Plan"). As of September 30, 2013, the maximum number of 2,763,271 shares of the Company's common stock authorized for issuance under the Plan may be issued in the form of stock options and other equity interests under the Plan and, of such shares, 191,994 were available for issuance under the Plan as of September 30, 2013. Under the terms of the Plan, options and other equity interests may be granted to employees, officers, directors, consultants and advisors of the Company. The exercise price of each stock option shall be the fair market value as determined in good faith by the Board of Directors (the Board) at the time each option is granted. The Company has granted service-based options under the Plan. Service-based option grants under the Plan generally vest as follows: 25% of the shares vest one calendar year from the vesting start date, 2.083% of the shares vest on the first day of each month thereafter. The options granted under the Plan generally expire in 10 years.

In connection with all share-based payment awards, total stock-based compensation expense recognized is as follows:

Three Months ended September 30,		Nine Months ended September 30,		Period from December 22, 2008 (date of inception) to September 30, 2013
2013	2012	2013	2012	2013

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Research and development	\$	949	\$	151	\$	1,338	\$	305	\$	2,013
General and administrative		374		5		431		24		479
Total	\$	1,323	\$	156	\$	1,769	\$	329	\$	2,492

**Stock options**

The following table summarizes stock option activity for employees and nonemployees.

	Shares	Weighted- average price per share	Weighted- average remaining contractual term (years)	Aggregate intrinsic value
Outstanding at December 31, 2012	691,367	\$ 0.46		
Granted	1,268,757	\$ 4.69		
Exercised(1)	(138,636)	\$ 2.41		
Forfeited	(45,895)	\$ 1.49		
Outstanding at September 30, 2013	1,775,593	\$ 3.30	9.3	\$ 15,768
Exercisable at September 30, 2013	281,035	\$ 0.23	7.7	\$ 3,354
Vested and expected to vest at September 30, 2013(2)	1,637,094	\$ 3.30	9.3	\$ 14,555

(1) Exercises include the issuance of 63,636 shares of non-vested restricted stock pursuant to the exercise of stock options prior to vesting. The Company has the right to repurchase the unvested shares under certain circumstances.

(2) This represents the number of vested options as of September 30, 2013, plus the number of unvested options expected to vest as of September 30, 2013, based on the unvested options at September 30, 2013, adjusted for the estimated forfeiture rate

The Company estimates the fair value of each employee and non-employee stock award using the Black-Scholes option-pricing model using the following assumptions:

	Nine Months ended September 30,	
	2013	2012
Expected volatility	85% - 93%	75% - 92%
Expected term (in years)	6.25 - 10	6.25 - 10
Risk-free interest rate	1.07% - 2.74%	0.85% - 1.76%
Expected dividend yield	0%	0%

### Restricted stock

A summary of the Company's non-vested restricted stock as of September 30, 2013 and changes during the nine months ended September 30, 2013 is as follows:

	Shares	Weighted- average purchase price per share
Non-vested at December 31, 2012	362,596	\$ 0.04
Vested	(316,535)	\$ 0.04
Non-vested at September 30, 2013(1)	46,061	\$ 0.09

(1) Excludes 177,955 shares of non-vested restricted stock remaining from the early exercise of stock options as of September 30, 2013.

### 8. Subsequent Events

In October 2013, the Company's board of directors adopted and the Company's stockholders approved, the 2013 Stock Incentive Plan (the "2013 Plan"). The 2013 Plan became effective immediately prior to the closing of the IPO and provides for the grant of incentive stock options, nonstatutory stock options, stock appreciation rights, restricted stock awards, restricted stock unit awards and other stock-based awards. The number of shares of Common Stock reserved for issuance under the 2013 Plan is equal to the sum of (1) 969,696 shares plus (2) the number of shares (up to 2,126,377 shares) equal to the sum of the number of shares of Common Stock then available for issuance under the 2010 Plan and the number of shares of Common Stock subject to outstanding awards under the 2010 Plan that expire, terminate or are otherwise surrendered,

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cancelled, forfeited or repurchased by the Company at their original issuance price pursuant to a contractual repurchase right plus (3) an annual increase, to be added on the first day of each fiscal year, beginning with the fiscal year ending December 31, 2014 and continuing until, and including, the fiscal year ending December 31, 2023, equal to the least of (A) 1,939,393 shares of Common Stock, (B) 4% of the number of shares of Common Stock outstanding on the first day of such fiscal year, and (C) an amount determined by the Company's board of directors. The Company will grant no further stock options or other awards under the 2010 Plan.

In December 2013, the Company incorporated Karyopharm Securities Corp, a wholly owned Massachusetts corporation.



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

**Forward-looking Information**

This Quarterly Report on Form 10-Q contains forward-looking statements that involve substantial risks and uncertainties. All statements, other than statements related to present facts or current conditions or of historical facts, contained in this Quarterly Report on Form 10-Q, including statements regarding our strategy, future operations, future financial position, future revenues, projected costs, prospects, plans and objectives of management, including the development of our drug candidates, the timeline for clinical development and regulatory approval of our drug candidates, the structure of our planned clinical trials and our ability to fund our operations, are forward-looking statements. The words anticipate, believe, estimate, expect, intend, may, plan, predict, project, target, potential, will, would, could, should, and other expressions are intended 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 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, our ability to raise additional capital to support our development programs 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 protect and maintain our intellectual property and the ability of our licensors, if any, to obtain and maintain patent protection for the technology or products that we license from them, the outcome of research and development activities and the fact that the preclinical and clinical testing of our drug candidates 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 Risk Factors in Item 1A of Part II and elsewhere in this report.

