

PROSPECTUS SUPPLEMENT
(To Prospectus Dated April 24, 2019)



Up to \$75,000,000

Common Stock

We have entered into an Open Market Sale AgreementSM, or sales agreement, with Jefferies LLC, or Jefferies, dated August 17, 2018, relating to the sale of shares of our common stock offered by this prospectus supplement and the accompanying prospectus. In accordance with the terms of the sales agreement, under this prospectus supplement we may offer and sell shares of our common stock, \$0.0001 par value per share, having an aggregate offering price of up to \$75,000,000 from time to time through Jefferies, acting as our agent. We originally filed a prospectus supplement for the offer and sale of up to \$75,000,000 of shares of our common stock pursuant to the sales agreement under the shelf registration statement on Form S-3 (Registration Statement No. 333-226038). To continue the offer and sale of shares pursuant to the sales agreement following the amendment of the registration statement due to our no longer qualifying as a well-known seasoned issuer, we are filing this prospectus supplement to the registration statement and accompanying prospectus, dated April 24, 2019, referenced above. As of the date of this prospectus supplement, we have not sold any shares of our common stock pursuant to the sales agreement.

Sales of our common stock, if any, under this prospectus supplement and the accompanying prospectus may be made by any method permitted that is deemed an “at the market offering” as defined in Rule 415(a)(4) promulgated under the Securities Act of 1933, as amended, or the Securities Act, including sales made directly on or through The Nasdaq Global Select Market, the existing trading market for our common stock. Jefferies is not required to sell any specific amount, but will act as our sales agent using commercially reasonable efforts consistent with its normal trading and sales practices. There is no arrangement for funds to be received in any escrow, trust or similar arrangement.

Jefferies will be entitled to compensation at a commission rate of up to 3.0% of the gross sales price per share sold under the sales agreement. See “Plan of Distribution” beginning on page S-14 for additional information regarding the compensation to be paid to Jefferies. In connection with the sale of our common stock on our behalf, Jefferies will be deemed to be an “underwriter” within the meaning of the Securities Act and the compensation of Jefferies will be deemed to be underwriting commissions or discounts. We have also agreed to provide indemnification and contribution to Jefferies with respect to certain liabilities, including liabilities under the Securities Act.

INVESTING IN OUR SECURITIES INVOLVES RISKS. SEE THE “[RISK FACTORS](#)” ON PAGE S-6 OF THIS PROSPECTUS SUPPLEMENT AND IN THE DOCUMENTS INCORPORATED BY REFERENCE IN THIS PROSPECTUS SUPPLEMENT CONCERNING FACTORS YOU SHOULD CONSIDER BEFORE INVESTING IN OUR COMMON STOCK.

Our common stock is listed on The Nasdaq Global Select Market under the symbol “KPTL.” On May 9, 2019, the closing sale price of our common stock on The Nasdaq Global Select Market was \$4.63 per share.

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.

Jefferies

The date of this prospectus supplement is May 10, 2019.

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ABOUT THIS PROSPECTUS SUPPLEMENT

This prospectus supplement and the accompanying prospectus relate to the offering of our common stock. Before buying any of the common stock that we are offering, we urge you to carefully read this prospectus supplement and the accompanying prospectus, together with the information incorporated by reference as described under the heading “Incorporation of Certain Information by Reference” in this prospectus supplement. These documents contain important information that you should consider when making your investment decision.

This document is in two parts. The first part is this prospectus supplement, which describes the specific terms of the common stock we are offering and also adds to and updates information contained in the accompanying prospectus and the documents incorporated by reference herein or therein. 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 herein or 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 or in the accompanying prospectus 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 agreement, 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.

You should rely only on the information contained in, or incorporated by reference in this prospectus supplement, the accompanying prospectus and in any free writing prospectus that we may authorize for use in connection with this offering. We have not, and Jefferies has not, authorized anyone to provide any information other than that contained or incorporated by reference in this prospectus supplement, in the accompanying prospectus or in any free writing prospectus prepared by or on behalf of us or to which we have referred you. We and Jefferies take no responsibility for, and can provide no assurance as to the reliability of, any other information that others may give you. We are not, and Jefferies is not, making an offer to sell, or soliciting 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. The information contained in this prospectus supplement, the accompanying prospectus, the documents incorporated by reference herein or therein, and in any free writing prospectus prepared by or on behalf of us that we may authorize for use in connection with this filing is accurate only as of the date of those respective documents. Our business, financial condition, results of operations and prospectus may have changed since those dates. It is important for you to read and consider all information contained in this prospectus supplement, the accompanying prospectus, the documents incorporated by reference herein and therein, and any free writing prospectus prepared by or on behalf of us that we may authorize for use in connection with this offering, in their entirety, before making an 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.

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

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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. This prospectus supplement and the accompanying prospectus do not constitute, and may not be used in connection with, an offer to sell, or a solicitation of an offer to buy, any securities offered by this prospectus supplement and the accompanying prospectus by any person in any jurisdiction in which it is unlawful for such person to make such an offer or solicitation.

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.

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 and our name and logo used together. Third-party product and company names mentioned herein may be the trademarks of their respective owners.

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 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,” “continue” and similar 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 preclinical 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 our collaborators;
- our intellectual property position;
- 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 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 Part II, Item 1A “Risk Factors” of our most recent quarterly report on Form 10-Q filed with the Securities and Exchange Commission, or the SEC, on May 9, 2019, which are incorporated by reference in this prospectus supplement, and in the “Risk Factors” section of this prospectus supplement, 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.

PROSPECTUS SUPPLEMENT SUMMARY

This summary highlights certain information about us, this offering and selected information contained elsewhere in this prospectus supplement and the accompanying prospectus and in the documents we incorporate by reference. This summary is not complete and does not contain all of the information you should consider before investing in our common stock. For a more complete understanding of our company and this offering, you should carefully read this entire prospectus supplement and the accompanying prospectus, including the information incorporated herein and therein and any free writing prospectus that we may authorize for use in connection with this offering, including the “Risk Factors” section beginning on page S-6 of this prospectus supplement and in Part II, Item 1A “Risk Factors” of our quarterly report on Form 10-Q filed with the SEC on May 9, 2019, which is incorporated by reference in this prospectus supplement, along with our consolidated financial statements and notes to those consolidated financial statements and the other documents incorporated by reference in this prospectus supplement and the accompanying prospectus.

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 **Selective Inhibitor of Nuclear Export (SINE)** compounds that inhibit the nuclear export protein exportin 1 (XPO1). These SINE compounds represent a new class of drug candidates with a novel mechanism of action that have the potential to treat a variety of diseases in areas of unmet medical need. Our SINE compounds were the first oral XPO1 inhibitors in clinical development.

Our focus is on seeking the regulatory approval and commercialization of our lead drug candidate, selinexor (KPT-330), as an oral agent in cancer indications with significant unmet clinical need, initially for hematologic malignancies. We then plan to seek additional approvals for the use of selinexor in combination therapies to expand the patient populations that are eligible for selinexor, as well as to move selinexor towards front-line cancer therapy. We are also advancing the clinical development of selinexor in multiple solid tumor indications. Oral selinexor is being evaluated in company- and investigator-sponsored clinical trials in advanced hematologic malignancies and solid tumors. Clinical trials evaluating selinexor include the Phase 2b STORM (**S**elinexor **T**reatment **o**f **R**efractory **M**yeloma) study in multiple myeloma, the Phase 1b/2 STOMP (**S**elinexor and Backbone **T**reatments **o**f **M**ultiple Myeloma **P**atients) study in combination with standard therapies in multiple myeloma, the Phase 2b SADAL (**S**elinexor **A**gainst **D**iffuse **A**ggressive **L**ymphoma) study in diffuse large B-cell lymphoma (DLBCL), the pivotal, randomized Phase 3 BOSTON (**B**ortezomib, **S**elinexor and **D**examethasone) study in multiple myeloma, the Phase 2/3 SEAL (**S**elinexor in **A**dvanced **L**iposarcoma) study in liposarcoma and the Phase 3 SIENDO (**S**elinexor/Placebo After Combination Chemotherapy **I**n Patients with advanced or recurrent **E**NDOMETRIAL cancer). During 2018, we reported positive top-line data from the STORM and SADAL studies as well as updated interim data for the STOMP and SEAL studies. As a result of the positive top-line results from the STORM and SADAL studies, we are pursuing or plan to pursue marketing approvals for selinexor in the United States and Europe.

Following the positive outcome from the expanded cohort for the STORM study, in August 2018, we announced the completion of the rolling submission of a New Drug Application (NDA) to the U.S. Food and Drug Administration (FDA) with a request for accelerated approval for selinexor as a new treatment for patients based on the results of the STORM study in penta-refractory multiple myeloma. Patients with penta-refractory multiple myeloma have previously received the two proteasome inhibitors (PIs), Velcade® (bortezomib) and Kyprolis® (carfilzomib), the two immunomodulatory drugs (IMiDs), Revlimid® (lenalidomide) and Pomalyst®

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(pomalidomide), and the anti-CD38 monoclonal antibody Darzalex® (daratumumab), as well as alkylating agents; their disease is refractory to glucocorticoids, at least one PI and at least one IMiD, Darzalex®; and their disease has progressed following their most recent therapy. The FDA previously granted orphan drug designation and fast track designation to selinexor for the treatment of patients with penta-refractory multiple myeloma. In October 2018, the FDA accepted for filing our NDA and also granted our request for priority review of the NDA and assigned an action date of April 6, 2019 under the Prescription Drug User Fee Act (PDUFA).

In February 2019, the FDA convened its Oncologic Drugs Advisory Committee (ODAC) to review data supporting our NDA requesting accelerated approval of selinexor and hold an advisory vote. The proposed indication discussed at the ODAC meeting was for selinexor in combination with dexamethasone for the treatment of patients with refractory multiple myeloma who have received at least three prior therapies and whose disease is refractory to at least one PI, one IMiD, and one anti-CD38 monoclonal antibody. During the ODAC meeting, the FDA presented issues of concern, including the limitations of single arm studies, especially those involving the combination of two agents, the toxicities associated with selinexor therapy and whether the selinexor dose has been optimized. The ODAC recommended by a vote of eight to five that the FDA delay the approval of selinexor until the results of the randomized Phase 3 BOSTON study in multiple myeloma are available. We are working with the FDA as it continues to review our NDA requesting accelerated approval of selinexor. In March 2019, the FDA extended the PDUFA action date from April 6, 2019 until July 6, 2019. We submitted additional, existing clinical information as an amendment to the NDA, which allowed the FDA to extend the PDUFA action date by three months.

Provided that marketing approval is granted by the FDA, we plan to commercialize selinexor in the United States as a treatment of patients in the approved indication in mid-2019. We are completing the development of our U.S. commercial capabilities to support a potential launch of selinexor in the United States and recently hired our U.S. sales force and expanded our marketing and market access teams. We will either work with existing and potential partners to establish a commercial infrastructure outside the United States or may, in certain geographies, elect to establish the commercial infrastructure ourselves.

We also announced the submission of a Marketing Authorization Application to the European Medicines Agency (EMA) in January 2019 with a request for conditional approval based on the results of the STORM study. The EMA's Committee for Medicinal Products for Human Use (CHMP) granted accelerated assessment for the selinexor Marketing Authorization Application (MAA). As a customary part of the MAA review process, we received the consolidated list of questions from EMA in early May 2019 and anticipate receiving additional feedback based on routine site audits and other activities. We plan to promptly address the questions and feedback with EMA. To provide adequate time to evaluate the application and allow us to respond to questions and feedback, the EMA has switched from an accelerated review to a traditional review. We expect to receive a decision on the application by the end of 2019.

