

NEKTAR THERAPEUTICS
 Form 424B5
 October 17, 2016
Table of Contents

Filed Pursuant to Rule 424(b)(5)
 Registration No. 333-193454

The information contained in this preliminary prospectus supplement and the accompanying prospectus is not complete and may be changed. A registration statement relating to the securities has become effective under the Securities Act of 1933. This preliminary prospectus supplement and the accompanying prospectus are not an offer to sell these securities and are not soliciting an offer to buy these securities in any jurisdiction where the offer or sale is not permitted.

Subject to completion, dated October 17, 2016

Prospectus supplement to Prospectus dated January 21, 2014

\$175,000,000

Common stock

We are offering _____ shares of our common stock. Our common stock is listed on The NASDAQ Global Select Market under the symbol NKTR. The last reported sale price of our common stock on The NASDAQ Global Select Market on October 14, 2016 was \$15.89 per share.

	Per share	Total
Public offering price	\$	\$
Underwriting discounts and commissions	\$	\$
Proceeds to Nektar, before expenses	\$	\$

We have granted the underwriters an option for a period of 30 days from the date of this prospectus supplement to purchase up to \$26,250,000 of additional shares of our common stock. If the underwriters exercise the option in full, the total underwriting discounts and commissions payable by us will be \$ _____ and the total proceeds to us, before expenses, will be \$ _____.

Investing in our common stock involves a high degree of risk. Please read Risk factors beginning on page S-7.

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

The underwriters expect to deliver the shares of common stock to investors on or about October _____, 2016.

J.P. Morgan

October , 2016

Table of Contents**Table of contents**

	Page
Prospectus supplement	
<u>About this prospectus supplement</u>	S-iii
<u>Prospectus supplement summary</u>	S-1
<u>The offering</u>	S-6
<u>Risk factors</u>	S-7
<u>Special note regarding forward-looking statements</u>	S-10
<u>Use of proceeds</u>	S-11
<u>Dilution</u>	S-12
<u>Underwriting</u>	S-14
<u>Legal matters</u>	S-25
<u>Experts</u>	S-25
<u>Where you can find more information</u>	S-25
<u>Incorporation of certain information by reference</u>	S-26
	Page
Prospectus	
<u>About this prospectus</u>	1
<u>About our company</u>	2
<u>Ratio of earnings to fixed charges</u>	3
<u>Forward-looking statements</u>	4
<u>Risk factors</u>	5
<u>Use of proceeds</u>	6
<u>Dividend policy</u>	7
<u>General description of securities</u>	8
<u>Description of capital stock</u>	10
<u>Description of debt securities</u>	14
<u>Description of warrants</u>	23
<u>Legal ownership of securities</u>	26
<u>Plan of distribution</u>	30
<u>Legal matters</u>	32
<u>Experts</u>	33
<u>Where you can find more information</u>	34
<u>Incorporation of documents by reference</u>	34

Table of Contents

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 have authorized for use in connection with this offering. We and the underwriters have not authorized anyone to provide you with different information. If anyone provides you with different or inconsistent information, you should not rely on it. We and the underwriters are not making an offer to sell these securities in any jurisdiction where the offer or sale is not permitted. You should assume that the information appearing in this prospectus supplement, the accompanying prospectus, the documents incorporated by reference in this prospectus supplement and the accompanying prospectus, and in any free writing prospectus that we have authorized for use in connection with this offering, is accurate only as of the date of those respective documents. Our business, financial condition, results of operations and prospects may have changed since those dates. You should read this prospectus supplement, the accompanying prospectus, the documents incorporated by reference in this prospectus supplement and the accompanying prospectus, and any free writing prospectus that we have authorized 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 of this prospectus supplement titled [Where you can find more information](#) and [Incorporation of certain information by reference](#).

Table of Contents

About this prospectus supplement

This document is in two parts. The first part is this prospectus supplement, which describes the terms of this offering of common stock and also adds to and updates information contained in the accompanying prospectus and the documents incorporated by reference in this prospectus supplement and the accompanying prospectus. The second part, the accompanying prospectus dated January 21, 2014, including the documents incorporated by reference therein, 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, on the one hand, and the information contained in the accompanying prospectus or in any document incorporated by reference that was filed with the Securities and Exchange Commission, or the SEC, before the date of this prospectus supplement, on the other hand, you should rely on the information in this prospectus supplement. 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.