As a result of these and other factors, we may not actually achieve the plans, intentions or expectations 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.

**Management Overview**

We are a clinical-stage pharmaceutical company founded in December 2008 by Dr. Sharon Shacham. We are focused on the discovery and development of novel first-in-class drugs directed against nuclear transport targets for the treatment of cancer and other major diseases. Our scientific expertise is focused on the understanding of the regulation of intracellular transport between the nucleus and the cytoplasm. We have discovered and developed novel, small molecule, Selective Inhibitors of Nuclear Export, or SINE, compounds that inhibit the nuclear export protein XPO1. We have worldwide rights to these SINE compounds. Our lead drug candidate, Selinexor (KPT-330), is an XPO1 inhibitor being evaluated in multiple open-label Phase 1 clinical trials in patients with heavily pretreated relapsed and/or refractory hematological and solid tumor malignancies. As of September 20, 2013, we had administered Selinexor to over 170 patients in these trials. Preliminary evidence of anti-cancer activity has been observed in some patients and Selinexor has been sufficiently well-tolerated to allow many of these patients to remain on therapy for prolonged periods, including several who have remained on study for over 8-12 months. To our knowledge, no other XPO1 inhibitors are in clinical development at the present time.

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We have devoted substantially all of our efforts to research and development. 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. Through September 30, 2013, we financed our operations primarily with the net proceeds from the private placements of our preferred stock.

Since inception, we have incurred significant operating losses. Our net loss was \$21.8 million and \$11.7 million for the nine months ended September 30, 2013 and 2012, respectively. As of September 30, 2013, we had an accumulated deficit of \$50.4 million. We have not generated any revenue to date from 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;
- identify additional drug candidates;

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- initiate additional clinical trials for our drug candidates;
- seek marketing approvals for any of our drug candidates that successfully complete clinical trials;
- ultimately 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;
- hire additional clinical, quality control and scientific personnel;
- 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 transition to 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.

It is important that the discussion of our operating results that follows be read in conjunction with the critical accounting policies disclosed in Prospectus filed related to Accrued Research and Development Expenses and Stock-Based Compensation.

### Results of Operations

#### Comparison of the Three Months ended September 30, 2013 and September 30, 2012

	Three Months Ended September 30,		Dollar Change
	2013	2012 (in thousands)	
Contract and grant revenue	\$	\$ 34	\$ (34)
<b>Operating expenses:</b>			
Research and development	7,738	2,997	4,741
General and administrative	1,583	672	911
Loss from operations	(9,321)	(3,635)	(5,686)

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Interest income

Net loss	\$	(9,321)	\$	(3,635)	\$	(5,686)
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*Contract and grant revenue.* Contract and grant revenue for the three months ended September 30, 2013 (the 2013 Quarter ) was zero compared to \$34,000 for the three months ended September 30, 2012 (the 2012 Quarter ). The decrease was due to the completion of the work required under the grant in the second quarter of 2013.

*Research and development expense.* Research and development expense for 2013 Quarter was \$7.7 million compared to \$3.0 million for the 2012 Quarter. The \$4.7 million increase from the 2012 Quarter to the 2013 Quarter was primarily related to an increase of \$2.9 million in clinical trial costs, an increase of \$1.2 million in consulting fees, an increase of \$411,000 in personnel costs, and an increase of \$173,000 in discovery expenses, which includes including preclinical studies and screening.

*General and administrative expense.* General and administrative expense for the 2013 Quarter was \$1.6 million compared to \$672,000 for the 2012 Quarter. The \$911,000 increase from the 2012 Quarter to the 2013 Quarter primarily resulted from an increase of \$541,000 in consulting fees and an increase of \$323,000 in personnel costs which includes an increase in stock-based compensation of \$107,000.

*Interest income.* Interest income was nominal for the 2013 Quarter and the 2012 Quarter.

**Comparison of the Nine Months ended September 30, 2013 and September 30, 2012**

	Nine Months Ended September 30,		Dollar Change
	2013	2012 (in thousands)	
Contract and grant revenue	\$ 366	\$ 601	\$ (235)
<b>Operating expenses:</b>			
Research and development	18,763	10,429	8,334
General and administrative	3,405	1,824	1,581
Loss from operations	(21,802)	(11,652)	(10,150)
Interest income	1	2	(1)
Net loss	\$ (21,801)	\$ (11,650)	\$ (10,151)

*Contract and grant revenue.* Contract and grant revenue for the nine months ended September 30, 2013 (the 2013 Period ) was \$366,000 compared to \$601,000 for the nine months ended September 30, 2012 (the 2012 Period ). The decrease in revenue is due to the completion of the work required under the grant in the second quarter of 2013.

