

Karyopharm Therapeutics Inc.
Form 424B5
April 26, 2017
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As Filed Pursuant to Rule 424(b)(5)

Registration No. 333-214489

PROSPECTUS SUPPLEMENT

(To Prospectus dated December 1, 2016)

3,902,439 Shares

Common Stock

We are offering 3,902,439 shares of our common stock.

Our common stock is listed on The NASDAQ Global Select Market under the symbol KPTI. On April 24, 2017, the last reported sale price of our common stock on The NASDAQ Global Select Market was \$11.31 per share.

We are an emerging growth company under federal securities laws and are subject to reduced public company disclosure standards. See Prospectus Supplement Summary Implications of Being an Emerging Growth Company.

Investing in our common stock involves a high degree of risk. Please read the information contained in and incorporated by reference under the heading Risk Factors beginning on page S-9 of this prospectus supplement and under a similar heading in our Annual Report on Form 10-K for the year ended December 31, 2016.

Neither the Securities and Exchange Commission nor any state securities commission has approved or disapproved of these securities or passed on the adequacy or accuracy of this prospectus supplement or the accompanying prospectus. Any representation to the contrary is a criminal offense.

PER SHARE TOTAL

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Public Offering Price	\$	10.25	\$ 40,000,000
Underwriting Discounts and Commissions ⁽¹⁾	\$	0.50	\$ 1,951,220
Proceeds to Karyopharm Therapeutics Inc. (before expenses)	\$	9.75	\$ 38,048,780

(1) See Underwriting for a description of compensation payable to the underwriter.

The underwriter expects to deliver the shares of common stock against payment on or about April 28, 2017. We have granted the underwriter an option for a period of 30 days to purchase up to an additional 585,365 shares of our common stock. If the underwriter exercises the option in full, the total underwriting discounts and commissions payable by us will be \$2,243,902 and the total proceeds to us, before expenses, will be \$43,756,089.

Sole Book-Running Manager

Cantor Fitzgerald & Co.

The date of this prospectus supplement is April 24, 2017.

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ABOUT THIS PROSPECTUS SUPPLEMENT

This document is in two parts and is part of the registration statement that we filed with the Securities and Exchange Commission, or the SEC, using a shelf registration process. The first part is this prospectus supplement, which describes the specific terms of this common stock offering and also adds to and updates information contained in the accompanying prospectus and the documents incorporated by reference herein. The second part, the accompanying prospectus, provides more general information. Generally, when we refer to this prospectus, we are referring to both parts of this document combined. To the extent there is a conflict between the information contained in this prospectus supplement and the information contained in the accompanying prospectus or any document incorporated by reference therein filed prior to the date of this prospectus supplement, you should rely on the information in this prospectus supplement; provided that if any statement in one of these documents is inconsistent with a statement in another document having a later date—for example, a document incorporated by reference in the accompanying prospectus—the statement in the document having the later date modifies or supersedes the earlier statement.

We further note that the representations, warranties and covenants made by us in any agreement that is filed as an exhibit to any document that is incorporated by reference herein were made solely for the benefit of the parties to such agreement, including, in some cases, for the purpose of allocating risk among the parties to such agreements, and should not be deemed to be a representation, warranty or covenant to you. Moreover, such representations, warranties or covenants were accurate only as of the date when made. Accordingly, such representations, warranties and covenants should not be relied on as accurately representing the current state of our affairs.

Neither we nor the underwriter has authorized anyone to provide any information other than that contained or incorporated by reference in this prospectus supplement, the accompanying prospectus or in any free writing prospectus prepared by or on behalf of us or to which we have referred you. We take no responsibility for, and can provide no assurance as to the reliability of, any other information that others may give you. The information contained in this prospectus supplement or the accompanying prospectus, or incorporated by reference herein or therein is accurate only as of the respective dates thereof, regardless of the time of delivery of this prospectus supplement and the accompanying prospectus or of any sale of our common stock. It is important for you to read and consider all information contained in this prospectus supplement and the accompanying prospectus, including the documents incorporated by reference herein and therein, in making your investment decision. You should also read and consider the information in the documents to which we have referred you in the sections entitled “Where You Can Find More Information” and “Incorporation of Certain Information by Reference” in this prospectus supplement and in the accompanying prospectus.