Based on the positive results of the SADAL study, we plan to submit an NDA to the FDA with a request for accelerated approval for selinexor as a new treatment for patients with relapsed and/or refractory DLBCL after at least two prior multi-agent therapies and who are ineligible for stem cell transplantation (high dose chemotherapy with stem cell rescue), including chimeric antigen receptor modified T (CAR-T) cell therapy. In November 2018, the FDA granted fast track designation to selinexor for the treatment of patients that have relapsed and/or refractory DLBCL after at least two prior multi-agent therapies and who are ineligible for transplantation, including high dose chemotherapy with stem cell rescue. We also plan to submit a MAA to the EMA with a request for conditional approval. We anticipate filing the NDA and MAA between the end of 2019 and the end of the first half of 2020.

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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.

The Offering	
Common stock offered by us	Shares of our common stock having an aggregate offering price of up to \$75,000,000.
Common stock to be outstanding after this offering	Up to 16,198,704 shares, assuming sales at a price of \$4.63 per share, which was the closing price of our common stock on The Nasdaq Global Select Market on May 9, 2019. The actual number of shares issued will vary depending on the sales price under this offering.
Manner of offering	“At the market offering” that may be made from time to time on The Nasdaq Global Select Market, the existing trading market for our common stock, through our agent, Jefferies LLC. See the section entitled “Plan of Distribution” on page S-14 of this prospectus supplement.
Use of proceeds	<p>We currently intend to use the net proceeds from this offering:</p> <ul style="list-style-type: none">• to maintain and grow the infrastructure to support the potential commercial launch of selinexor in the United States, including further developing our sales, marketing and market access functions along with related general and administrative capabilities;• to support continued clinical development of selinexor, including in our BOSTON study and other current and planned pivotal studies, in hematologic malignancies and solid tumors;• to conduct ongoing activities to support regulatory submissions for oral selinexor as a potential new treatment for patients with multiple myeloma based on the results of the STORM study and as a potential new treatment for patients with diffuse large B-cell lymphoma based on the results of the SADAL study;• for conducting clinical trials of two of our pipeline drug candidates in oncology, eltanexor, a second-generation SINE compound, and KPT-9274, a dual acting p21-activated kinase 4 (PAK4) allosteric modulator and nicotinamide phosphoribosyltransferase (NAMPT) inhibitor; and• for working capital and other general corporate purposes. <p>See the section entitled “Use of Proceeds” on page S-11 of this prospectus supplement.</p>
Risk factors	See “Risk Factors” beginning on page S-6 of this prospectus supplement and the other information included in, or incorporated by reference into, this prospectus supplement for a discussion of certain factors you should carefully consider before deciding to invest in 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 60,864,445 shares of our common stock issued and outstanding as of March 31, 2019 and excludes:

- 10,519,696 shares of our common stock issuable upon the exercise of stock options outstanding as of March 31, 2019, at a weighted-average exercise price of \$12.76 per share;
- 949,600 shares of our common stock issuable upon the vesting of restricted stock units outstanding as of March 31, 2019; and
- 1,692,547 and 819,589 additional shares of our common stock available for future issuance, as of March 31, 2019, under our 2013 stock incentive plan and our 2013 employee stock purchase plan, respectively.

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 in Part II, Item IA “Risk Factors” of our most recent quarterly report on Form 10-Q filed with the SEC on May 9, 2019, together with the other information contained in this prospectus supplement, the accompanying prospectus and in our filings with the SEC that we have incorporated by reference in this prospectus supplement and the accompanying prospectus and in any free writing prospectus that we may authorize for use in connection with this offering. We expect to update these Risk Factors from time to time in the periodic and current reports we file with the SEC after the date of this prospectus supplement. These updated Risk Factors will be incorporated by reference in this prospectus supplement. There may be other unknown or unpredictable economic, business, competitive, regulatory or other factors that could have material adverse effects on our future results. If any of the following 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 May 9, 2019, 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 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. Assuming that an aggregate of 16,198,704 shares of our common stock are sold at a price of \$4.63 per share, the last reported sale price of our common stock on The Nasdaq Global Select Market on May 9, 2019, for aggregate proceeds to us of \$73.3 million after deducting commissions and estimated aggregate offering expenses payable by us, you will experience immediate dilution of \$2.10 per share, representing the difference between our as adjusted net tangible book value per share as of March 31, 2019 after giving effect to this offering and the assumed offering price. 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.

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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Sales of a significant number of shares of our common stock in the public markets, or the perception that such sales could occur, could depress the market price of our common stock.

Sales of a substantial number of shares of our common stock in the public markets, or the perception that such sales could occur, could depress the market price of our common stock and impair our ability to raise capital through the sale of additional equity securities. We have agreed, without the prior written consent of Jefferies and subject to certain exceptions set forth in the sales agreement, not to sell or otherwise dispose of any common stock or securities convertible into or exchangeable for shares of common stock, warrants or any rights to purchase or acquire common stock during the period beginning on the fifth trading day immediately prior to the delivery of any placement notice delivered by us to Jefferies and ending on the fifth trading day immediately following the final settlement date with respect to the shares sold pursuant to such notice. We have further agreed, subject to certain exceptions set forth in the sales agreement, not to sell or otherwise dispose of any common stock or securities convertible into or exchangeable for shares of common stock, warrants or any rights to purchase or acquire common stock in any other “at-the-market” or continuous equity transaction prior to the termination of the sales agreement with Jefferies. Therefore, it is possible that we could issue and sell additional shares of our common stock in the public markets. We cannot predict the effect that future sales of our common stock would have on the market price of our common stock.

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 \$3.92. On May 9, 2019, the closing sale price of our common stock on The Nasdaq Global Select Market was \$4.63 per share. The stock market in general and the market for pharmaceutical and biotechnology companies in particular have experienced extreme volatility that has often been unrelated to the operating performance of particular companies. The market price for our common stock may be influenced by many factors, including:

- the success of competitive drugs or technologies;
- results of clinical trials of our drug candidates or those of our competitors;
- our success in commercializing our drug candidates, if and when approved;
- 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 and in Part II, Item 1A “Risk Factors” of our quarterly report on Form 10-Q filed with the SEC on May 9, 2019, which are incorporated by reference into this prospectus supplement.

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

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experienced significant stock price volatility in recent years. We may also face securities class action litigation if we cannot obtain regulatory approvals for, or if we otherwise fail to commercialize, selinexor or other of our drug candidates. 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 have incurred increased costs as a result of operating as a public company, and our management is required to devote substantial time to compliance initiatives and corporate governance practices.

As a public company, we 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 devote a substantial amount of time to these compliance initiatives. Moreover, these rules and regulations have increased our legal and financial compliance costs and have made some activities more time-consuming and costly especially since we are no longer an "emerging growth company," as defined in the Jumpstart Our Business Startups Act of 2012, and are no longer able to take advantage of certain exemptions from various reporting requirements that are applicable to public companies that are "emerging growth companies" and that were applicable to us prior to January 1, 2019.

Section 404 of the Sarbanes-Oxley Act of 2002 requires us, on an annual basis, to review and evaluate our internal controls. To maintain compliance with Section 404, we are required to document and evaluate our internal control over financial reporting, which has been both costly and challenging. We will need to continue to dedicate internal resources, continue to engage outside consultants and follow a detailed work plan to continue to assess and document the adequacy of internal control over financial reporting, continue 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 in the future 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. If we identify one or more material weaknesses, it could result in an adverse reaction in the financial markets due to a loss of confidence in the reliability of our financial statements.

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

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

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

Sales of a substantial number of shares of our common stock in the public market could occur at any time. These sales, or the perception in the market that the holders of a large number of shares intend to sell shares, could reduce the market price of our common stock. We had 60,864,445 shares outstanding as of March 31, 2019. Of such shares, at least 7.8 million shares are eligible for sale in the public market under Rule 144 of the Securities Act of 1933, as amended, or the Securities Act, subject to the volume limitations and other conditions of Rule 144. The holders of these shares may at any time decide to sell their shares in the public market. We have also registered all shares of common stock that we may issue under our equity compensation plans. As a result, these shares can be freely sold in the public market upon issuance, subject to volume limitations applicable to affiliates, to the extent applicable.

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

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

USE OF PROCEEDS

Except as described in any free writing prospectus that we may authorize to be provided to you, we currently intend to use the net proceeds from this offering:

- to maintain and grow the infrastructure to support the potential commercial launch of selinexor in the United States, including further developing our sales, marketing and market access functions along with related general and administrative capabilities;
- to support continued clinical development of selinexor, including in our BOSTON study and other current and planned pivotal studies, in hematologic malignancies and solid tumors;
- to conduct ongoing activities to support regulatory submissions for oral selinexor as a potential new treatment for patients with multiple myeloma based on the results of the STORM study and as a potential new treatment for patients with diffuse large B-cell lymphoma based on the results of the SADAL study;
- for conducting clinical trials of two of our pipeline drug candidates in oncology, eltanexor, a second-generation SINE compound, and KPT-9274, a dual acting PAK4 allosteric modulator and NAMPT inhibitor; 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.

DILUTION

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 March 31, 2019 was approximately \$121.3 million, or \$1.99 per share.

After giving effect to the sale of our common stock pursuant to this prospectus supplement and accompanying prospectus in the aggregate amount of \$75 million at an assumed offering price of \$4.63 per share, the last reported sale price of our common stock on The Nasdaq Global Select Market on May 9, 2019, and after deducting commissions and estimated aggregate offering expenses payable by us, our net tangible book value as of March 31, 2019 would have been \$194.6 million, or \$2.53 per share of common stock. This represents an immediate increase in the net tangible book value of \$0.54 per share to our existing stockholders and an immediate dilution in net tangible book value of \$2.10 per share to new investors. The following table illustrates this per share dilution:

Assumed offering price per share	\$4.63
Net tangible book value per share as of March 31, 2019	\$1.99
Increase per share attributable to new investors	<u>\$0.54</u>
As-adjusted net tangible book value per share as of March 31, 2019 after giving effect to this offering	\$2.53
Dilution per share to new investors purchasing shares in this offering	<u>\$2.10</u>

The table above assumes for illustrative purposes that an aggregate of 16,198,704 shares of our common stock are sold pursuant to this prospectus supplement and the accompanying prospectus at a price of \$4.63 per share, the last reported sale price of our common stock on The Nasdaq Global Select Market on May 9, 2019, for aggregate gross proceeds of \$75 million. The shares sold in this offering, if any, will be sold from time to time at various prices. An increase of \$1.00 per share in the price at which the shares are sold from the assumed offering price to \$5.63 per share, assuming all of our common stock in the aggregate amount of \$75 million is sold at that price, would result in an adjusted net tangible book value per share after the offering of \$2.62 per share and would increase the dilution in net tangible book value per share to new investors in this offering to \$3.01 per share, after deducting commissions and estimated aggregate offering expenses payable by us. A decrease of \$1.00 per share in the price at which the shares are sold from the assumed offering price to \$3.63 per share, assuming all of our common stock in the aggregate amount of \$75 million is sold at that price, would result in an adjusted net tangible book value per share after the offering of \$2.39 per share and would decrease the dilution in net tangible book value per share to new investors in this offering to \$1.24 per share, after deducting commissions and estimated aggregate offering expenses payable by us. This information is supplied for illustrative purposes only.

The above discussion and table are based on 60,864,445 shares of our common stock issued and outstanding as of March 31, 2019 and excludes the following:

- 10,519,696 shares of our common stock issuable upon the exercise of stock options outstanding as of March 31, 2019, at a weighted-average exercise price of \$12.76 per share;
- 949,600 shares of our common stock issuable upon the vesting of restricted stock units outstanding as of March 31, 2019; and
- 1,692,547 and 819,589 additional shares of our common stock available for future issuance, as of March 31, 2019, under our 2013 stock incentive plan and our 2013 employee stock purchase plan, respectively.