*Research and development expense.* Research and development expense for the 2013 Period was \$18.8 million compared to \$10.4 million for the 2012 Period. The \$8.4 million increase from the 2012 Period to the 2013 Period was primarily related to an increase of \$6.2 million in clinical trial costs, an increase of \$1.7 million in consulting fees, an increase of \$695,000 in personnel costs, and an increase of \$532,000 in discovery expenses, including preclinical studies and screening. These increases were partially offset by a decreases of \$486,000 in collaboration expense and \$378,000 in toxicology and efficacy studies.

*General and administrative expense.* General and administrative expense for the 2013 Period was \$3.4 million compared to \$1.8 million for the 2012 Period. The \$1.6 million increase from the 2012 Period to the 2013 Period primarily resulted from an increase of \$826,000 in consulting fees, an increase of \$384,000 in personnel costs, which includes an increase in stock-based compensation of \$107,000, an increase of \$213,000 in professional fees and an increase of \$105,000 travel expenses.

*Interest income.* Interest income decreased to \$1,000 for the 2013 Period from \$2,000 for the 2012 Period.

**LIQUIDITY AND CAPITAL RESOURCES****Sources of liquidity**

As of September 30, 2013, we have not generated any material revenues. Through September 30, 2013, we financed our operations primarily through private placements of our preferred stock. As of September 30, 2013, we had \$52.9 million in cash and cash equivalents.

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In November 2013, we closed an initial public offering ( IPO ) of our common stock, which resulted in the sale of 6,800,000 shares of our common stock at a public offering price of \$16.00 per share. In December 2013, we issued and sold 1,020,000 shares of common stock upon the exercise by the underwriters of their option to purchase additional shares at the public offering price. We received net proceeds from the IPO of approximately \$113.7 million, after deducting underwriting discounts and estimated expenses payable by us.

**Cash flows**

The following table provides information regarding our cash flows:

	Nine Months Ended, September 30,		
	2013	2012	
	(in thousands)		
Net cash used in operating activities	\$ (20,212)	\$ (11,533)	
Net cash used in investing activities	(25)	(121)	
Net cash provided by financing activities	72,774	7,009	
Net increase (decrease) in cash and cash equivalents	\$ 52,537	\$ (4,645)	

***Net Cash Used in Operating Activities***

The use of cash in both periods resulted primarily from our net losses adjusted for non-cash charges and changes in components of working capital. Net cash used in operating activities was \$20.2 million during the 2013 Period compared to \$11.5 million during the 2012 Period. The increase in cash used in operating activities during the 2013 Period was driven primarily by an increase in our net loss and by changes in components of working capital, including a decrease in accounts payable and accrued expenses.

***Net Cash Used in Investing Activities***

Net cash used in investing activities was \$25,000 during the 2013 Period compared to \$121,000 during the 2012 Period. The cash used in investing activities was for the purchase of property and equipment.

***Net Cash Provided by Financing Activities***

Net cash provided by financing activities was \$72.8 million during the 2013 Period compared to \$7.0 million during the 2012 Period. The increase in cash provided by financing activities during the 2013 Period was driven primarily by the proceeds from the sale of preferred stock.

**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

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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 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 the net proceeds of our IPO, completed in the fourth quarter of 2013, together with our existing cash and cash equivalents, will enable us to fund our current operating plan and capital expenditure requirements for at least the next 30 months. 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;



- 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 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.

#### **Contractual Obligations**

During the three months ended September 30, 2013, there were no material changes to our contractual obligations and commitments described under Management's Discussion and Analysis of Financial Condition and Results of Operations in the Prospectus.

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

We are exposed to market risk related to changes in interest rates. We had cash and cash equivalents of \$52.9 million and \$391,000 as of September 30, 2013 and December 31, 2012, respectively. 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 our investments are in cash and cash equivalents. 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 portfolio.

We are also exposed to market risk related to change in foreign currency exchange rates. We contract with contract research organizations ( CROs ) and contract manufacture organizations ( CMOs ) that are located in Canada and Europe, such contracts require payments by us 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. As of September 30, 2013 and December 31, 2012, we had payables and accrued expenses of \$283,000 and \$535,000, respectively, denominated in foreign currencies.

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

**Evaluation of Disclosure Controls and Procedures**

Our management, with the participation of our Chief Executive Officer and Senior Vice President, Finance & Administration, evaluated the effectiveness of our disclosure controls and procedures as of September 30, 2013. 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 September 30, 2013, our Chief Executive Officer and Senior Vice President,

Finance & Administration concluded that, as of such date, our disclosure controls and procedures were effective at the reasonable assurance level.

## PART II OTHER INFORMATION

### Item 1A. Risk Factors.

Our business is subject to numerous risks. We caution you that the following important factors, among others, could cause our actual results to differ materially from those expressed in forward-looking statements made by us or on our behalf in filings with the SEC, press releases, communications with investors and oral statements. Any or all of our forward-looking statements in this Quarterly Report on Form 10-Q and in any other public statements we make may turn out to be wrong. They can be affected by inaccurate assumptions we might make or by known or unknown risks and uncertainties. Many factors mentioned in the discussion below will be important in determining future results. Consequently, no forward-looking statement can be guaranteed. Actual future results may differ materially from those anticipated in our forward-looking statements. We undertake no obligation to update any forward-looking statements, whether as a result of new information, future events or otherwise. You are advised, however, to consult any further disclosure we make in our reports filed with the SEC. These risk factors restate and supersede the risk factors set forth under the heading "Risk Factors" in the Prospectus.