This prospectus supplement and the accompanying prospectus do not constitute an offer to sell, or a solicitation of an offer to purchase, the securities offered by this prospectus supplement and the accompanying prospectus in any jurisdiction to or from any person to whom or from whom it is unlawful to make such offer or solicitation of an offer in such jurisdiction. We are offering to sell, and seeking offers to buy, shares of our common stock only in jurisdictions where offers and sales are permitted. The distribution of this prospectus supplement and the accompanying prospectus and the offering of the common stock in certain jurisdictions may be restricted by law. Persons outside the United States who come into possession of this prospectus supplement and the accompanying prospectus must inform themselves about, and observe any restrictions relating to, the offering of the common stock and the distribution of this prospectus supplement and the accompanying prospectus outside the United States.

Unless otherwise stated, all references in this prospectus supplement and the accompanying prospectus to we, us, our, Karyopharm, the Company and similar designations refer, collectively, to Karyopharm Therapeutics Inc., a Delaware corporation, and, where appropriate, its consolidated subsidiaries.

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The trademarks and registered trademarks of Karyopharm Therapeutics Inc. and its subsidiaries referred to herein include, but are not limited to, Karyopharm Therapeutics, our logo, our name and logo used together and

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SINE. Third-party product and company names mentioned herein may be the trademarks of their respective owners. Solely for convenience, the trademarks and trade names in this prospectus may be referred to without the ® and symbols, but such references should not be construed as any indicator that their respective owners will not assert, to the fullest extent under applicable law, their rights thereto.

No action is being taken in any jurisdiction outside the United States to permit a public offering of the securities or possession or distribution of this prospectus supplement or the accompanying prospectus in that jurisdiction. Persons who come into possession of this prospectus supplement or the accompanying prospectus in jurisdictions outside the United States are required to inform themselves about and to observe any restrictions as to this offering and the distribution of this prospectus supplement or the accompanying prospectus applicable to that jurisdiction.

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CAUTIONARY NOTE REGARDING FORWARD-LOOKING STATEMENTS

This prospectus supplement, the accompanying prospectus and the information incorporated by reference herein and therein include forward-looking statements within the meaning of Section 27A of the Securities Act of 1933, as amended, or the Securities Act, and Section 21E of the Securities Exchange Act of 1934, as amended, or the Exchange Act. All statements, other than statements of historical facts, included in this prospectus supplement, the accompanying prospectus and the information incorporated by reference herein and therein regarding our strategy, future operations, future financial position, future revenue, projected costs, prospects, plans, objectives of management and expected market growth are forward-looking statements. The words anticipate, believe, estimate, expect, intend, may, plan, predict, project, target, potential, will, would, could, should, co expressions are intended to identify forward-looking statements, although not all forward-looking statements contain these identifying words. These forward-looking statements include, among other things, statements about:

the timing, progress and results of current and future preclinical studies and clinical trials, and our research and development programs;

our plans to develop and commercialize our drug candidates;

adverse results in our drug discovery and clinical development activities;

the timing or likelihood of regulatory filings and approvals;

decisions made by the U.S. Food and Drug Administration and other regulatory authorities with respect to the development and commercialization of our drug candidates;

our commercialization, marketing and manufacturing capabilities and strategy;

our ability to obtain, maintain and enforce intellectual property rights for our drug candidates;

dependence on any collaborators we may have in the future;

our competitive position;

developments and projections relating to our competitors and our industry;

our ability to obtain any necessary financing to conduct our planned activities;

our expectations regarding the time during which we will be an emerging growth company under the Jumpstart Our Business Startups Act of 2012, or the JOBS Act;

our expectations related to the use of proceeds from this offering; and

our estimates regarding expenses, future revenue, capital requirements and needs for additional financing. 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. Actual results or events could differ materially from the plans, intentions and expectations disclosed in the forward-looking statements we make. We have included important factors in the cautionary statements included in this prospectus supplement, the accompanying prospectus, and the information incorporated by reference herein and therein, particularly in the Risk Factors section of this prospectus supplement and of our Annual Report on Form 10-K for the year ended December 31, 2016, which is incorporated by reference herein, that could cause actual results or events to differ materially from the forward-looking statements that we make. Our forward-looking statements do not reflect the potential impact of any future acquisitions, mergers, dispositions, joint ventures or investments that we may make.