DIVIDEND POLICY

We have not declared or paid any cash dividends on our capital stock since our inception. We currently intend to retain future earnings, if any, to finance the operation and expansion of our business and do not anticipate paying any cash dividends in the foreseeable future. Payment of future dividends, if any, will be at the discretion of our board of directors and will depend on our financial condition, results of operations, capital requirements, restrictions contained in current or future financing instruments, provisions of applicable law and other factors the board deems relevant.

PLAN OF DISTRIBUTION

We have entered into a sales agreement with Jefferies under which we may issue and sell shares of our common stock from time to time through the third anniversary of the effective date of such agreement up to an aggregate sales price of \$75,000,000 through Jefferies. The sales agreement is filed with the SEC and incorporated by reference into the registration statement of which this prospectus supplement is a part. Sales of our common stock, if any, under this prospectus supplement will be made by any method that is deemed an “at the market offering” as defined in Rule 415(a) (4) under the Securities Act, including sales made directly on or through The Nasdaq Global Select Market, the existing trading market for our common stock.

When requested by us, Jefferies will offer the shares of common stock subject to the terms and conditions of the sales agreement, which may be on a daily basis for periods of time, or as we may otherwise agree with Jefferies. We will designate the maximum amount of shares of common stock to be sold through Jefferies when we request Jefferies to do so. Jefferies has agreed, subject to the terms and conditions of the sales agreement, to use its commercially reasonable efforts to execute our orders to sell, as our sales agent and on our behalf, shares of our common stock submitted to Jefferies from time to time by us, consistent with its normal sales and trading practices. We may instruct Jefferies not to place shares of common stock at or below a price designated by us. We or Jefferies may suspend the offering of shares of common stock under the sales agreement upon proper notice to the other party.

We will pay Jefferies a commission of up to 3.0% of the gross proceeds of any shares sold through it pursuant to this prospectus supplement, and reimburse Jefferies for up to \$50,000 of its expenses, including fees and disbursements to its legal counsel. The estimated offering expenses payable by us, in addition to such commission and expenses, are approximately \$120,000, which includes legal, accounting and printing costs and various other fees associated with registering the shares of common stock. The remaining sale proceeds, after deducting any other transaction fees, will equal our net proceeds from the sale of such shares.

Jefferies will provide written confirmation to us before the open on The Nasdaq Global Select Market on the day following each day on which shares of common stock are sold under the sales agreement. Each confirmation will include the number of shares sold on that day, the aggregate gross proceeds of such sales and the proceeds to the Company. Settlement for sales of common stock will occur, unless otherwise agreed, on the third business day following the date on which such sales were made.

In connection with the sale of our common stock on our behalf, Jefferies will be deemed to be an “underwriter” within the meaning of the Securities Act and the compensation of Jefferies will be deemed to be underwriting commissions or discounts. We have agreed to indemnify Jefferies against certain liabilities, including liabilities under the Securities Act. We have also agreed to contribute to payments Jefferies may be required to make in respect of such liabilities.

The offering of shares of common stock pursuant to the sales agreement will terminate upon the earliest of (i) the sale of all shares of common stock subject to the sales agreement and this prospectus supplement, (ii) the termination of the sales agreement according to its terms by either Jefferies or us and (iii) August 17, 2021.

Jefferies and its affiliates may in the future provide various investment banking, commercial banking, financial advisory and other services to us and our affiliates and may in the future receive customary fees. In the course of its business, Jefferies may actively trade our securities for its own account or for the accounts of customers, and, accordingly, Jefferies may at any time hold long or short positions in such securities.

LEGAL MATTERS

The validity of the shares of common stock offered hereby will be passed upon for us by Wilmer Cutler Pickering Hale and Dorr LLP, Boston, Massachusetts. Jefferies LLC is being represented in connection with this offering by Cooley LLP, New York, New York.

EXPERTS

The consolidated financial statements of Karyopharm Therapeutics Inc. appearing in Karyopharm Therapeutics Inc.'s Annual Report (Form 10-K) for the year ended December 31, 2018, and the effectiveness of Karyopharm Therapeutics Inc.'s internal control over financial reporting as of December 31, 2018, have been audited by Ernst & Young LLP, independent registered public accounting firm, as set forth in their reports thereon, included therein, and incorporated herein by reference. Such consolidated financial statements are incorporated herein by reference in reliance upon such reports given on the authority of such firm as experts in accounting and auditing.

WHERE YOU CAN FIND MORE INFORMATION

We file annual, quarterly and current reports, proxy statements and other information with the SEC. Our SEC filings are available to the public over the Internet at the SEC's website at www.sec.gov. Copies of certain information filed by us with the SEC are also available on our website at www.karyopharm.com. Our website is not a part of this prospectus supplement and is not incorporated by reference in this prospectus supplement.

This prospectus supplement is part of a registration statement that we filed with the SEC. The registration statement contains more information than this prospectus supplement and the accompanying prospectus regarding us and the securities, including certain exhibits and schedules. You can obtain a copy of the registration statement from the SEC's website.

INCORPORATION OF CERTAIN INFORMATION BY REFERENCE

The SEC allows us to incorporate by reference in this prospectus supplement and the accompanying prospectus much of the information we file with the SEC, which means that we can disclose important information to you by referring you to those publicly available documents. The information that we incorporate by reference in this prospectus supplement and the accompanying prospectus is considered to be part of this prospectus supplement and the accompanying prospectus. Because we are incorporating by reference future filings with the SEC, this prospectus supplement and the accompanying prospectus is continually updated and those future filings may modify or supersede some of the information included or incorporated in this prospectus supplement and the accompanying prospectus. This means that you must look at all of the SEC filings that we incorporate by reference to determine if any of the statements in this prospectus supplement, the accompanying prospectus or in any document previously incorporated by reference have been modified or superseded. This prospectus supplement and the accompanying prospectus incorporate by reference the documents listed below (File No. 001-36167) and any future filings we make with the SEC under Sections 13(a), 13(c), 14 or 15(d) of the Exchange Act (in each case, other than those documents or the portions of those documents not deemed to be filed) until the offering of the securities under the registration statement is terminated or completed:

- Annual Report on [Form 10-K](#) for the fiscal year ended December 31, 2018, including the information specifically incorporated by reference into the Annual Report on Form 10-K from our definitive proxy statement for the 2019 Annual Meeting of Stockholders;
- Quarterly Report on [Form 10-Q](#) for the fiscal quarter ended March 31, 2019;
- Current Reports on Form 8-K filed [January 18, 2019](#), [February 19, 2019](#), [February 25, 2019](#) and [March 15, 2019](#); and
- The description of our common stock contained in our Registration Statement on [Form 8-A](#) filed on November 1, 2013, including any amendments or reports filed for the purpose of updating such description.

You may request a copy of these filings, at no cost, by writing or telephoning us at the following address or phone number:

Karyopharm Therapeutics Inc.
85 Wells Avenue
2nd Floor
Newton, Massachusetts 02459
Attn: Investor Relations
(617) 658-0600

PROSPECTUS



\$300,000,000

**Debt Securities
Common Stock
Preferred Stock
Warrants
Units**

We may offer and sell up to \$300,000,000 in the aggregate of securities from time to time in one or more offerings. These securities are inclusive of \$75,000,000 of shares of common stock that we may issue and sell pursuant to the previously-announced Open Market Sale AgreementSM that we entered into with Jefferies LLC on August 17, 2018. This prospectus describes the general terms of these securities and the general manner in which these securities will be offered. We will provide the specific terms of these securities in supplements to this prospectus. The prospectus supplements will also describe the specific manner in which these securities will be offered and may also supplement, update or amend information contained in this document. You should read this prospectus and any applicable prospectus supplement before you invest.

We may offer these securities in amounts, at prices and on terms determined at the time of offering. The securities may be sold directly to you, through agents, or through underwriters and dealers. If agents, underwriters or dealers are used to sell the securities, we will name them and describe their compensation in a prospectus supplement.

Our common stock is listed on The Nasdaq Global Select Market under the symbol "KPTI."

Investing in these securities involves certain risks. See "Risk Factors" on page 4, in any accompanying prospectus supplement and in the documents incorporated by reference in this prospectus for a discussion of the factors you should carefully consider before deciding to purchase these securities.

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

The date of this prospectus is April 24, 2019

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ABOUT THIS PROSPECTUS

This prospectus is part of a registration statement that we filed with the Securities and Exchange Commission, which we refer to as the “SEC,” utilizing a “shelf” registration process. Under this shelf registration process, we may from time to time sell any combination of the securities described in this prospectus, either separately or in units, in one or more offerings up to a total dollar amount of \$300,000,000 (inclusive of \$75,000,000 of shares of common stock that we may issue and sell pursuant to the previously-announced Open Market Sale AgreementSM that we entered into with Jefferies LLC on August 17, 2018).

This prospectus provides you with a general description of the securities we may offer. Each time we sell securities, we will provide one or more prospectus supplements that will contain specific information about the terms of the offering. The prospectus supplement may also add, update or change information contained in this prospectus. You should read both this prospectus and the accompanying prospectus supplement together with the additional information described under the heading “Where You Can Find More Information” beginning on page 2 of this prospectus.

You should rely only on the information contained in or incorporated by reference in this prospectus, any accompanying prospectus supplement or in any related free writing prospectus filed by us with the SEC. We have not authorized anyone to provide you with different information. This prospectus and any accompanying prospectus supplement do not constitute an offer to sell or the solicitation of an offer to buy any securities other than the securities described in this prospectus or such accompanying prospectus supplement or an offer to sell or the solicitation of an offer to buy such securities in any circumstances in which such offer or solicitation is unlawful. You should assume that the information appearing in this prospectus, any prospectus supplement, the documents incorporated by reference and any related free writing prospectus is accurate only as of their respective dates. Our business, financial condition, results of operations and prospects may have changed materially since those dates.

Unless the context otherwise indicates, references in this prospectus to “we,” “our” and “us” refer, collectively, to Karyopham Therapeutics Inc., a Delaware corporation, and its consolidated subsidiaries.

WHERE YOU CAN FIND MORE INFORMATION

We file annual, quarterly and current reports, proxy statements and other information with the SEC. Our SEC filings are available to the public over the Internet at the SEC's website at <http://www.sec.gov>. Copies of certain information filed by us with the SEC are also available on our website at www.karyopharm.com. Our website is not a part of this prospectus and is not incorporated by reference in this prospectus.

This prospectus is part of a registration statement we filed with the SEC. This prospectus omits some information contained in the registration statement in accordance with SEC rules and regulations. You should review the information and exhibits in the registration statement for further information about us and our consolidated subsidiaries and the securities we are offering. Statements in this prospectus concerning any document we filed as an exhibit to the registration statement or that we otherwise filed with the SEC are not intended to be comprehensive and are qualified by reference to these filings. You should review the complete document to evaluate these statements.

INCORPORATION BY REFERENCE

The SEC allows us to incorporate by reference much of the information we file with the SEC, which means that we can disclose important information to you by referring you to those publicly available documents. The information that we incorporate by reference in this prospectus is considered to be part of this prospectus. Because we are incorporating by reference future filings with the SEC, this prospectus is continually updated and those future filings may modify or supersede some of the information included or incorporated in this prospectus. This means that you must look at all of the SEC filings that we incorporate by reference to determine if any of the statements in this prospectus or in any document previously incorporated by reference have been modified or superseded. This prospectus incorporates by reference the documents listed below (File No. 001-36167) and any future filings we make with the SEC under Sections 13(a), 13(c), 14 or 15(d) of the Securities Exchange Act of 1934, as amended, or the Exchange Act (in each case, other than those documents or the portions of those documents not deemed to be filed) between the date of the initial registration statement and the effectiveness of the registration statement and following the effectiveness of the registration statement until the offering of the securities under the registration statement is terminated or completed:

- Annual Report on [Form 10-K](#) for the fiscal year ended December 31, 2018;
- Current Reports on Form 8-K filed [January 18, 2019](#), [February 19, 2019](#) and [February 25, 2019](#); and
- The description of our common stock contained in our Registration Statement on [Form 8-A](#) filed on November 1, 2013, including any amendments or reports filed for the purpose of updating such description.