#### 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.*

Since inception, we have incurred significant operating losses. Our net loss was \$9.3 million, \$3.6 million, \$21.8 million, and \$11.7 million for the three months ended September 30, 2013 and 2012, and for the nine months ended September 30, 2013 and 2012, respectively. As of September 30, 2013, we had an accumulated deficit of \$50.4 million. We have not generated any revenue to date from sales of any drugs and have financed our operations principally through private placements of our preferred stock. We have devoted substantially all of our efforts to research and development. Our lead drug candidate, Selinexor (KPT-330), is in Phase 1 clinical development and our other drug candidates for the treatment of human disease are in preclinical 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;
- identify additional drug candidates;
- initiate additional clinical trials for our drug candidates;
- seek marketing approvals for any of our drug candidates that successfully complete clinical trials;
- ultimately 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;

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- hire additional clinical, quality control and scientific personnel;
- 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 transition to a public company.

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.

*Our short operating history may make it difficult for you to evaluate the success of our business to date and to assess our future viability.*

We are an early-stage company. We were incorporated in December 2008 and commenced operations in the first half of 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-stage clinical

trials of our drug candidates. Our lead drug candidate is currently in Phase 1 clinical trials and all of our other drug candidates for the treatment of human disease are in preclinical development. We have not yet demonstrated our ability to successfully complete any late-stage clinical trials in humans, including large-scale, pivotal 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 available for treating patients. Consequently, any predictions you 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, you 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 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 and cash equivalents and the proceeds from our IPO will enable us to fund our operating expenses and capital expenditure requirements for at least the next 30 months. 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 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, your ownership interest will be diluted, and the terms of these securities may include liquidation or other preferences that adversely affect your rights as a common stockholder. 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 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.***

As has been widely reported, global credit and financial markets have experienced extreme disruptions over the past several years, including severely 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 further 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 current equity and credit markets deteriorate, or do not improve, 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 these difficult economic times, which could directly affect our ability to attain our operating goals on schedule and on budget.

#### **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 Phase 1 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 we do not expect to occur for several years, if ever, will depend heavily on the successful development, regulatory approval and eventual commercialization of Selinexor.



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We cannot commercialize drug candidates in the United States without first obtaining regulatory approval for the drug from the United States 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 a third party 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 future 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 clinical trials designed to potentially serve as the basis for an application seeking approval, which we refer to as registration-directed 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-directed 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.

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 have limited experience in designing clinical trials and 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.

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 registration-directed 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 reviewing and providing comments or advice on a protocol for a pivotal 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. In addition, 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 no discussions with the FDA or non-U.S. regulatory authorities regarding the design of our planned registration-directed clinical trials for Selinexor. We plan to commence two registration-directed clinical trials in the first half of 2014 and, assuming positive results, we plan to seek regulatory approvals of Selinexor in North America and Europe and we may seek such approvals in other geographies. 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 planned registration-directed clinical trials to be sufficient to serve as the basis for 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 Phase 1 clinical trials that may be required prior to commencing either of our planned registration-directed clinical trials, or an additional Phase 3 clinical trial following completion of our planned registration-directed 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.

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The results to date in preclinical studies that conducted by us or our academic collaborators and in Phase 1 clinical trials that we are currently conducting include the response of tumors to Selinexor. We expect that the primary endpoint in any randomized pivotal trials of Selinexor will be either progression free survival, meaning the length of time on treatment until objective tumor progression, or overall survival. We have no clinical data in humans relating to the impact of Selinexor on overall survival; we are gathering information on progression free survival. We have no comparative clinical data between Selinexor and standard or supportive care. If Selinexor does not demonstrate a progression free or 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

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period. For some types of cancer, following discussions with regulatory authorities, we may use overall response rate as a primary endpoint. If Selinexor does not demonstrate a sufficient overall response rate for a particular indication, it will likely not be approved for that indication.

***We are very early in our development efforts and have only one drug candidate in clinical development. All of our other drug candidates are still in preclinical 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 very early in our development efforts and have only one drug candidate, Selinexor, in clinical development. The success of Selinexor and any of our other drug candidates will depend on several factors, including the following:

- successful completion of preclinical 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;
- 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 a continued 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, and possibly 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 or current clinical-stage cancer drug candidates 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 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 proving 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.*

A key element of our strategy is to use our technology platform to build a pipeline of novel drug candidates. The drug discovery that we are conducting using our proprietary technology 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;
- 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, the results of our Phase 1 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 have 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:

- regulators 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 regulators may require us, to conduct additional 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;

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- 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 future collaborators that 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.

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 or allow our competitors to bring drugs to market before we do and impair our ability to successfully commercialize our drug candidates and may harm our business and results of operations.

*If we experience delays or difficulties in the enrollment of patients in 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;
- perceived risks and benefits of the drug candidate under study;
- 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.

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.*

Our lead drug candidate Selinexor is in Phase 1 clinical development and our other drug candidates are in preclinical development. 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



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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, even though Selinexor has generally been well-tolerated by patients in our Phase 1 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 minority of patients have withdrawn from our Phase 1 solid tumor malignancy trial as a result of AEs. We do not gather data relating to patient withdrawals as a result of AEs for our other Phase 1 clinical trials. A small minority of patients across our Phase 1 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 adverse events 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.