You should read this prospectus supplement, the accompanying prospectus and the information incorporated by reference herein and therein completely and with the understanding that our actual future results may be materially different from what we expect. Any forward-looking statement speaks only as of the date of this prospectus supplement. 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.

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PROSPECTUS SUPPLEMENT SUMMARY

*This summary highlights selected information contained elsewhere in this prospectus supplement and the accompanying prospectus and in the documents we incorporate by reference. This summary does not contain all of the information you should consider before investing in our common stock. You should read this entire prospectus supplement and the accompanying prospectus, including the documents incorporated by reference herein and therein, carefully, especially the risks of investing in our common stock discussed under **Risk Factors** beginning on page S-9 of this prospectus supplement and the **Risk Factors** section of our Annual Report on Form 10-K for the year ended December 31, 2016, along with our consolidated financial statements and notes to those consolidated financial statements, before making an investment decision.*

Karyopharm Therapeutics Inc.

Overview

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

Our initial focus is on seeking the regulatory approval and commercialization of our lead drug candidate, selinexor (KPT-330), as an oral agent in cancer indications with significant unmet clinical need, initially for hematologic malignancies. We then plan to seek additional approvals for the use of selinexor in combination therapies to expand the patient populations that are eligible for selinexor, as well as to move selinexor towards front-line cancer therapy. We are also advancing the clinical development of selinexor in multiple solid tumor indications. To date, over 1,900 patients have been treated with oral selinexor in company- and investigator-sponsored clinical trials in advanced hematologic malignancies and solid tumors. Selinexor is currently being evaluated in several mid- and later-stage clinical trials, including, among others, the Phase 2b STORM (**S**elinexor **T**reatment **o**f **R**efractory **M**yeloma) study in multiple myeloma, the Phase 1b/2 STOMP (**S**elinexor and Backbone **T**reatments **o**f **M**ultiple Myeloma **P**atients) study in combination with backbone therapies in multiple myeloma, the Phase 2b SADAL (**S**elinexor **A**gainst **D**iffuse **A**ggressive **L**ymphoma) study in diffuse large B-cell lymphoma (DLBCL), and the Phase 2/3 SEAL (**S**elinexor in **A**dvanced **L**iposarcoma) study in liposarcoma.

We plan to initiate the pivotal, randomized Phase 3 BOSTON (**B**ortezomib, **S**elinexor and **D**examethasone) study in multiple myeloma in May 2017. We expect to provide final topline data for the SADAL study in mid-2018, topline data for the Phase 2 portion of the SEAL study in mid-2017 and topline data from the expanded cohort for the STORM study in early 2018. We are also preparing to establish the commercial infrastructure to support a potential launch of selinexor in North America and Western Europe. We intend to enter into collaborations for further development, marketing and commercialization of selinexor in particular geographies outside of North America and Western Europe at an appropriate time.

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. To date, we have financed our operations principally through private placements of our preferred stock and proceeds from our

initial public offering, follow-on offerings of common stock and at-the-market offerings.

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Certain Preliminary Financial Results and Recent Developments

As of March 31, 2017, we had approximately \$150.6 million in cash, cash equivalents, restricted cash and short- and long-term investments. This amount is unaudited and preliminary, is subject to completion of financial closing procedures that could result in changes to the amount, and does not present all information necessary for an understanding of our financial condition as of March 31, 2017.

On November 7, 2016, we entered into Amendment No. 1 to the Controlled Equity OfferingSM Sales Agreement, dated December 7, 2015, with Cantor Fitzgerald & Co., as agent, to which we refer, as so amended, as our Sales Agreement. Under the Sales Agreement, from time to time, we may issue and sell shares of our common stock having an additional aggregate offering price of up to \$50.0 million, of which approximately \$31.3 million remains available as of April 24, 2017. Since November 7, 2016, we have issued and sold a total of 1,677,185 shares of our common stock under the Sales Agreement for gross proceeds of approximately \$18.7 million, of which 401,168 shares were issued between November 7, 2016 and December 31, 2016 for gross proceeds of approximately \$3.9 million and 1,276,017 shares were issued after March 31, 2017 for gross proceeds of approximately \$14.8 million.