You may request a copy of these filings, at no cost, by writing or telephoning us at the following address or telephone number:

Karyopharm Therapeutics Inc.
85 Wells Avenue, 2nd Floor
Newton, MA 02459
Attn: Investor Relations
(617) 658-0600

FORWARD-LOOKING STATEMENTS

This prospectus and the information incorporated by reference in this prospectus 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 Exchange Act. All statements, other than statements of historical facts, included in this 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,” “continue” and similar 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 our collaborators;
- our intellectual property position;
- 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; 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. You are cautioned that these forward-looking statements are only predictions and are subject to risks, uncertainties and assumptions that are referenced in the section of any accompanying prospectus supplement entitled “Risk Factors.” You should also carefully review the risk factors and cautionary statements described in the other documents we file from time to time with the SEC, specifically our most recent Annual Report on Form 10-K, our Quarterly Reports on Form 10-Q and our Current Reports on Form 8-K. 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 and the information incorporated by reference herein completely and with the understanding that our actual future results may be materially different from what we expect. 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.

RISK FACTORS

An investment in our securities involves a high degree of risk. Before deciding whether to invest in our securities, you should consider carefully the risks and uncertainties described under the section captioned “Risk Factors” in the applicable prospectus supplement and contained in our most recent Annual Report on Form 10-K and Quarterly Report on Form 10-Q and other filings we make with the SEC from time to time, which are incorporated by reference herein in their entirety, together with other information in this prospectus, the information and documents incorporated by reference in this prospectus, and in any prospectus supplement or free writing prospectus that we authorize for use in connection with this offering. If any event related to these risks actually occurs, our business, financial condition, results of operations or cash flow could suffer materially. In such event, you might lose all or part of your investment.

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 **Selective Inhibitor of Nuclear Export**, or SINE, compounds that inhibit the nuclear export protein exportin 1, or 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.

Corporate Information

We were incorporated under the laws of the State of Delaware in December 2008. Our executive offices are located at 85 Wells Avenue, Newton, Massachusetts 02459, and our telephone number is (617) 658-0600. Our website address is www.karyopharm.com. We have included our website address in this prospectus solely as an inactive textual reference. The trademarks, trade names and service marks appearing in this prospectus are the property of their respective owners.

USE OF PROCEEDS

We intend to use the net proceeds from the sale of any securities offered under this prospectus for general corporate purposes unless otherwise indicated in the applicable prospectus supplement. General corporate purposes may include research and development expenditures, the acquisition or licensing of other products, businesses or technologies, working capital and capital expenditures. We have not determined the amount of net proceeds to be used specifically for such purposes. As a result, management will retain broad discretion over the allocation of net proceeds.

DESCRIPTION OF DEBT SECURITIES

We may offer debt securities which may be senior or subordinated. We refer to the senior debt securities and the subordinated debt securities collectively as debt securities. The following description summarizes the general terms and provisions of the debt securities. We will describe the specific terms of the debt securities and the extent, if any, to which the general provisions summarized below apply to any series of debt securities in the prospectus supplement relating to the series and any applicable free writing prospectus that we authorize to be delivered. When we refer to “the Company,” “we,” “our,” and “us” in this section, we mean Karyopharm Therapeutics Inc. excluding, unless the context otherwise requires or as otherwise expressly stated, our subsidiaries.

We may issue senior debt securities from time to time, in one or more series under a senior indenture to be entered into between us and a senior trustee to be named in a prospectus supplement, which we refer to as the senior trustee. We may issue subordinated debt securities from time to time, in one or more series under a subordinated indenture to be entered into between us and a subordinated trustee to be named in a prospectus supplement, which we refer to as the subordinated trustee. The forms of senior indenture and subordinated indenture are filed as exhibits to the registration statement of which this prospectus forms a part. The senior indenture and the subordinated indenture are referred to individually as an indenture and together as the indentures and the senior trustee and the subordinated trustee are referred to individually as a trustee and together as the trustees. This section summarizes some of the provisions of the indentures and is qualified in its entirety by the specific text of the indentures, including definitions of terms used in the indentures. Wherever we refer to particular sections of, or defined terms in, the indentures, those sections or defined terms are incorporated by reference in this prospectus or the applicable prospectus supplement. You should review the indentures that are filed as exhibits to the registration statement of which this prospectus forms a part for additional information.

Neither indenture will limit the amount of debt securities that we may issue. The applicable indenture will provide that debt securities may be issued up to an aggregate principal amount authorized from time to time by us and may be payable in any currency or currency unit designated by us or in amounts determined by reference to an index.

General

The senior debt securities will constitute our unsecured and unsubordinated general obligations and will rank equally in right of payment with our other unsecured and unsubordinated obligations. The subordinated debt securities will constitute our unsecured and subordinated general obligations and will be junior in right of payment to our senior indebtedness (including senior debt securities), as described under the heading “— Certain Terms of the Subordinated Debt Securities—Subordination.” The debt securities will be structurally subordinated to all existing and future indebtedness and other liabilities of our subsidiaries unless such subsidiaries expressly guarantee such debt securities.

The debt securities will be our unsecured obligations. Any secured debt or other secured obligations will be effectively senior to the debt securities to the extent of the value of the assets securing such debt or other obligations.

The applicable prospectus supplement and/or free writing prospectus will include any additional or different terms of the debt securities of any series being offered, including the following terms:

- the title and type of the debt securities;
- whether the debt securities will be senior or subordinated debt securities, and, with respect to any subordinated debt securities the terms on which they are subordinated;
- the initial aggregate principal amount of the debt securities;

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- the price or prices at which we will sell the debt securities;
- the maturity date or dates of the debt securities and the right, if any, to extend such date or dates;
- the rate or rates, if any, at which the debt securities will bear interest, or the method of determining such rate or rates;
- the date or dates from which such interest will accrue, the interest payment dates on which such interest will be payable or the method of determination of such dates;
- the right, if any, to extend the interest payment periods and the duration of that extension;
- the manner of paying principal and interest and the place or places where principal and interest will be payable;
- provisions for a sinking fund, purchase fund or other analogous fund, if any;
- any redemption dates, prices, obligations and restrictions on the debt securities;
- the currency, currencies or currency units in which the debt securities will be denominated and the currency, currencies or currency units in which principal and interest, if any, on the debt securities may be payable;
- any conversion or exchange features of the debt securities;
- whether the debt securities will be subject to the defeasance provisions in the indenture;
- whether the debt securities will be issued in definitive or global form or in definitive form only upon satisfaction of certain conditions;
- whether the debt securities will be guaranteed as to payment or performance;
- any special tax implications of the debt securities;
- any events of defaults or covenants in addition to or in lieu of those set forth in the indenture; and
- any other material terms of the debt securities.

When we refer to “principal” in this section with reference to the debt securities, we are also referring to “premium, if any.”

We may from time to time, without notice to or the consent of the holders of any series of debt securities, create and issue further debt securities of any such series ranking equally with the debt securities of such series in all respects (or in all respects other than (1) the payment of interest accruing prior to the issue date of such further debt securities or (2) the first payment of interest following the issue date of such further debt securities). Such further debt securities may be consolidated and form a single series with the debt securities of such series and have the same terms as to status, redemption or otherwise as the debt securities of such series.

You may present debt securities for exchange and you may present debt securities for transfer in the manner, at the places and subject to the restrictions set forth in the debt securities and the applicable prospectus supplement. We will provide you those services without charge, although you may have to pay any tax or other governmental charge payable in connection with any exchange or transfer, as set forth in the indenture.

Debt securities may bear interest at a fixed rate or a floating rate. Debt securities bearing no interest or interest at a rate that at the time of issuance is below the prevailing market rate (original issue discount securities) may be sold at a discount below their stated principal amount. U.S. federal income tax considerations applicable to any such discounted debt securities or to certain debt securities issued at par which are treated as having been issued at a discount for U.S. federal income tax purposes will be described in the applicable prospectus supplement.

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We may issue debt securities with the principal amount payable on any principal payment date, or the amount of interest payable on any interest payment date, to be determined by reference to one or more currency exchange rates, securities or baskets of securities, commodity prices or indices. You may receive a payment of principal on any principal payment date, or a payment of interest on any interest payment date, that is greater than or less than the amount of principal or interest otherwise payable on such dates, depending on the value on such dates of the applicable currency, security or basket of securities, commodity or index. Information as to the methods for determining the amount of principal or interest payable on any date, the currencies, securities or baskets of securities, commodities or indices to which the amount payable on such date is linked and certain related tax considerations will be set forth in the applicable prospectus supplement.

Certain Terms of the Senior Debt Securities

Covenants. Unless we indicate otherwise in a prospectus supplement with respect to a particular series of senior debt securities, the senior debt securities will not contain any financial or restrictive covenants, including covenants restricting either us or any of our subsidiaries from incurring, issuing, assuming or guaranteeing any indebtedness secured by a lien on any of our or our subsidiaries' property or capital stock, or restricting either us or any of our subsidiaries from entering into sale and leaseback transactions.

Consolidation, Merger and Sale of Assets. Unless we indicate otherwise in a prospectus supplement with respect to a particular series of senior debt securities, we may not consolidate with or merge into any other person, in a transaction in which we are not the surviving corporation, or convey, transfer or lease our properties and assets substantially as an entirety to any person, in either case, unless:

- the successor entity, if any, is a U.S. corporation, limited liability company, partnership or trust;
- the successor entity assumes our obligations on the senior debt securities and under the senior indenture;
- immediately after giving effect to the transaction, no default or event of default shall have occurred and be continuing; and
- we have delivered to the senior trustee an officer's certificate and an opinion of counsel, each stating that the consolidation, merger, conveyance, transfer or lease and, if a supplemental indenture is required in connection with such transaction, such supplemental indenture, comply with the senior indenture and all conditions precedent provided for in the senior indenture relating to such transaction have been complied with.

The restrictions described in the bullets above do not apply (1) to our consolidation with or merging into one of our affiliates, if our board of directors determines in good faith that the purpose of the consolidation or merger is principally to change our state of incorporation or our form of organization to another form or (2) if we merge with or into a single direct or indirect wholly-owned subsidiary of ours.

The surviving business entity will succeed to, and be substituted for, us under the senior indenture and the senior debt securities and, except in the case of a lease, we shall be released from all obligations under the senior indenture and the senior debt securities.

No Protection in the Event of a Change in Control. Unless we indicate otherwise in a prospectus supplement with respect to a particular series of senior debt securities, the senior debt securities will not contain any provisions that may afford holders of the senior debt securities protection in the event we have a change in control or in the event of a highly leveraged transaction (whether or not such transaction results in a change in control).

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Events of Default. Unless we indicate otherwise in a prospectus supplement with respect to a particular series of senior debt securities, the following are events of default under the senior indenture with respect to senior debt securities of each series:

- failure to pay interest on any senior debt securities of such series when due and payable, if that default continues for a period of 30 days (or such other period as may be specified for such series);
- failure to pay principal on the senior debt securities of such series when due and payable whether at maturity, upon redemption, by declaration or otherwise (and, if specified for such series, the continuance of such failure for a specified period);
- default in the performance of or breach of any of our covenants or agreements in the senior indenture applicable to senior debt securities of such series, other than a covenant breach which is specifically dealt with elsewhere in the senior indenture, and that default or breach continues for a period of 90 days after we receive written notice from the trustee or from the holders of 25% or more in aggregate principal amount of the senior debt securities of such series;
- certain events of bankruptcy or insolvency, whether or not voluntary; and
- any other event of default provided for in such series of senior debt securities as may be specified in the applicable prospectus supplement.