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

If any of our drug candidates receive marketing approval, they may nonetheless fail to gain sufficient market acceptance by physicians, patients, healthcare 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;

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- 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 enter into 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 do not have a sales or marketing infrastructure and have no experience in the sale or marketing of pharmaceutical drugs. To date, we have not entered into a strategic collaboration that provides us with access to a collaborator's resources in selling or marketing drugs. To achieve commercial success for any approved drug for which sales and marketing is not the responsibility of any strategic collaborator that we 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 some of our drug candidates if and when they are approved, or enter into collaborations with respect to the sale and marketing of our drug candidates.

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:

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- 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.

If we enter into arrangements with third parties to perform sales and marketing services, our revenues from the sale of drug or the profitability of these revenues to us are likely to be lower than if we were to market and sell any drugs that we develop ourselves. In addition, we may not be successful in entering into 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.

***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.

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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 become subject to unfavorable pricing regulations, third-party reimbursement practices or healthcare reform initiatives, which would harm our business.*

The regulations that govern marketing approvals, pricing and reimbursement for new drugs vary widely from country to country. In the United States, recently enacted legislation may significantly change the approval requirements in ways that could involve additional costs and cause delays in obtaining approvals. 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. 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.

Our ability to commercialize any drugs successfully also 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. 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. 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. 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 to 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 purposes for which the drug is approved by the FDA or similar 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;

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- 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.

We currently hold clinical trial liability insurance coverage for up to \$5.0 million, 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.

*Verdinexor (KPT-335) is our clinical drug candidate for the treatment of pet dogs with newly-diagnosed and first time relapse lymphomas. We expect that we will submit the safety and effectiveness sections of a New Animal Drug Application, or NADA, for Verdinexor to the FDA by early 2014. If this clinical trial does not produce positive results or if Verdinexor is not approved by the FDA, this may raise safety and efficacy concerns for Selinexor, as the anti-cancer activity and adverse event profile of Verdinexor in dogs with lymphomas provided support for our decision to move Selinexor into Phase 1 clinical trials.*

As part of the drug discovery and development process, we have used spontaneously occurring pet dog cancers as a surrogate model for human malignancies. Dog lymphomas respond to chemotherapy in a manner similar to their human counterparts (human non-Hodgkin's lymphomas) and display a comparable genetic profile. The anti-cancer activity of our drug candidate Verdinexor (KPT-335) in a Phase 1 clinical trial in dogs with certain lymphomas provided support for our decision to move Selinexor, our closely-related human drug candidate, into Phase 1 clinical trials. We conducted a Phase 2b clinical trial of Verdinexor in dogs with newly-diagnosed or first time relapse lymphomas. We have received a Minor Use / Minor Species, or MUMS, designation from the Center for Veterinary Medicine of the FDA for the treatment of newly-diagnosed or after first relapse lymphomas in dogs with Verdinexor. Our Phase 2b clinical trial is intended to support regulatory approval under the MUMS designation. We expect that we will submit the safety and effectiveness sections of a NADA for Verdinexor to the FDA by early 2014. If this clinical trial of Verdinexor fails to demonstrate safety and efficacy to the satisfaction of the FDA or does not otherwise produce positive results or if Verdinexor is not otherwise approved by the FDA for the indication with respect to which we are submitting an application, this may raise questions regarding Selinexor because we have used dog cancers as a surrogate model for human malignancies. In such an event, Verdinexor's clinical trial results may cause the FDA or non-U.S. regulatory authorities to require more information, including additional preclinical or clinical data to support approval of Selinexor. If the Phase 2b clinical trial of Verdinexor fails to demonstrate safety and efficacy to the satisfaction of the FDA or does 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 Verdinexor. In such an event, we also may not be able to realize our potential to generate revenue from the commercialization of Verdinexor, either on our own or with a collaborator.

#### **Risks Related To Our Dependence On Third Parties**

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

We intend to seek third-party collaborators for the development, marketing and/or commercialization of our drug candidates. For example, while we currently plan to conduct two registration-directed clinical trials of Selinexor and make regulatory filings in North America and Europe with respect to the potential approval of Selinexor without a collaborator, we anticipate that we will seek to enter into a collaboration for marketing and commercialization of Selinexor at the appropriate time in the future. In addition, we intend to seek one or more collaborators to aid in the further development, marketing and/or commercialization of selected SINE compounds for inflammatory conditions, viral disorders and wound healing. Our likely collaborators for any collaboration arrangements include large and mid-size pharmaceutical companies, regional and national pharmaceutical companies and biotechnology companies. If we do enter into any such arrangements with any 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;



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- 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 future collaborators or acquirers.

Collaboration agreements may not lead to development or commercialization of drug candidates in the most efficient manner, or at all.

*If we are not able to establish 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 collaborate with pharmaceutical and biotechnology companies for the development and/or commercialization of our drug candidates.

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.