Company Information

We were incorporated under the laws of the State of Delaware in December 2008. Our executive offices are located at 85 Wells Avenue, 2nd Floor, Newton, Massachusetts 02459, and our telephone number is (617) 658-0600. Our website address is www.karyopharm.com. The information contained in, or accessible through, our website does not constitute part of this prospectus supplement. We have included our website address in this prospectus supplement solely as an inactive textual reference.

Implications of Being an Emerging Growth Company

As a company with less than \$1 billion in revenue during our last fiscal year, we qualify as an emerging growth company as defined in the JOBS Act. As an emerging growth company, we may take advantage of specified reduced disclosure and other requirements that are otherwise applicable generally to public companies. These provisions include:

reduced disclosure about our executive compensation arrangements;

exemption from holding the non-binding advisory votes on executive compensation, including golden parachute arrangements; and

exemption from the auditor attestation requirement in the assessment of our internal controls over financial reporting.

We have taken advantage of certain reduced reporting burdens in this prospectus supplement, the accompanying prospectus and the information incorporated by reference herein and therein. Accordingly, the information contained herein and therein may be different than the information you receive from other public companies in which you hold stock.

We will remain an emerging growth company until the earliest of (i) the last day of the fiscal year in which we have total annual gross revenues of \$1.07 billion or more; (ii) December 31, 2018; (iii) the date on which we have issued more than \$1.0 billion in nonconvertible debt during the previous three years; or (iv) the date on which we are deemed to be a large accelerated filer under the rules of the SEC based on the market value of our common stock held by non-affiliates.

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

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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, are subject to the same new or revised accounting standards as other public companies that are not emerging growth companies.

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THE OFFERING

Common stock offered by us	3,902,439 shares
Common stock to be outstanding after this offering	45,790,268 shares
Option to purchase additional shares	We have granted the underwriter an option for a period of 30 days to purchase up to an additional 585,365 shares of our common stock.
Use of Proceeds	<p>We estimate that the net proceeds to us from the shares sold by us to the underwriter in this offering, after deducting the underwriting discounts and commissions and estimated offering expenses payable by us, will be approximately \$37.8 million. We currently intend to use the net proceeds from this offering:</p> <p>to support continued clinical development of selinexor in multiple myeloma, lymphoma and other oncology indications as a single agent and in combination with other therapies, including in combination with existing therapies in solid tumors and hematologic malignancies;</p> <p>for early clinical trials of two of our pipeline drug candidates in oncology, KPT-8602, a second generation SINE compound, and KPT-9274, a dual acting p21-activated kinase 4, or PAK4, Allosteric Modulator and nicotinamide phosphoribosyltransferase, or NAMPT, inhibitor;</p> <p>to continue preparing to establish the commercial infrastructure for the potential launch of selinexor in North America and Western Europe; and</p> <p>for working capital and other general corporate purposes.</p>

See Use of Proceeds for more information.

Risk Factors

Investing in our common stock involves a high degree of risk. You should read the Risk Factors section of this prospectus supplement, as well as those risk factors that are incorporated by reference in this prospectus supplement and the accompanying prospectus, for a discussion of factors to consider carefully before deciding to purchase shares of our common stock.

NASDAQ Global Select Market symbol

KPTI

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The number of shares of our common stock to be outstanding after this offering is based on 41,887,829 shares of our common stock issued and outstanding as of December 31, 2016 and excludes:

5,574,179 shares of our common stock issuable upon the exercise of stock options outstanding as of December 31, 2016, at a weighted-average exercise price of \$16.55 per share;

214,300 shares of our common stock issuable upon the vesting of restricted stock units outstanding as of December 31, 2016;

689,615 and 491,093 shares of our common stock available for future issuance, as of December 31, 2016, under our 2013 stock incentive plan and our 2013 employee stock purchase plan, respectively; and

1,276,017 shares of common stock issued and sold after December 31, 2016, pursuant to our Controlled Equity OfferingSM Sales Agreement with Cantor Fitzgerald & Co.

Unless otherwise indicated, this prospectus supplement reflects and assumes the following:

no exercise of outstanding stock options described above;

no purchases of shares of our common stock by our existing stockholders in this offering; and

no exercise by the underwriter of its option to purchase additional shares of our common stock.