This prospectus supplement and the accompanying prospectus dated January 21, 2014 are part of a registration statement on Form S-3 (File No. 333-193454) we filed with the SEC as a well-known seasoned issuer, as defined in Rule 405 under the Securities Act of 1933, as amended, or the Securities Act, using a shelf registration process. Under this shelf registration process, we may sell common stock, preferred stock, debt securities or warrants from time to time in one or more offerings described in the accompanying prospectus.

All references in this prospectus supplement and the accompanying prospectus to Nektar, NKTR, the Company, we, us, our or similar refer to Nektar Therapeutics, a Delaware corporation, and its subsidiaries, except where the context otherwise requires or as otherwise indicated.

This prospectus supplement, the accompanying prospectus and the information incorporated herein and therein by reference, include trademarks, service marks and trade names owned by us or other companies. All trademarks, service marks and trade names included or incorporated by reference in this prospectus supplement or the accompanying prospectus are the property of their respective owners.

Table of Contents**Prospectus supplement summary**

This summary highlights certain information about us, this offering and selected information contained elsewhere in or incorporated by reference in this prospectus supplement and the accompanying prospectus. This summary is not complete and does not contain all of the information that you should consider before deciding whether to invest in our common stock. For a more complete understanding of our company and this offering, we encourage you to read and consider carefully the more detailed information in this prospectus supplement and the accompanying prospectus, including the information incorporated by reference in this prospectus supplement and the accompanying prospectus, and the information included in any free writing prospectus that we have authorized for use in connection with this offering, including the information referred to under the heading "Risk factors" in this prospectus supplement beginning on page S-7.

Company overview

We are a biopharmaceutical company developing a pipeline of drug candidates that utilize our PEGylation and advanced polymer conjugate technology platforms, which are designed to enable the development of new molecular entities that target known mechanisms of action. Our current proprietary pipeline is comprised of drug candidates across a number of therapeutic areas including oncology, pain, anti-infectives, and immunology. Our research and development activities involve small molecule drugs, peptides and protein biologic drug candidates. We create innovative drug candidates by using our proprietary advanced polymer conjugate technologies and expertise to modify the chemical structure of pharmacophores to create new molecular entities. Polymer chemistry is a science focused on the synthesis or bonding of polymer architectures with drug molecules to alter the properties of a molecule. Additionally, we may utilize established pharmacologic targets to engineer a new drug candidate relying on a combination of the known properties of these targets and our proprietary polymer chemistry technology and expertise. Our drug candidates are designed to improve the overall benefits and use of a drug for patients by improving the metabolism, distribution, pharmacokinetics, pharmacodynamics, half-life and/or bioavailability of drugs. Our objective is to apply our advanced polymer conjugate technology platform to create new drug candidates in multiple therapeutic areas that address large potential markets.

Commercial Stage Partnered Portfolio

In 2014, we achieved the first approval of one of our proprietary drug candidates based on our polymer conjugation technology, MOVANTIK™ (naloxegol), under a global license agreement with AstraZeneca AB (AstraZeneca). MOVANTIK™ is an oral peripherally-acting opioid antagonist, for the treatment of opioid-induced constipation, or OIC, a side effect caused by chronic administration of prescription opioid pain medicines. AstraZeneca markets and sells MOVANTIK™ in the United States in collaboration with Daiichi Sankyo, Inc. (Daiichi). On March 31, 2015, AstraZeneca and Daiichi launched MOVANTIK™ in the United States. On March 1, 2016, AstraZeneca entered into an agreement with ProStrakan Group plc (ProStrakan), a subsidiary of Kyowa Hakko Kirin Co. Ltd., granting ProStrakan exclusive marketing rights to MOVENTIG® (the naloxegol brand name in the EU) in the EU, Iceland, Liechtenstein, Norway and Switzerland. Under the terms of that agreement, ProStrakan made a \$70 million upfront payment to AstraZeneca and will make future payments based on achieving market access milestones, tiered net sales royalties, as well as sales milestones. Under our license agreement, AstraZeneca and Nektar shared the upfront payment and will share the market access milestones, royalties and sales milestones from ProStrakan with AstraZeneca receiving 60% and Nektar receiving 40%.

Table of Contents

We have a collaboration with Baxalta Incorporated (Baxalta) to develop and commercialize PEGylated drug candidates with the objective of providing new long-acting therapies for hemophilia patients. Under this collaboration, we worked with Baxalta to develop ADYNOVATE™, an extended half-life recombinant factor VIII (rFVIII) treatment for Hemophilia A based on ADVATE®. In November 2015, ADYNOVATE™ was approved by the U.S. Food and Drug Administration (FDA) for use in adults and adolescents, aged 12 years and older, who have Hemophilia A. Baxalta announced the launch and first shipments of ADYNOVATE™ on November 30, 2015. On April 4, 2016, Baxalta announced that the Ministry of Health, Labour and Welfare in Japan approved ADYNOVATE™ for patients aged 12 years and older with Hemophilia A. ADYNOVATE™ is also under regulatory review in Europe, Switzerland and Canada.