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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 third parties to 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 third parties, such as contract research organizations, clinical data management organizations, medical institutions and clinical investigators, to 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 and Health Canada also require 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 intend to 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 intend to rely on academic and private non-academic institutions to conduct and sponsor clinical trials relating to Selinexor and our other drug candidates. We will not control the design or conduct of the investigator-sponsored trials, and it is possible that the FDA or 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. To date, we have obtained starting materials for our supply of the current good manufacturing practices, or cGMP, bulk drug substance for our drug candidates from one third-party manufacturer. We have engaged a separate third-party manufacturer for fill-and-finish services. We do not have a long term supply agreement with either 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 future 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 specifications;
- the possible failure of the third party to manufacture our drug candidate according to our schedule, or at all;
- the possible misappropriation 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 cGMP regulations or similar regulatory requirements outside of the United States. Our failure, or the failure of our third-party manufacturers, to comply with applicable regulations could result in sanctions being imposed on us, including 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.

Any performance failure on the part of our existing or future manufacturers could delay clinical development or marketing approval. We do not currently have arrangements in place for redundant supply or a second source for cGMP bulk drug substance or fill-and-finish services. 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, one patent has issued that relates to XPO1 inhibitors, other than our key drug candidates, and their use in targeted therapeutics. We cannot be certain that any patents will issue with claims that cover any of our key drug candidates or other discoveries or drug candidates.

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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 patent 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.

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 may infringe our patents and other intellectual property rights. To counter infringement or unauthorized use, we may be required to file infringement claims, which can be expensive and time-consuming. In addition, in an infringement proceeding, a court may decide 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 future collaborators that we may have 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; however, if we are found to infringe a third party's intellectual property rights, we could be required 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



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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.

***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 a 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.

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In the United States, only a single patent can be extended for each FDA approval, and any patent can be extended only once, 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 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.

***We have not yet registered our trademarks. Failure to secure those registrations could adversely affect our business.***

We have not yet registered our trademarks in the United States or other countries. 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. We have also not yet registered trademarks for any of our drug candidates in any jurisdiction. When we file trademark applications for our drug candidates those applications may not be allowed for registration, and registered trademarks may not be obtained, maintained or enforced. 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 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 collaborators we may have in the future, will obtain marketing approval to commercialize a drug candidate.***

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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 collaborators we may have in the future, receive approval of an 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 collaborators we may have in the future, ultimately obtain may be limited or subject to restrictions or post-approval commitments that render the approved drug not commercially viable.

Any delay in obtaining or failure to obtain required approvals could materially adversely affect our ability or that of any collaborators we may have 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.

***Failure to obtain marketing approval in international jurisdictions would prevent our drug candidates from being marketed abroad.***

In order to market and sell our drugs in the European Union and many other jurisdictions, we, and any collaborators we may have in the future, 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 any collaborators we may have in the future, 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.

***Even if we, or any collaborators we may have in the future, 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 any collaborators we may have in the future, 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 any collaborators we may have in the future, 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 future 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 future collaborators, receive marketing approval for one or more of our drug candidates, we, and our future 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 future collaborators, are not able to comply with post-approval regulatory requirements, we, and our future collaborators, could have the marketing approvals for our drugs withdrawn by regulatory authorities and our, or our future 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.

*Any of our drug candidates for which we, or our future collaborators, obtain marketing approval in the future could be subject to post-marketing restrictions or withdrawal from the market and we, and our future 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 future 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.

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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 future 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 Federal Food, Drug, and Cosmetic Act 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 adverse events 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;
- fines, 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.

***Recently-enacted and future legislation may increase the difficulty and cost for us and our future collaborators to obtain marketing approval of 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 prevent or delay marketing approval of our drug candidates, restrict or regulate post-approval activities and affect our ability, or the ability of our future 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 be adopted in the future, may result in more rigorous coverage criteria and in additional downward pressure on the price that we, or our future collaborators, may receive for any approved drugs.

In the United States, the Medicare Prescription Drug, Improvement, and Modernization Act of 2003, or the MMA, changed the way Medicare covers and pays for pharmaceutical products and could decrease the coverage and price that we, or our future collaborators, may receive for any approved drugs. While the MMA only addresses drug benefits for Medicare beneficiaries, private payors often follow Medicare coverage policy and payment limitations in setting their own reimbursement rates. Therefore, any reduction in reimbursement that results from the MMA may result in a similar reduction in payments from private payors.

More recently, in March 2010, President Obama signed into law the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Affordability Reconciliation Act, or collectively the PPACA.

Among the provisions of the PPACA of potential importance to our drug candidates are the following:

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- 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 False Claims Act and the Anti-Kickback Statute, new government investigative powers and enhanced penalties for non-compliance;
- a new Medicare Part D coverage gap discount program, in which manufacturers must agree to offer 50% point-of-sale discounts off negotiated prices;
- 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;
- new requirements to report 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.

In addition, other legislative changes have been proposed and adopted since the PPACA was enacted. 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 drug candidates for which marketing approval is obtained.

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

Legislative and regulatory proposals have been made to expand post-approval requirements and restrict sales and promotional activities for pharmaceutical products. 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 United States Congress of the FDA's approval process may significantly delay or prevent marketing approval, as well as subject us and our future 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.***

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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;

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- **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.

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.