In addition, the number of shares outstanding immediately after this offering does not include shares of common stock that we may sell in the future pursuant to our Sales Agreement. Under the Sales Agreement, from time to time, we may issue and sell shares of our common stock having an additional aggregate offering price of up to \$50.0 million, of which approximately \$31.3 million remains available as of April 24, 2017. After the expiration or waiver of the 60-day lock-up period applicable to us and described under the section of this prospectus supplement entitled

Underwriting, we may issue and sell shares of our common stock having aggregate sales proceeds of up to \$31.3 million from time to time in such amounts as we may determine, subject to certain limitations under applicable securities laws, under our Sales Agreement.

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RISK FACTORS

*Investing in our common stock involves a high degree of risk. Before investing in our common stock, you should consider carefully the risks described below and under the heading **Risk Factors** in our Annual Report on Form 10-K for the year ended December 31, 2016, filed with the Securities and Exchange Commission, or SEC, on March 16, 2017, which is incorporated by reference into this prospectus supplement, together with the other information contained in this prospectus supplement, the accompanying prospectus and in our other filings with the SEC that we have incorporated by reference in this prospectus supplement and the accompanying prospectus. If any of these risks occur, our business, financial condition, results of operations and future growth prospects could be materially and adversely affected. In these circumstances, the market price of our common stock could decline, and you may lose all or part of your investment.*

Risks Related to Our Common Stock and This Offering

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

As of December 31, 2016, our executive officers, directors and a small number of stockholders own more than a majority of our outstanding common stock. As a result, if these stockholders were to choose to act together, they would be able to control all matters submitted to our stockholders for approval, as well as our management and affairs. For example, these persons, if they choose to act together, would control the election of directors and approval of any merger, consolidation or sale of all or substantially all of our assets. This concentration of voting power could delay or prevent an acquisition of our company on terms that other stockholders may desire.

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

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

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

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

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

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

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

limit who may call stockholder meetings;

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

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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 you purchase shares of common stock in this offering, you will suffer immediate and substantial dilution in the book value of your investment.

The price per share of our common stock in this offering may exceed the net tangible book value per share of our common stock outstanding prior to this offering. Therefore, if you purchase shares of our common stock in this offering, you may pay a price per share that substantially exceeds our net tangible book value per share after this offering. To the extent shares are issued under outstanding options at exercise prices lower than the price of our common stock in this offering, you will incur further dilution. See the section entitled **Dilution** below for a more detailed illustration of the dilution you would incur if you participate in this offering.

You may experience future dilution as a result of future equity offerings.

In order to raise additional capital, we may in the future offer additional shares of our common stock or other securities convertible into or exchangeable for our common stock at prices that may not be the same as the price per share in this offering. We may sell shares or other securities in any other offering at a price per share that is less than the price per share paid by investors in this offering, and investors purchasing shares or other securities in the future could have rights superior to existing stockholders. The price per share at which we sell additional shares of our common stock, or securities convertible or exchangeable into common stock, in future transactions may be higher or lower than the price per share paid by investors in this offering. In addition, on November 7, 2016, we entered into Amendment No. 1 to the Controlled Equity OfferingSM Sales Agreement, dated December 7, 2015, with Cantor Fitzgerald & Co., as agent, which we refer to, as so amended, as our Sales Agreement, under which we may issue and sell from time to time through Cantor Fitzgerald & Co. shares of our common stock, in an aggregate amount not to exceed \$50 million, of which approximately \$31.3 million remains available as of April 24, 2017, after the expiration or waiver of the 60-day lock-up period applicable to us and described under the section of this prospectus supplement entitled **Underwriting**. To the extent that we sell shares of our common stock pursuant to our Sales Agreement with Cantor Fitzgerald & Co., investors purchasing shares of common stock in this offering could experience further dilution.

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

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

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

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

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

Our stock price has been and is likely to be volatile and may fluctuate substantially. For example, since January 1, 2015, our common stock has traded at prices per share as high as \$38.47 and as low as \$4.83. 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 have broad discretion in the use of our cash and cash equivalents, including the net proceeds we receive in this offering, and may not use them effectively.