The default by us under any other debt, including any other series of debt securities, is not a default under the senior indenture.

If an event of default other than an event of default specified in the fourth bullet point above occurs with respect to a series of senior debt securities and is continuing under the senior indenture, then, and in each such case, either the trustee or the holders of not less than 25% in aggregate principal amount of such series then outstanding under the senior indenture (each such series voting as a separate class) by written notice to us and to the trustee, if such notice is given by the holders, may, and the trustee at the request of such holders shall, declare the principal amount of and accrued interest on such series of senior debt securities to be immediately due and payable, and upon this declaration, the same shall become immediately due and payable.

If an event of default specified in the fourth bullet point above occurs and is continuing, the entire principal amount of and accrued interest on each series of senior debt securities then outstanding shall automatically become immediately due and payable.

Unless otherwise specified in the prospectus supplement relating to a series of senior debt securities originally issued at a discount, the amount due upon acceleration shall include only the original issue price of the senior debt securities, the amount of original issue discount accrued to the date of acceleration and accrued interest, if any.

Upon certain conditions, declarations of acceleration may be rescinded and annulled and past defaults may be waived by the holders of a majority in aggregate principal amount of all the senior debt securities of such series affected by the default, each series voting as a separate class. Furthermore, subject to various provisions in the senior indenture, the holders of a majority in aggregate principal amount of a series of senior debt securities, by notice to the trustee, may waive a continuing default or event of default with respect to such senior debt securities and its consequences, except a default in the payment of principal of or interest on such senior debt securities (other than any such default in payment resulting solely from an acceleration of the senior debt securities) or in respect of a covenant or provision of the senior indenture which cannot be modified or amended without the consent of the holders of each such senior debt security. Upon any such waiver, such default shall cease to exist, and any event of default with respect to such senior debt securities shall be deemed to have been cured, for every purpose of the senior indenture; but no such waiver shall extend to any subsequent or other default or event of default or impair any right consequent thereto.

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The holders of a majority in aggregate principal amount of a series of senior debt securities may direct the time, method and place of conducting any proceeding for any remedy available to the trustee or exercising any trust or power conferred on the trustee with respect to such senior debt securities. However, the trustee may refuse to follow any direction that conflicts with law or the senior indenture, that may involve the trustee in personal liability or that the trustee determines in good faith may be unduly prejudicial to the rights of holders of such series of senior debt securities not joining in the giving of such direction and may take any other action it deems proper that is not inconsistent with any such direction received from holders of such series of senior debt securities. A holder may not pursue any remedy with respect to the senior indenture or any series of senior debt securities unless:

- the holder gives the trustee written notice of a continuing event of default;
- the holders of at least 25% in aggregate principal amount of such series of senior debt securities make a written request to the trustee to pursue the remedy in respect of such event of default;
- the requesting holder or holders offer the trustee indemnity satisfactory to the trustee against any costs, liability or expense;
- the trustee does not comply with the request within 60 days after receipt of the request and the offer of indemnity; and
- during such 60-day period, the holders of a majority in aggregate principal amount of such series of senior debt securities do not give the trustee a direction that is inconsistent with the request.

These limitations, however, do not apply to the right of any holder of a senior debt security of any affected series to receive payment of the principal of and interest on such senior debt security in accordance with the terms of such debt security, or to bring suit for the enforcement of any such payment in accordance with the terms of such debt security, on or after the due date for the senior debt securities, which right shall not be impaired or affected without the consent of the holder.

The senior indenture requires certain of our officers to certify, on or before a fixed date in each year in which any senior debt security is outstanding, as to their knowledge of our compliance with all covenants, agreements and conditions under the senior indenture.

Satisfaction and Discharge. We can satisfy and discharge our obligations to holders of any series of debt securities if:

- we have paid or caused to be paid the principal of and interest on all senior debt securities of such series (with certain limited exceptions) when due and payable; or
- we deliver to the senior trustee for cancellation all senior debt securities of such series theretofore authenticated under the senior indenture (with certain limited exceptions); or
- all senior debt securities of such series have become due and payable or will become due and payable within one year (or are to be called for redemption within one year under arrangements satisfactory to the senior trustee) and we deposit in trust an amount of cash or a combination of cash and U.S. government or U.S. government agency obligations (or in the case of senior debt securities denominated in a foreign currency, foreign government securities or foreign government agency securities) sufficient to make interest, principal and any other payments on the debt securities of that series on their various due dates;

and if, in any such case, we also pay or cause to be paid all other sums payable under the senior indenture, as and when the same shall be due and payable and we deliver to the senior trustee an officer's certificate and an opinion of counsel, each stating that these conditions have been satisfied.

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Under current U.S. federal income tax law, the deposit and our legal release from the debt securities would be treated as though we took back your debt securities and gave you your share of the cash and debt securities or bonds deposited in trust. In that event, you could recognize gain or loss on the debt securities you give back to us. Purchasers of the debt securities should consult their own advisers with respect to the tax consequences to them of such deposit and discharge, including the applicability and effect of tax laws other than the U.S. federal income tax law.

Defeasance. Unless the applicable prospectus supplement provides otherwise, the following discussion of legal defeasance and covenant defeasance will apply to any series of debt securities issued under the indentures.

Legal Defeasance. We can legally release ourselves from any payment or other obligations on the debt securities of any series (called “legal defeasance”) if certain conditions are met, including the following:

- We deposit in trust for your benefit and the benefit of all other direct holders of the debt securities of the same series cash or a combination of cash and U.S. government or U.S. government agency obligations (or, in the case of senior debt securities denominated in a foreign currency, foreign government or foreign government agency obligations) that will generate enough cash to make interest, principal and any other payments on the debt securities of that series on their various due dates.
- There is a change in current U.S. federal income tax law or an IRS ruling that lets us make the above deposit without causing you to be taxed on the debt securities any differently than if we did not make the deposit and instead repaid the debt securities ourselves when due. Under current U.S. federal income tax law, the deposit and our legal release from the debt securities would be treated as though we took back your debt securities and gave you your share of the cash and debt securities or bonds deposited in trust. In that event, you could recognize gain or loss on the debt securities you give back to us.
- We deliver to the trustee a legal opinion of our counsel confirming the tax law change or ruling described above.

If we accomplish legal defeasance, as described above, you would have to rely solely on the trust deposit for repayment of the debt securities. You could not look to us for repayment in the event of any shortfall.

Covenant Defeasance. Without any change in current U.S. federal tax law, we can make the same type of deposit described above and be released from some of the covenants in the debt securities (called “covenant defeasance”). In that event, you would lose the protection of those covenants but would gain the protection of having money and securities set aside in trust to repay the debt securities. In order to achieve covenant defeasance, we must do the following (among other things):

- We must deposit in trust for your benefit and the benefit of all other direct holders of the debt securities of the same series cash or a combination of cash and U.S. government or U.S. government agency obligations (or, in the case of senior debt securities denominated in a foreign currency, foreign government or foreign government agency obligations) that will generate enough cash to make interest, principal and any other payments on the debt securities of that series on their various due dates.
- We must deliver to the trustee a legal opinion of our counsel confirming that under current U.S. federal income tax law we may make the above deposit without causing you to be taxed on the debt securities any differently than if we did not make the deposit and instead repaid the debt securities ourselves when due.

If we accomplish covenant defeasance, you could still look to us for repayment of the debt securities if there were a shortfall in the trust deposit. In fact, if one of the events of default occurred (such as our bankruptcy) and the debt securities become immediately due and payable, there may be such a shortfall. Depending on the events causing the default, you may not be able to obtain payment of the shortfall.

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Modification and Waiver. We and the trustee may amend or supplement the senior indenture or the senior debt securities of any series without the consent of any holder:

- to convey, transfer, assign, mortgage or pledge any assets as security for the senior debt securities of one or more series;
- to evidence the succession of a corporation, limited liability company, partnership or trust to us, and the assumption by such successor of our covenants, agreements and obligations under the senior indenture or to otherwise comply with the covenant relating to mergers, consolidations and sales of assets;
- to comply with requirements of the SEC in order to effect or maintain the qualification of the senior indenture under the Trust Indenture Act of 1939, as amended (the “Trust Indenture Act”);
- to add to our covenants such new covenants, restrictions, conditions or provisions for the protection of the holders, and to make the occurrence, or the occurrence and continuance, of a default in any such additional covenants, restrictions, conditions or provisions an event of default;
- to cure any ambiguity, defect or inconsistency in the senior indenture or in any supplemental indenture or to conform the senior indenture or the senior debt securities to the description of senior debt securities of such series set forth in this prospectus or any applicable prospectus supplement;
- to provide for or add guarantors with respect to the senior debt securities of any series;
- to establish the form or forms or terms of the senior debt securities as permitted by the senior indenture;
- to evidence and provide for the acceptance of appointment under the senior indenture by a successor trustee, or to make such changes as shall be necessary to provide for or facilitate the administration of the trusts in the senior indenture by more than one trustee;
- to add to, change or eliminate any of the provisions of the senior indenture in respect of one or more series of senior debt securities, provided that any such addition, change or elimination shall (a) neither (1) apply to any senior debt security of any series created prior to the execution of such supplemental indenture and entitled to the benefit of such provision nor (2) modify the rights of the holder of any such senior debt security with respect to such provision or (b) become effective only when there is no senior debt security described in clause (a)(1) outstanding;
- to make any change to the senior debt securities of any series so long as no senior debt securities of such series are outstanding; or
- to make any change that does not adversely affect the rights of any holder in any material respect.

Other amendments and modifications of the senior indenture or the senior debt securities issued may be made, and our compliance with any provision of the senior indenture with respect to any series of senior debt securities may be waived, with the consent of the holders of a majority of the aggregate principal amount of the outstanding senior debt securities of each series affected by the amendment or modification (voting as separate series); provided, however, that each affected holder must consent to any modification, amendment or waiver that:

- extends the final maturity of any senior debt securities of such series;
- reduces the principal amount of any senior debt securities of such series;
- reduces the rate, or extends the time for payment of, interest on any senior debt securities of such series;
- reduces the amount payable upon the redemption of any senior debt securities of such series;
- changes the currency of payment of principal of or interest on any senior debt securities of such series;

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- reduces the principal amount of original issue discount securities payable upon acceleration of maturity or the amount provable in bankruptcy;
- waives a continuing default in the payment of principal of or interest on the senior debt securities (other than any such default in payment resulting solely from an acceleration of the senior debt securities);
- changes the provisions relating to the waiver of past defaults or impairs the right of holders to receive payment or to institute suit for the enforcement of any payment or conversion of any senior debt securities of such series on or after the due date therefor;
- modifies any of the provisions of these restrictions on amendments and modifications, except to increase any required percentage or to provide that certain other provisions cannot be modified or waived without the consent of the holder of each senior debt security of such series affected by the modification;
- adversely affects the right to convert or exchange senior debt securities into common stock or other property in accordance with the terms of the senior debt securities; or
- reduces the above-stated percentage of outstanding senior debt securities of such series whose holders must consent to a supplemental indenture or modifies or amends or waives certain provisions of or defaults under the senior indenture.

It shall not be necessary for the holders to approve the particular form of any proposed amendment, supplement or waiver, but it shall be sufficient if the holders' consent approves the substance thereof. After an amendment, supplement or waiver of the senior indenture in accordance with the provisions described in this section becomes effective, the trustee must give to the holders affected thereby certain notice briefly describing the amendment, supplement or waiver. Any failure by the trustee to give such notice, or any defect therein, shall not, however, in any way impair or affect the validity of any such amendment, supplemental indenture or waiver.