***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.

***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

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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.*

If we expand our operations outside of the United States, we must comply with numerous laws and regulations in each jurisdiction in which we plan to operate. The creation and implementation of international business practices compliance programs is costly and such programs are difficult to enforce, particularly where reliance on third parties is required.

The Foreign Corrupt Practices Act, or 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. If we expand our presence outside of the United States, it will 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.

*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, particularly 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 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 these persons could impede the achievement of our research, development and commercialization 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.

***Michael Kauffman, M.D., Ph.D. and Sharon Shacham, Ph.D., M.B.A. are married. 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. 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 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, potentially, 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.***

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, natural disasters, fire, terrorism, war and telecommunication and electrical 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 and the further development of our drug candidates could be delayed.

## **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 December 16, 2013, 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 you might otherwise receive a premium for your shares. These provisions could also limit the price that investors might be willing to pay in the future for

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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.

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.

***If securities analysts do not 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. 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 may be volatile and fluctuate substantially.***

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Our stock price is likely to be volatile. 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.

### ***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 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 for up to five years. 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, 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, only two years of audited financial statements and a correspondingly reduced Management's Discussion and Analysis of Financial Condition and Results of Operations disclosure, 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 incur increased costs as a result of operating as a public company, and our management will be required to devote substantial time to new compliance initiatives.*

As a public company, and particularly after we are no longer an emerging growth company, we will incur significant legal, accounting and other expenses that we did not incur as a private company. 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 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. For example, we expect that these rules and regulations may make it more difficult and more expensive for us to obtain director and officer liability insurance. We estimate that our incremental costs resulting from operating as a public company may be between \$2.0 million and \$4.0 million per year.

Pursuant to Section 404 of the Sarbanes-Oxley Act of 2002, or Section 404, we will be required to furnish a report by our management on our internal control over financial reporting, including an attestation report on internal control over financial reporting issued by our independent registered public accounting firm. However, while we remain an emerging growth company, we will not be 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 will be 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 continuous reporting and improvement process for internal control over financial reporting. In the course of the preparation and external audit of our consolidated financial statements, we and our independent registered public accounting firm identified significant deficiencies in our internal control over financial reporting related to the insufficient staffing of our finance department. A significant deficiency is a deficiency, or combination of deficiencies, in internal control over financial reporting that is less severe than a material weakness, yet important enough to

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merit attention by those responsible for oversight of a company's financial reporting. Following the identification of these control deficiencies, we have taken actions and measures to improve our internal control over financial reporting by hiring additional employees and consultants at various appropriate levels. Our remediation efforts may not, however, enable us to avoid material weaknesses or other significant deficiencies in the future. 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.

*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 your sole source of gain.*

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 your sole source of gain 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. Of the approximately 29.7 million shares of our common stock outstanding as of December 16, 2013, approximately 21.9 million shares are currently subject to restrictions on transfer under 180-day lock-up arrangements with either the underwriters for our IPO or under stock option or restricted stock agreements entered into between us and the holders of those shares. The restrictions under the 180-day lock-up arrangements with the underwriters for our IPO are due to expire on May 4, 2014, resulting in these shares becoming eligible for public sale on May 5, 2014 if they are registered under the Securities Act of 1933, as amended (the Securities Act), or if they qualify for an exemption from registration under the Securities Act, including under Rules 144 or 701.

Moreover, holders of an aggregate of approximately 19.1 million shares of our common stock 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. Once we register these shares, they can be freely sold in the public market, subject to the lock-up arrangements described above.

## **Item 2. Unregistered Sales of Equity Securities and Use of Proceeds.**

### **Recent Sales of Unregistered Securities**

#### *(a) Issuances of Preferred Stock*

In July 2013, we issued and sold an aggregate of 8,636,362 shares of our series B-1 preferred stock at a purchase price per share of \$2.20, for an aggregate purchase price of \$18,999,996.

In August 2013, we issued (i) an aggregate of 6,100,000 shares of our series A-2 preferred stock at a purchase price per share of \$1.15, for an aggregate purchase price of \$7,015,000, (ii) an aggregate of 1,764,706 shares of our series A-3 preferred stock at a purchase price per share of \$1.70, for an aggregate purchase price of \$3,000,000, and (iii) an aggregate of 1,538,461 shares of our series A-4 preferred stock, at a purchase price per share of \$1.30, for an aggregate purchase price of \$1,999,999.

In September 2013, we issued and sold an aggregate of 12,500,000 shares of our series B preferred stock at a purchase price per share of \$2.00, for an aggregate purchase price of \$25,000,000.

No underwriters were involved in the foregoing sales of preferred stock. The preferred stock was issued to third parties pursuant to Regulation D promulgated under the Securities Act or pursuant to Regulation S promulgated under the Securities Act, in each case related to transactions by an issuer not involving any public offering.

In November 2013, upon the closing of our initial public offering, all shares of our then-outstanding preferred stock were automatically converted into shares of our common stock at conversion rate of 1 share of common stock for 3.3 shares of preferred stock.

*(b) Issuances of Common Stock*

In July 2013, we issued an aggregate of 12,121 shares of our common stock (after giving effect to the 1-for-3.3 reverse stock split of our common stock that was effected on October 25, 2013) to the holders of our special participation stock, in connection with the election of the holders of a majority of such shares of special participation stock to convert all outstanding shares of special participation stock into common stock. The common stock was issued pursuant to the exemption from the registration requirements of the Securities Act provided by Section 3(a)(9) of the Securities Act.