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

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

We are an emerging growth company, as defined in the JOBS Act, and may remain an emerging growth company through 2018. For so long as we remain an emerging growth company, we are permitted and intend to rely on exemptions from certain disclosure requirements that are applicable to other public companies that are

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

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

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

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

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

Pursuant to Section 404, we are required to furnish a report by our management on our internal control over financial reporting. However, while we remain an emerging growth company, we are not required to include an attestation report on internal control over financial reporting issued by our independent registered public accounting firm. To achieve compliance with Section 404 within the prescribed period, we are engaged in a process to document and evaluate our internal control over financial reporting, which is both costly and challenging. In this regard, we will need to continue to dedicate internal resources, potentially engage outside consultants and adopt a detailed work plan to assess and document the adequacy of internal control over financial reporting, continue steps to improve control processes as appropriate, validate through testing that controls are functioning as documented and implement a continuous reporting and improvement process for internal control over financial reporting. There is a risk that neither we nor our independent registered public accounting firm will be able to conclude within the prescribed timeframe that our internal control over financial reporting is effective as required by Section 404. This could result in an adverse reaction in the financial markets due to a loss of confidence in the reliability of our financial statements. In addition, if we identify one or more material weaknesses, it could result in an adverse reaction in the financial markets due to a

loss of confidence in the reliability of our financial statements.

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

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

Sales of a significant number of shares of our common stock in the public markets, or the perception that such sales could occur, 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. After this offering, we will have outstanding shares of common stock based on 41,887,829 shares outstanding as of December 31, 2016 and 1,276,017 shares issued and sold under the Sales Agreement after December 31, 2016. This includes the shares that we are selling in this offering, which may be resold in the public market immediately without restriction, unless purchased by our affiliates. Of the remaining shares, approximately 12.2 million shares are subject to a contractual lock-up with the underwriter for this offering for 60 days following the date of the underwriting agreement. These shares are eligible for sale in the public market under Rule 144 of the Securities Act, subject to the volume limitations and other conditions of Rule 144, after the earlier of the expiration of, or release from, the lock-up period. The holders of these shares may at any time decide to sell their shares in the public market

Moreover, holders of an aggregate of approximately 11.7 million shares of our common stock as of December 31, 2016 have rights, subject to some conditions, to require us to file registration statements covering their shares or to include their shares in registration statements that we may file for ourselves or other stockholders. We have also registered all shares of common stock that we may issue under our equity compensation plans. As a result, these shares can be freely sold in the public market upon issuance, subject to volume limitations applicable to affiliates and the lock-up agreements described above, to the extent applicable.

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

Under the provisions of the Internal Revenue Code of 1986, as amended, or the Code, our net operating loss and tax credit carryforwards are subject to review and possible adjustment by the Internal Revenue Service (and state tax authorities under relevant state tax rules). The use of net operating loss and tax credit carryforwards may become subject to an annual limitation under Sections 382 and 383 of the Code, respectively, and similar state provisions in the event of certain cumulative changes in the ownership interest of significant shareholders in excess of 50 percent over a three-year period. This could limit the amount of tax attributes that can be utilized annually to offset future taxable income or tax liabilities. The amount of the annual limitation is determined based on the value of a company immediately prior to the ownership change. Subsequent ownership changes may further affect the limitation in future years. Our company has completed several financings since its inception which resulted in an ownership change under Sections 382 and 383 of the Code. In addition, future changes in our stock ownership, including in connection with this offering, some of which are outside of our control, could result in ownership changes in the future. For these reasons, we may not be able to use some or all of our net operating loss and tax credit carryforwards, even if we attain profitability prior to the expiration of our net operating loss and tax credit carryforwards.

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USE OF PROCEEDS

We estimate that the net proceeds from the sale of shares of common stock to the underwriter in this offering will be approximately \$37.8 million (\$43.5 million if the underwriter's option to purchase additional shares is exercised in full), after deducting the underwriting discounts and commissions and estimated offering expenses payable by us.

We currently intend to use the net proceeds from this offering:

to support continued clinical development of selinexor in multiple myeloma, lymphoma and other oncology indications as a single agent and in combination with other therapies, including in combination with existing therapies in solid tumors and hematologic malignancies;

for early clinical trials of two of our pipeline drug candidates in oncology, KPT-8602, a second generation SINE compound, and KPT-9274, a dual acting PAK4 Allosteric Modulator and NAMPT inhibitor;

to continue preparing to establish the commercial infrastructure for the potential launch of selinexor in North America and Western Europe; and

for working capital and other general corporate purposes.