No Personal Liability of Incorporators, Stockholders, Officers, Directors. The senior indenture provides that no recourse shall be had under any obligation, covenant or agreement of ours in the senior indenture or any supplemental indenture, or in any of the senior debt securities or because of the creation of any indebtedness represented thereby, against any of our incorporators, stockholders, officers or directors, past, present or future, or of any predecessor or successor entity thereof under any law, statute or constitutional provision or by the enforcement of any assessment or by any legal or equitable proceeding or otherwise. Each holder, by accepting the senior debt securities, waives and releases all such liability.

Concerning the Trustee. The senior indenture provides that, except during the continuance of an event of default, the trustee will not be liable except for the performance of such duties as are specifically set forth in the senior indenture. If an event of default has occurred and is continuing, the trustee will exercise such rights and powers vested in it under the senior indenture and will use the same degree of care and skill in its exercise as a prudent person would exercise under the circumstances in the conduct of such person's own affairs.

The senior indenture and the provisions of the Trust Indenture Act incorporated by reference therein contain limitations on the rights of the trustee thereunder, should it become a creditor of ours or any of our subsidiaries, to obtain payment of claims in certain cases or to realize on certain property received by it in respect of any such claims, as security or otherwise. The trustee is permitted to engage in other transactions, provided that if it acquires any conflicting interest (as defined in the Trust Indenture Act), it must eliminate such conflict or resign.

We may have normal banking relationships with the senior trustee in the ordinary course of business.

Unclaimed Funds. All funds deposited with the trustee or any paying agent for the payment of principal, premium, interest or additional amounts in respect of the senior debt securities that remain unclaimed for two

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years after the date upon which such amounts became due and payable will be repaid to us. Thereafter, any right of any holder of senior debt securities to such funds shall be enforceable only against us, and the trustee and paying agents will have no liability therefor.

Governing Law. The senior indenture and the senior debt securities will be governed by, and construed in accordance with, the internal laws of the State of New York.

Certain Terms of the Subordinated Debt Securities

Other than the terms of the subordinated indenture and subordinated debt securities relating to subordination or otherwise as described in the prospectus supplement relating to a particular series of subordinated debt securities, the terms of the subordinated indenture and subordinated debt securities are identical in all material respects to the terms of the senior indenture and senior debt securities.

Additional or different subordination terms may be specified in the prospectus supplement applicable to a particular series.

Subordination. The indebtedness evidenced by the subordinated debt securities is subordinate to the prior payment in full of all of our senior indebtedness, as defined in the subordinated indenture. During the continuance beyond any applicable grace period of any default in the payment of principal, premium, interest or any other payment due on any of our senior indebtedness, we may not make any payment of principal or interest on the subordinated debt securities (except for certain sinking fund payments). In addition, upon any payment or distribution of our assets upon any dissolution, winding-up, liquidation or reorganization, the payment of the principal of and interest on the subordinated debt securities will be subordinated to the extent provided in the subordinated indenture in right of payment to the prior payment in full of all our senior indebtedness. Because of this subordination, if we dissolve or otherwise liquidate, holders of our subordinated debt securities may receive less, ratably, than holders of our senior indebtedness. The subordination provisions do not prevent the occurrence of an event of default under the subordinated indenture.

The term “senior indebtedness” of a person means with respect to such person the principal of, premium, if any, interest on, and any other payment due pursuant to any of the following, whether outstanding on the date of the subordinated indenture or incurred by that person in the future:

- all of the indebtedness of that person for money borrowed;
- all of the indebtedness of that person evidenced by notes, debentures, bonds or other securities sold by that person for money;
- all of the lease obligations that are capitalized on the books of that person in accordance with generally accepted accounting principles;
- all indebtedness of others of the kinds described in the first two bullet points above and all lease obligations of others of the kind described in the third bullet point above that the person, in any manner, assumes or guarantees or that the person in effect guarantees through an agreement to purchase, whether that agreement is contingent or otherwise; and
- all renewals, extensions or refundings of indebtedness of the kinds described in the first, second or fourth bullet point above and all renewals or extensions of leases of the kinds described in the third or fourth bullet point above;

unless, in the case of any particular indebtedness, renewal, extension or refunding, the instrument creating or evidencing it or the assumption or guarantee relating to it expressly provides that such indebtedness, renewal, extension or refunding is not superior in right of payment to the subordinated debt securities. Our senior debt securities constitute senior indebtedness for purposes of the subordinated indenture.

DESCRIPTION OF CAPITAL STOCK

The following description of our capital stock is intended as a summary only and therefore is not a complete description of our capital stock. This description is based upon, and is qualified by reference to, our certificate of incorporation, our by-laws and applicable provisions of Delaware corporate law. You should read our certificate of incorporation and by-laws, which are filed as exhibits to the registration statement of which this prospectus forms a part, for the provisions that are important to you.

Our authorized capital stock consists of 100,000,000 shares of common stock, par value \$0.0001 per share, and 5,000,000 shares of preferred stock, par value \$0.0001 per share. As of February 26, 2019, 60,859,445 shares of common stock were outstanding and no shares of preferred stock were outstanding.

Common Stock

Annual Meeting. Annual meetings of our stockholders are held on the date designated in accordance with our by-laws. Written notice must be mailed to each stockholder entitled to vote not less than ten nor more than 60 days before the date of the meeting. The presence in person or by proxy of the holders of record of a majority of our issued and outstanding shares entitled to vote at such meeting constitutes a quorum for the transaction of business at meetings of the stockholders. Special meetings of the stockholders may be called for any purpose by the board of directors, the chairman of the board or the chief executive officer. Except as may be otherwise provided by applicable law, our certificate of incorporation or our by-laws, all elections shall be decided by a plurality, and all other questions shall be decided by a majority, of the votes cast by stockholders entitled to vote thereon at a duly held meeting of stockholders at which a quorum is present.

Voting Rights. Each holder of common stock is entitled to one vote for each share held on all matters to be voted upon by stockholders.

Dividends. Subject to the rights, powers and preferences of any outstanding preferred stock, and except as provided by law or in our certificate of incorporation, dividends may be declared and paid or set aside for payment on the common stock out of legally available assets or funds when and as declared by the board of directors.

Liquidation and Dissolution. Subject to the rights, powers and preferences of any outstanding preferred stock, in the event of our liquidation or dissolution, our net assets will be distributed pro rata to the holders of our common stock.

Other Rights. Holders of the common stock have no right to:

- convert the stock into any other security;
- have the stock redeemed;
- purchase additional stock; or
- maintain their proportionate ownership interest.

The common stock does not have cumulative voting rights. Holders of shares of the common stock are not required to make additional capital contributions.

Transfer Agent and Registrar. Computershare Trust Company, N.A., is transfer agent and registrar for the common stock.

Preferred Stock

We are authorized to issue “blank check” preferred stock, which may be issued in one or more series upon authorization of our board of directors. Our board of directors is authorized to fix the designations, powers,

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preferences and the relative, participating, optional or other special rights and any qualifications, limitations and restrictions of the shares of each series of preferred stock. The authorized shares of our preferred stock are available for issuance without further action by our stockholders, unless such action is required by applicable law or the rules of any stock exchange on which our securities may be listed. If the approval of our stockholders is not required for the issuance of shares of our preferred stock, our board may determine not to seek stockholder approval. The specific terms of any series of preferred stock offered pursuant to this prospectus will be described in the prospectus supplement relating to that series of preferred stock.

A series of our preferred stock could, depending on the terms of such series, impede the completion of a merger, tender offer or other takeover attempt. Our board of directors will make any determination to issue preferred shares based upon its judgment as to the best interests of our stockholders. Our directors, in so acting, could issue preferred stock having terms that could discourage an acquisition attempt through which an acquirer may be able to change the composition of our board of directors, including a tender offer or other transaction that some, or a majority, of our stockholders might believe to be in their best interests or in which stockholders might receive a premium for their stock over the then-current market price of the stock.

The preferred stock has the terms described below unless otherwise provided in the prospectus supplement relating to a particular series of preferred stock. You should read the prospectus supplement relating to the particular series of preferred stock being offered for specific terms, including:

- the designation and stated value per share of the preferred stock and the number of shares offered;
- the amount of liquidation preference per share;
- the price at which the preferred stock will be issued;
- the dividend rate, or method of calculation of dividends, the dates on which dividends will be payable, whether dividends will be cumulative or noncumulative and, if cumulative, the dates from which dividends will commence to accumulate;
- any redemption or sinking fund provisions;
- if other than the currency of the United States, the currency or currencies including composite currencies in which the preferred stock is denominated and/or in which payments will or may be payable;
- any conversion provisions; and
- any other rights, preferences, privileges, limitations and restrictions on the preferred stock.

The preferred stock will, when issued, be fully paid and non-assessable. Unless otherwise specified in the prospectus supplement, each series of preferred stock will rank equally as to dividends and liquidation rights in all respects with each other series of preferred stock. The rights of holders of shares of each series of preferred stock will be subordinate to those of our general creditors.

Rank. Unless otherwise specified in the prospectus supplement, the preferred stock will, with respect to dividend rights and rights upon our liquidation, dissolution or winding up of our affairs, rank:

- senior to our common stock and to all equity securities ranking junior to such preferred stock with respect to dividend rights or rights upon our liquidation, dissolution or winding up of our affairs;
- on a parity with all equity securities issued by us, the terms of which specifically provide that such equity securities rank on a parity with the preferred stock with respect to dividend rights or rights upon our liquidation, dissolution or winding up of our affairs; and
- junior to all equity securities issued by us, the terms of which specifically provide that such equity securities rank senior to the preferred stock with respect to dividend rights or rights upon our liquidation, dissolution or winding up of our affairs.

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The term “equity securities” does not include convertible debt securities.

Dividends. Holders of the preferred stock of each series will be entitled to receive, when, as and if declared by our board of directors, cash dividends at such rates and on such dates described in the prospectus supplement. Different series of preferred stock may be entitled to dividends at different rates or based on different methods of calculation. The dividend rate may be fixed or variable or both. Dividends will be payable to the holders of record as they appear on our stock books on record dates fixed by our board of directors, as specified in the applicable prospectus supplement.

Dividends on any series of preferred stock may be cumulative or noncumulative, as described in the applicable prospectus supplement. If our board of directors does not declare a dividend payable on a dividend payment date on any series of noncumulative preferred stock, then the holders of that noncumulative preferred stock will have no right to receive a dividend for that dividend payment date, and we will have no obligation to pay the dividend accrued for that period, whether or not dividends on that series are declared payable on any future dividend payment dates. Dividends on any series of cumulative preferred stock will accrue from the date we initially issue shares of such series or such other date specified in the applicable prospectus supplement.

No dividends may be declared or paid or funds set apart for the payment of any dividends on any parity securities unless full dividends have been paid or set apart for payment on the preferred stock. If full dividends are not paid, the preferred stock will share dividends pro rata with the parity securities.

No dividends may be declared or paid or funds set apart for the payment of dividends on any junior securities unless full dividends for all dividend periods terminating on or prior to the date of the declaration or payment will have been paid or declared and a sum sufficient for the payment set apart for payment on the preferred stock.