In November 2013, upon the closing of our initial public offering, all shares of our then-outstanding convertible preferred stock were automatically converted into 19,114,241 shares of common stock. The common stock was issued pursuant to the exemption from the registration requirements of the Securities Act provided by Section 3(a)(9) or Section 4(2) of the Securities Act.

(c) *Stock Option Grants*

In July 2013, pursuant to the terms of our 2010 Plan, we granted to certain of our executive officers, employees and consultants options to purchase an aggregate of 110,605 shares of our common stock, at an exercise price of \$4.75 per share. The issuance of such options and the common stock issuable upon the exercise of such options were issued pursuant to written compensatory plans or arrangements with our employees, directors and consultants, in reliance on the exemption from the registration requirements of the Securities Act provided by Rule 701 promulgated under the Securities Act.

In September 2013, pursuant to the terms of our 2010 Plan, we granted to certain of our directors, executive officers, employees and consultants options to purchase an aggregate of 1,131,667 shares of our common stock, at an exercise price of \$4.75 per share. The issuance of such options and the common stock issuable upon the exercise of such options were issued pursuant to written compensatory plans or arrangements with our employees, directors and consultants, in reliance on the exemption from the registration requirements of the Securities Act provided by Rule 701 promulgated under the Securities Act, or pursuant to Section 4(2) under the Securities Act.

In October 2013, pursuant to the terms of our 2010 Plan, we granted to certain of our directors, employees and consultants options to purchase an aggregate of 113,330 shares of our common stock, at an exercise price of \$5.64 per share. The issuance of such options and the common stock issuable upon the exercise of such options were issued pursuant to written compensatory plans or arrangements with our employees, directors and consultants, in reliance on the exemption from the registration requirements of the Securities Act provided by Rule 701 promulgated under the Securities Act.

The number of shares underlying the option grants listed above and the exercise price for each such underlying share give effect to the 1-for-3.3 reverse stock split of our common stock that was effected on October 25, 2013.

**Use of Proceeds from Registered Securities**

On November 12, 2013, we issued and sold 6,800,000 shares of our common stock in the IPO at a public offering price of \$16.00 per share, for aggregate gross proceeds of \$108.8 million. On December 10, 2013, we issued and sold 1,020,000 shares of our common stock pursuant to the underwriters' full exercise of their option to purchase additional shares in the IPO at \$16.00 per share for gross proceeds of \$16.3 million. All of the shares issued and sold in the IPO were registered under the Securities Act pursuant to a Registration Statement on Form S-1 (File No. 333-191584), which was declared effective by the SEC on November 5, 2013, and a Registration Statement on Form S-1 (File No. 333-192110) filed pursuant to Rule 462(b) of the Securities Act. Merrill Lynch, Pierce, Fenner & Smith Incorporated and Leerink Swann LLC acted as joint-book-running managers of the offering and as representatives of the underwriters. JMP Securities LLC and Oppenheimer & Co. Inc. acted as co-managers for the offering. The offering commenced on November 5, 2013 and terminated on December 5, 2013.



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The net offering proceeds to us, after deducting underwriting discounts of \$8.8 million and estimated offering expenses payable by us totaling \$2.6 million, were approximately \$113.7 million. No offering expenses were paid directly or indirectly to any of our directors or officers (or their associates) or persons owning 10.0% or more of any class of our equity securities or to any other affiliates.

There has been no material change in our planned use of the net proceeds from the offering described in the Prospectus.

### **Item 6. Exhibits.**

The exhibits filed as part of this Quarterly Report on Form 10-Q are set forth on the Exhibit Index, which Exhibit Index is incorporated herein by reference.

**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.

Date: December 20, 2013

**KARYOPHARM THERAPEUTICS INC.**

By: /s/ PAUL BRANNELLY

Paul Brannelly  
*Senior Vice President, Finance & Administration*  
*(Principal financial and accounting officer)*

## EXHIBIT INDEX

Exhibit Number	Description of Exhibit	Incorporated by Reference			Exhibit Number	Filed Herewith
		Form	File Number	Date of Filing		
3.1	Restated Certificate of Incorporation	8-K				
3.2	Amended and Restated By-Laws	8-K				
10.1	2013 Stock Incentive Plan	S-1/A	333-191584	10/28/13	10.3	
10.2	Form of Incentive Stock Option Agreement under 2013 Stock Incentive Plan	S-1/A	333-191584	10/28/13	10.4	
10.3	Form of Nonstatutory Stock Option Agreement under 2013 Stock Incentive Plan	S-1/A	333-191584	10/28/13	10.5	
10.4	2013 Employee Stock Purchase Plan	S-1/A	333-191584	10/28/13	10.6	
31.1	Certification of principal executive officer pursuant to Rule 13a-14(a)/15d-14(a) of the Securities Exchange Act of 1934, as amended.					X
31.2	Certification of principal financial officer pursuant to Rule 13a-14(a)/15d-14(a) of the Securities Exchange Act of 1934, as amended.					X
32.1	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.					X
32.2	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.					X