The expected use of net proceeds from this offering represents our intentions based upon our current plans and business conditions, which could change in the future as our plans and business conditions evolve. The amounts and timing of our actual expenditures may vary significantly depending on numerous factors, including the progress of our development, feedback from regulatory authorities, the status of and results from clinical trials, as well as any collaborations that we may enter into with third parties for our drug candidates, and any unforeseen cash needs. As a result, our management will retain broad discretion over the allocation of the net proceeds from this offering. We may find it necessary or advisable to use the net proceeds from this offering for other purposes, and we will have broad discretion in the application of net proceeds.

Pending use of the proceeds as described above, we intend to invest the proceeds in a variety of capital preservation investments, including short-term, interest-bearing instruments, investment-grade and U.S. government securities.

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If you invest in this offering, your ownership interest will be diluted immediately to the extent of the difference between the public offering price per share and the as-adjusted net tangible book value per share of our common stock after giving effect to this offering. We calculate net tangible book value per share by dividing the net tangible book value, which is tangible assets less total liabilities, by the number of outstanding shares of our common stock. Dilution represents the difference between the portion of the amount per share paid by purchasers of shares in this offering and the as adjusted net tangible book value per share of our common stock immediately after giving effect to this offering. Our net tangible book value as of December 31, 2016 was approximately \$162.2 million, or \$3.87 per share.

After giving effect to the sale of 3,902,439 shares of our common stock pursuant to this prospectus supplement and accompanying prospectus at the public offering price of \$10.25 per share, and after deducting commissions and estimated aggregate offering expenses payable by us, our net tangible book value as of December 31, 2016 would have been \$200.0 million, or \$4.37 per share of common stock. This represents an immediate increase in the net tangible book value of \$0.50 per share to our existing stockholders and an immediate dilution in net tangible book value of \$5.88 per share to new investors. The following table illustrates this per share dilution:

Public offering price per share	\$ 10.25
Net tangible book value per share as of December 31, 2016	\$ 3.87
Increase per share attributable to new investors	\$ 0.50
As adjusted net tangible book value per share as of December 31, 2016 after giving effect to this offering	\$ 4.37
Dilution per share to new investors purchasing shares in this offering	\$ 5.88

The above discussion and table are based on 41,887,829 shares of our common stock issued and outstanding as of December 31, 2016 and excludes the following:

5,574,179 shares of our common stock issuable upon the exercise of stock options outstanding as of December 31, 2016, at a weighted-average exercise price of \$16.55 per share;

214,300 shares of our common stock issuable upon the vesting of restricted stock units outstanding as of December 31, 2016;

689,615 and 491,093 shares of our common stock available for future issuance, as of December 31, 2016, under our 2013 stock incentive plan and our 2013 employee stock purchase plan, respectively; and

1,276,017 shares of common stock issued and sold after December 31, 2016, pursuant to our Controlled Equity OfferingSM Sales Agreement with Cantor Fitzgerald & Co.

To the extent that any options are exercised, new equity awards are granted under our equity incentive plans, or we otherwise issue additional shares of common stock in the future, there will be further dilution to new investors.

In addition, we may choose to raise additional capital due to market conditions or strategic considerations, even if we believe we have sufficient funds for our current or future operating plans. To the extent that additional capital is raised through the sale of equity or convertible debt securities, the issuance of these securities could result in further dilution to our stockholders.

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The following table sets forth the high and low intraday sale prices per share of our common stock, as reported on The NASDAQ Global Select Market, for the quarterly periods indicated:

	High	Low
Year ended December 31, 2015		
First Quarter	\$ 38.47	\$ 24.35
Second Quarter	\$ 35.65	\$ 24.72
Third Quarter	\$ 27.70	\$ 10.00
Fourth Quarter	\$ 19.41	\$ 10.35
Year ended December 31, 2016		
First Quarter	\$ 13.97	\$ 4.83
Second Quarter	\$ 10.45	\$ 6.63
Third Quarter	\$ 11.41	\$ 6.54
Fourth Quarter	\$ 10.30	\$ 6.27
Year ending December 31, 2017		
First Quarter	\$ 13.84	\$ 9.64
Second Quarter (through April 24, 2017)	\$ 12.61	\$ 10.55