Liquidation Preference. Upon any voluntary or involuntary liquidation, dissolution or winding up of our affairs, then, before we make any distribution or payment to the holders of any common stock or any other class or series of our capital stock ranking junior to the preferred stock in the distribution of assets upon any liquidation, dissolution or winding up of our affairs, the holders of each series of preferred stock shall be entitled to receive out of assets legally available for distribution to stockholders, liquidating distributions in the amount of the liquidation preference per share set forth in the prospectus supplement, plus any accrued and unpaid dividends thereon. Such dividends will not include any accumulation in respect of unpaid noncumulative dividends for prior dividend periods. Unless otherwise specified in the prospectus supplement, after payment of the full amount of their liquidating distributions, the holders of preferred stock will have no right or claim to any of our remaining assets. Upon any such voluntary or involuntary liquidation, dissolution or winding up, if our available assets are insufficient to pay the amount of the liquidating distributions on all outstanding preferred stock and the corresponding amounts payable on all other classes or series of our capital stock ranking on parity with the preferred stock and all other such classes or series of shares of capital stock ranking on parity with the preferred stock in the distribution of assets, then the holders of the preferred stock and all other such classes or series of capital stock will share ratably in any such distribution of assets in proportion to the full liquidating distributions to which they would otherwise be entitled.

Upon any such liquidation, dissolution or winding up and if we have made liquidating distributions in full to all holders of preferred stock, we will distribute our remaining assets among the holders of any other classes or series of capital stock ranking junior to the preferred stock according to their respective rights and preferences and, in each case, according to their respective number of shares. For such purposes, our consolidation or merger with or into any other corporation, trust or entity, or the sale, lease or conveyance of all or substantially all of our property or assets will not be deemed to constitute a liquidation, dissolution or winding up of our affairs.

Redemption. If so provided in the applicable prospectus supplement, the preferred stock will be subject to mandatory redemption or redemption at our option, as a whole or in part, in each case upon the terms, at the times and at the redemption prices set forth in such prospectus supplement.

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The prospectus supplement relating to a series of preferred stock that is subject to mandatory redemption will specify the number of shares of preferred stock that shall be redeemed by us in each year commencing after a date to be specified, at a redemption price per share to be specified, together with an amount equal to all accrued and unpaid dividends thereon to the date of redemption. Unless the shares have a cumulative dividend, such accrued dividends will not include any accumulation in respect of unpaid dividends for prior dividend periods. We may pay the redemption price in cash or other property, as specified in the applicable prospectus supplement. If the redemption price for preferred stock of any series is payable only from the net proceeds of the issuance of shares of our capital stock, the terms of such preferred stock may provide that, if no such shares of our capital stock shall have been issued or to the extent the net proceeds from any issuance are insufficient to pay in full the aggregate redemption price then due, such preferred stock shall automatically and mandatorily be converted into the applicable shares of our capital stock pursuant to conversion provisions specified in the applicable prospectus supplement. Notwithstanding the foregoing, we will not redeem any preferred stock of a series unless:

- if that series of preferred stock has a cumulative dividend, we have declared and paid or contemporaneously declare and pay or set aside funds to pay full cumulative dividends on the preferred stock for all past dividend periods and the then current dividend period; or
- if such series of preferred stock does not have a cumulative dividend, we have declared and paid or contemporaneously declare and pay or set aside funds to pay full dividends for the then current dividend period.

In addition, we will not acquire any preferred stock of a series unless:

- if that series of preferred stock has a cumulative dividend, we have declared and paid or contemporaneously declare and pay or set aside funds to pay full cumulative dividends on all outstanding shares of such series of preferred stock for all past dividend periods and the then current dividend period; or
- if that series of preferred stock does not have a cumulative dividend, we have declared and paid or contemporaneously declare and pay or set aside funds to pay full dividends on the preferred stock of such series for the then current dividend period.

However, at any time we may purchase or acquire preferred stock of that series (1) pursuant to a purchase or exchange offer made on the same terms to holders of all outstanding preferred stock of such series or (2) by conversion into or exchange for shares of our capital stock ranking junior to the preferred stock of such series as to dividends and upon liquidation.

If fewer than all of the outstanding shares of preferred stock of any series are to be redeemed, we will determine the number of shares that may be redeemed pro rata from the holders of record of such shares in proportion to the number of such shares held or for which redemption is requested by such holder or by any other equitable manner that we determine. Such determination will reflect adjustments to avoid redemption of fractional shares.

Unless otherwise specified in the prospectus supplement, we will mail notice of redemption at least 30 days but not more than 60 days before the redemption date to each holder of record of preferred stock to be redeemed at the address shown on our stock transfer books. Each notice shall state:

- the redemption date;
- the number of shares and series of preferred stock to be redeemed;
- the redemption price;
- the place or places where certificates for such preferred stock are to be surrendered for payment of the redemption price;

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- that dividends on the shares to be redeemed will cease to accrue on such redemption date;
- the date on which the holder's conversion rights, if any, as to such shares shall terminate; and
- the specific number of shares to be redeemed from each such holder if fewer than all the shares of any series are to be redeemed.

If notice of redemption has been given and we have set aside the funds necessary for such redemption in trust for the benefit of the holders of any shares called for redemption, then from and after the redemption date, dividends will cease to accrue on such shares, and all rights of the holders of such shares will terminate, except the right to receive the redemption price.

Voting Rights. Holders of preferred stock will not have any voting rights, except as required by law or as indicated in the applicable prospectus supplement.

Unless otherwise provided for under the terms of any series of preferred stock, no consent or vote of the holders of shares of preferred stock or any series thereof shall be required for any amendment to our certificate of incorporation that would increase the number of authorized shares of preferred stock or the number of authorized shares of any series thereof or decrease the number of authorized shares of preferred stock or the number of authorized shares of any series thereof (but not below the number of authorized shares of preferred stock or such series, as the case may be, then outstanding).

Conversion Rights. The terms and conditions, if any, upon which any series of preferred stock is convertible into our common stock will be set forth in the applicable prospectus supplement relating thereto. Such terms will include the number of shares of common stock into which the shares of preferred stock are convertible, the conversion price, rate or manner of calculation thereof, the conversion period, provisions as to whether conversion will be at our option or at the option of the holders of the preferred stock, the events requiring an adjustment of the conversion price and provisions affecting conversion in the event of the redemption.

Transfer Agent and Registrar. The transfer agent and registrar for the preferred stock will be set forth in the applicable prospectus supplement.

Provisions of Our Certificate of Incorporation and By-laws and Delaware Law That May Have Anti-Takeover Effects

Board of Directors. Our certificate of incorporation and by-laws provide for a board of directors divided as nearly equally as possible into three classes. Each class is elected to a term expiring at the annual meeting of stockholders held in the third year following the year of such election. The number of directors comprising our board of directors is fixed from time to time by the board of directors.

Removal of Directors by Stockholders. Our certificate of incorporation and by-laws provide that, subject to the rights of holders of any series of preferred stock, a member of our board of directors may only be removed for cause and only by an affirmative vote of the holders of at least 75% of the outstanding shares entitled to vote on the election of the directors.

Super-Majority Voting. The General Corporation Law of the State of Delaware, which we refer to as the DGCL, provides generally that the affirmative vote of a majority of the shares entitled to vote on any matter is required to amend a corporation's certificate of incorporation or by-laws, unless a corporation's certificate of incorporation or by-laws, as the case may be, requires a greater percentage. Subject to the rights of holders of any series of preferred stock, our by-laws may be amended or repealed by a majority vote of our board of directors or the affirmative vote of the holders of at least 75% of the votes that all our stockholders would be entitled to cast in any annual election of directors. In addition, the affirmative vote of the holders of at least 75% of the votes that all our stockholders would be entitled to cast in any annual election of directors is required to amend or repeal, or to adopt any provisions inconsistent with, any of the provisions of our certificate of incorporation described under the prior two paragraphs.

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Stockholder Nomination of Directors. Our by-laws provide that a stockholder must notify us in writing of any stockholder nomination of a director not earlier than 120 days but not later than 90 days prior to the first anniversary of the preceding year's annual meeting; provided, that if the date of the annual meeting is advanced by more than 20 days, or delayed by more than 60 days, from such anniversary date, notice by the stockholder to be timely must be so delivered not earlier than the 120th day prior to the date of such annual meeting and not later than close of business on the later of (x) the 90th day prior to the date of such meeting and (y) the 10th day following the day on which notice of the date of such annual meeting was mailed or public announcement of the date of such annual meeting is first made by us, whichever occurs first.

No Action By Written Consent. Our certificate of incorporation and our by-laws provide that our stockholders may not act by written consent and may only act at duly called meetings of stockholders. Our certificate of incorporation and our by-laws also provide that, except as otherwise required by law, special meetings of our stockholders can only be called by our board of directors, chairman of the board or chief executive officer. In addition, our by-laws establish an advance notice procedure for stockholder proposals to be brought before an annual meeting of stockholders, including proposed nominations of candidates for election to our board of directors.

Delaware Business Combination Statute. We are subject to Section 203 of the DGCL. Subject to certain exceptions, Section 203 prevents a publicly held Delaware corporation from engaging in a "business combination" with any "interested stockholder" for three years following the date that the person became an interested stockholder, unless the interested stockholder attained such status with the approval of the corporation's board of directors or unless the business combination is approved in a prescribed manner or the interested stockholder acquired at least 85% of the corporation's outstanding voting stock in the transaction in which it became an interested stockholder. A "business combination" includes, among other things, a merger or consolidation involving us and the "interested stockholder" and the sale of more than 10% of our assets. In general, an "interested stockholder" is any entity or person beneficially owning 15% or more of our outstanding voting stock and any entity or person affiliated with or controlling or controlled by such entity or person.

DESCRIPTION OF WARRANTS

We may issue warrants to purchase common stock, preferred stock or debt securities. We may offer warrants separately or together with one or more additional warrants, common stock, preferred stock or debt securities, or any combination of those securities in the form of units, as described in the applicable prospectus supplement. If we issue warrants as part of a unit, the accompanying prospectus supplement will specify whether those warrants may be separated from the other securities in the unit prior to the expiration date of the warrants. The applicable prospectus supplement will also describe the following terms of any warrants:

- the specific designation and aggregate number of, and the offering price at which we will issue, the warrants;
- the currency or currency units in which the offering price, if any, and the exercise price are payable;
- the date on which the right to exercise the warrants will begin and the date on which that right will expire or, if you may not continuously exercise the warrants throughout that period, the specific date or dates on which you may exercise the warrants;
- whether the warrants are to be sold separately or with other securities as parts of units;
- whether the warrants will be issued in definitive or global form or in any combination of these forms, although, in any case, the form of a warrant included in a unit will correspond to the form of the unit and of any security included in that unit;
- any applicable material U.S. federal income tax consequences;
- the identity of the warrant agent for the warrants and of any other depositaries, execution or paying agents, transfer agents, registrars or other agents;
- the proposed listing, if any, of the warrants or any securities purchasable upon exercise of the warrants on any securities exchange;
- the designation and terms of any equity securities purchasable upon exercise of the warrants;
- the designation, aggregate principal amount, currency and terms of any debt securities that may be purchased upon exercise of the warrants;
- if applicable, the designation and terms of the preferred stock with which the warrants are issued and the number of warrants issued with each security;
- if applicable, the date from and after which any warrants issued as part of a unit and the related debt securities, preferred stock or common stock will be separately transferable;
- the number of shares of common stock or preferred stock purchasable upon exercise of a warrant and the price at which those shares may be purchased;
- if applicable, the minimum or maximum amount of the warrants that may be exercised at any one time;
- information with respect to book-entry procedures, if any;
- the anti-dilution provisions of, and other provisions for changes to or adjustment in the exercise price of, the warrants, if any;
- any redemption or call provisions; and
- any additional terms of the warrants, including terms, procedures and limitations relating to the exchange or exercise of the warrants.

DESCRIPTION OF UNITS

We may issue units consisting of one or more of the other securities described in this prospectus in any combination, as described in the applicable prospectus supplement. We may issue units in one or more series, which will be described in the applicable prospectus supplement. The applicable prospectus supplement will also describe the following terms of any units:

- the designation and the terms of the units and of the securities constituting the units, including whether and under what circumstances the securities comprising the units may be traded separately;
- the identity of the unit agent for the units and of any other depositaries, execution or paying agents, transfer agents, registrars or other agents;
- any additional terms of the governing unit agreement;
- any additional provisions for the issuance, payment, settlement, transfer or exchange of the units or of the debt securities, common stock, preferred stock or warrants constituting the units; and
- any applicable material U.S. federal income tax consequences.

FORMS OF SECURITIES

Each debt security, warrant and unit will be represented either by a certificate issued in definitive form to a particular investor or by one or more global securities representing the entire issuance of securities. Unless the applicable prospectus supplement provides otherwise, certificated securities will be issued in definitive form and global securities will be issued in registered form. Definitive securities name you or your nominee as the owner of the security, and in order to transfer or exchange these securities or to receive payments other than interest or other interim payments, you or your nominee must physically deliver the securities to the trustee, registrar, paying agent or other agent, as applicable. Global securities name a depository or its nominee as the owner of the debt securities, warrants or units represented by these global securities. The depository maintains a computerized system that will reflect each investor's beneficial ownership of the securities through an account maintained by the investor with its broker/dealer, bank, trust company or other representative, as we explain more fully below.

Global Securities

We may issue the debt securities, warrants and units in the form of one or more fully registered global securities that will be deposited with a depository or its nominee identified in the applicable prospectus supplement and registered in the name of that depository or nominee. In those cases, one or more global securities will be issued in a denomination or aggregate denominations equal to the portion of the aggregate principal or face amount of the securities to be represented by global securities. Unless and until it is exchanged in whole for securities in definitive registered form, a global security may not be transferred except as a whole by and among the depository for the global security, the nominees of the depository or any successors of the depository or those nominees.

If not described below, any specific terms of the depository arrangement with respect to any securities to be represented by a global security will be described in the prospectus supplement relating to those securities. We anticipate that the following provisions will apply to all depository arrangements.

Ownership of beneficial interests in a global security will be limited to persons, called participants, that have accounts with the depository or persons that may hold interests through participants. Upon the issuance of a global security, the depository will credit, on its book-entry registration and transfer system, the participants' accounts with the respective principal or face amounts of the securities beneficially owned by the participants. Any dealers, underwriters or agents participating in the distribution of the securities will designate the accounts to be credited. Ownership of beneficial interests in a global security will be shown on, and the transfer of ownership interests will be effected only through, records maintained by the depository, with respect to interests of participants, and on the records of participants, with respect to interests of persons holding through participants. The laws of some states may require that some purchasers of securities take physical delivery of these securities in definitive form. These laws may impair your ability to own, transfer or pledge beneficial interests in global securities.

So long as the depository, or its nominee, is the registered owner of a global security, that depository or its nominee, as the case may be, will be considered the sole owner or holder of the securities represented by the global security for all purposes under the applicable indenture, warrant agreement or unit agreement. Except as described below, owners of beneficial interests in a global security will not be entitled to have the securities represented by the global security registered in their names, will not receive or be entitled to receive physical delivery of the securities in definitive form and will not be considered the owners or holders of the securities under the applicable indenture, warrant agreement or unit agreement. Accordingly, each person owning a beneficial interest in a global security must rely on the procedures of the depository for that global security and, if that person is not a participant, on the procedures of the participant through which the person owns its interest, to exercise any rights of a holder under the applicable indenture, warrant agreement or unit agreement. We understand that under existing industry practices, if we request any action of holders or if an owner of a beneficial interest in a global security desires to give or take any action that a holder is entitled to give or take

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under the applicable indenture, warrant agreement or unit agreement, the depositary for the global security would authorize the participants holding the relevant beneficial interests to give or take that action, and the participants would authorize beneficial owners owning through them to give or take that action or would otherwise act upon the instructions of beneficial owners holding through them.

Principal, premium, if any, and interest payments on debt securities, and any payments to holders with respect to warrants or units represented by a global security registered in the name of a depositary or its nominee will be made to the depositary or its nominee, as the case may be, as the registered owner of the global security. None of us, or any trustee, warrant agent, unit agent or other agent of ours, or any agent of any trustee, warrant agent or unit agent will have any responsibility or liability for any aspect of the records relating to payments made on account of beneficial ownership interests in the global security or for maintaining, supervising or reviewing any records relating to those beneficial ownership interests.

We expect that the depositary for any of the securities represented by a global security, upon receipt of any payment to holders of principal, premium, interest or other distribution of underlying securities or other property on that registered global security, will immediately credit participants' accounts in amounts proportionate to their respective beneficial interests in that global security as shown on the records of the depositary. We also expect that payments by participants to owners of beneficial interests in a global security held through participants will be governed by standing customer instructions and customary practices, as is now the case with the securities held for the accounts of customers or registered in "street name," and will be the responsibility of those participants.

If the depositary for any of the securities represented by a global security is at any time unwilling or unable to continue as depositary or ceases to be a clearing agency registered under the Exchange Act, and a successor depositary registered as a clearing agency under the Exchange Act is not appointed by us within 90 days, we will issue securities in definitive form in exchange for the global security that had been held by the depositary. Any securities issued in definitive form in exchange for a global security will be registered in the name or names that the depositary gives to the relevant trustee, warrant agent, unit agent or other relevant agent of ours or theirs. It is expected that the depositary's instructions will be based upon directions received by the depositary from participants with respect to ownership of beneficial interests in the global security that had been held by the depositary.

PLAN OF DISTRIBUTION

We may sell securities:

- through underwriters;
- through dealers;
- through agents;
- directly to purchasers; or
- through a combination of any of these methods of sale.

In addition, we may issue the securities as a dividend or distribution or in a subscription rights offering to our existing security holders. This prospectus may be used in connection with any offering of our securities through any of these methods or other methods described in the applicable prospectus supplement.

We may directly solicit offers to purchase securities, or agents may be designated to solicit such offers. We will, in the prospectus supplement relating to such offering, name any agent that could be viewed as an underwriter under the Securities Act, and describe any commissions that we must pay. Any such agent will be acting on a best efforts basis for the period of its appointment or, if indicated in the applicable prospectus supplement, on a firm commitment basis.

The distribution of the securities may be effected from time to time in one or more transactions:

- at a fixed price, or prices, which may be changed from time to time;
- at market prices prevailing at the time of sale;
- at prices related to such prevailing market prices; or
- at negotiated prices.

Each prospectus supplement will describe the method of distribution of the securities and any applicable restrictions.

The prospectus supplement with respect to the securities of a particular series will describe the terms of the offering of the securities, including the following:

- the name of the agent or any underwriters;
- the public offering or purchase price and the proceeds we will receive from the sale of the securities;
- any discounts and commissions to be allowed or re-allowed or paid to the agent or underwriters;
- all other items constituting underwriting compensation;
- any discounts and commissions to be allowed or re-allowed or paid to dealers; and
- any exchanges on which the securities will be listed.

If any underwriters or agents are utilized in the sale of the securities in respect of which this prospectus is delivered, we will enter into an underwriting agreement or other agreement with them at the time of sale to them, and we will set forth in the prospectus supplement relating to such offering the names of the underwriters or agents and the terms of the related agreement with them.

If a dealer is utilized in the sale of the securities in respect of which this prospectus is delivered, we will sell such securities to the dealer, as principal. The dealer may then resell such securities to the public at varying prices to be determined by such dealer at the time of resale.

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If we offer securities in a subscription rights offering to our existing security holders, we may enter into a standby underwriting agreement with dealers, acting as standby underwriters. We may pay the standby underwriters a commitment fee for the securities they commit to purchase on a standby basis. If we do not enter into a standby underwriting arrangement, we may retain a dealer-manager to manage a subscription rights offering for us.

Remarketing firms, agents, underwriters, dealers and other persons may be entitled under agreements which they may enter into with us to indemnification by us against certain civil liabilities, including liabilities under the Securities Act, and may be customers of, engage in transactions with or perform services for us in the ordinary course of business.

If so indicated in the applicable prospectus supplement, we will authorize underwriters or other persons acting as our agents to solicit offers by certain institutions to purchase securities from us pursuant to delayed delivery contracts providing for payment and delivery on the date stated in the prospectus supplement. Each contract will be for an amount not less than, and the aggregate amount of securities sold pursuant to such contracts shall not be less nor more than, the respective amounts stated in the prospectus supplement. Institutions with whom the contracts, when authorized, may be made include commercial and savings banks, insurance companies, pension funds, investment companies, educational and charitable institutions and other institutions, but shall in all cases be subject to our approval. Delayed delivery contracts will not be subject to any conditions except that:

- the purchase by an institution of the securities covered under that contract shall not at the time of delivery be prohibited under the laws of the jurisdiction to which that institution is subject; and
- if the securities are also being sold to underwriters acting as principals for their own account, the underwriters shall have purchased such securities not sold for delayed delivery. The underwriters and other persons acting as our agents will not have any responsibility in respect of the validity or performance of delayed delivery contracts.

Certain agents, underwriters and dealers, and their associates and affiliates may be customers of, have borrowing relationships with, engage in other transactions with, and/or perform services, including investment banking services, for us or one or more of our respective affiliates in the ordinary course of business.

In order to facilitate the offering of the securities, any underwriters may engage in transactions that stabilize, maintain or otherwise affect the price of the securities or any other securities the prices of which may be used to determine payments on such securities. Specifically, any underwriters may over allot in connection with the offering, creating a short position for their own accounts. In addition, to cover over allotments or to stabilize the price of the securities or of any such other securities, the underwriters may bid for, and purchase, the securities or any such other securities in the open market. Finally, in any offering of the securities through a syndicate of underwriters, the underwriting syndicate may reclaim selling concessions allowed to an underwriter or a dealer for distributing the securities in the offering if the syndicate repurchases previously distributed securities in transactions to cover syndicate short positions, in stabilization transactions or otherwise. Any of these activities may stabilize or maintain the market price of the securities above independent market levels. Any such underwriters are not required to engage in these activities and may end any of these activities at any time.

Under Rule 15c6-1 of the Exchange Act, trades in the secondary market generally are required to settle in two business days, unless the parties to any such trade expressly agree otherwise or the securities are sold by us to an underwriter in a firm commitment underwritten offering. The applicable prospectus supplement may provide that the original issue date for your securities may be more than two scheduled business days after the trade date for your securities. Accordingly, in such a case, if you wish to trade securities on any date prior to the second business day before the original issue date for your securities, you will be required, by virtue of the fact that your securities initially are expected to settle in more than two scheduled business days after the trade date for your securities, to make alternative settlement arrangements to prevent a failed settlement.

The securities may be new issues of securities and may have no established trading market. The securities may or may not be listed on a national securities exchange. We can make no assurance as to the liquidity of or the existence of trading markets for any of the securities.

LEGAL MATTERS

Unless the applicable prospectus supplement indicates otherwise, the validity of the securities in respect of which this prospectus is being delivered will be passed upon by Wilmer Cutler Pickering Hale and Dorr LLP.

EXPERTS

The consolidated financial statements of Karyopharm Therapeutics Inc. appearing in Karyopharm Therapeutics Inc.'s Annual Report (Form 10-K) for the year ended December 31, 2018, and the effectiveness of Karyopharm Therapeutics Inc.'s internal control over financial reporting as of December 31, 2018, have been audited by Ernst & Young LLP, independent registered public accounting firm, as set forth in their reports thereon, included therein, and incorporated herein by reference. Such consolidated financial statements are incorporated herein by reference in reliance upon such reports given on the authority of such firm as experts in accounting and auditing.



Up to \$75,000,000

Common Stock

PROSPECTUS SUPPLEMENT

Jefferies

May 10, 2019