Development Stage Partnered Portfolio

We have two significant drug development programs with Bayer. The first is a collaboration to develop BAY41-6551 (Amikacin Inhale, formerly known as NKTR-061), which is an inhaled solution of amikacin, an aminoglycoside antibiotic. We originally developed the liquid aerosol inhalation platform and the NKTR-061 drug candidate and entered into a collaboration agreement with Bayer to further advance the drug candidate's development and potential commercialization. Bayer is currently enrolling patients in a Phase 3 clinical study for Amikacin Inhale. Bayer is conducting this study under a Special Protocol Assessment process agreed to with the FDA and topline data is anticipated in the first quarter of 2017. The second is the Cipro DPI (Cipro Dry Powder Inhaler, previously called Cipro Inhale) program with Bayer. We retained significant royalty rights in this pulmonary program, but otherwise transferred development responsibility to Novartis as part of the 2008 pulmonary asset divestiture transaction. In August 2012, Bayer initiated a global Phase 3 program called RESPIRE for the Cipro DPI product candidate in patients with non-cystic fibrosis bronchiectasis. These programs represent a significant future economic opportunity for us.

We have a license, manufacturing and supply agreement with Ophthotech Corporation (Ophthotech) for Fovista®, an anti-platelet-derived growth factor (anti-PDGF) agent, currently in Phase 3 development for the treatment of wet age-related macular degeneration. Data for the Phase 3 program of Fovista® is anticipated in the fourth quarter of 2016. Ophthotech expected that, if the FDA grants priority review, Fovista® could be launched in U.S. as early as in the fourth quarter of 2017.

We have a license, manufacturing and supply agreement with Halozyme Therapeutics, Inc. for PEG-PH20, which is entering Phase 3 development for the treatment of pancreatic cancer. We have a license, manufacturing and supply agreement with UCB Pharma for dapirolizumab pegol, a monovalent pegylated Fab antibody fragment against the CD40 ligand (CD40L), being developed for the treatment of autoimmune diseases, including systemic lupus erythematosus for which the candidate is entering Phase 2 development with UCB partner Biogen. We also have a number of license, manufacturing and supply agreements with other leading biotechnology and pharmaceutical companies, including Amgen Inc., Allergan, Inc., Merck & Co., Inc., Pfizer, Inc. and F. Hoffmann-La Roche Ltd. A total of ten products using our PEGylation technology have received regulatory approval in the U.S. or EU. There are also a number of other products in clinical development that incorporate our advanced PEGylation and advanced polymer conjugate technologies.

Nektar Proprietary Portfolio

ONZEALD for metastatic breast cancer

NKTR-102 (etirinotecan pegol, also known as ONZEALD™) is our next-generation topoisomerase I inhibitor proprietary drug candidate. In 2015, we announced topline data from a Phase 3 clinical study for NKTR-102,

Table of Contents

which we call the BEACON study (BrEAsT Cancer Outcomes with NKTR-102), as a single-agent therapy for women with advanced metastatic breast cancer. The BEACON study compared NKTR-102 to an active control arm comprised of a single chemotherapy agent of physician's choice (TPC) in patients who were heavily pre-treated with a median of three prior therapies for metastatic disease. In a topline analysis of 852 patients from the trial, NKTR-102 provided a 2.1 month improvement in median overall survival over TPC (12.4 months for patients receiving NKTR-102 compared to 10.3 months for patients receiving TPC). Based on a stratified log-rank analysis, the primary endpoint measuring the hazard ratio for survival in the NKTR-102 group compared to the active control arm was 0.87 with a p-value of 0.08, which did not achieve statistical significance. Secondary endpoints in the BEACON study included objective response rate and progression-free survival, which did not achieve statistical significance in the study. We also announced that we observed a significant overall survival benefit in two pre-specified subgroups: patients with a history of brain metastases and patients with baseline liver metastases at study entry.

We have explored future regulatory and development paths forward for ONZEALD™ with the EU and U.S. health authorities. In Europe, we met with the National Authorities in Sweden and the United Kingdom to discuss the BEACON data. On May 26, 2016, the Committee for Medicinal Products for Human Use granted an accelerated assessment procedure for the planned ONZEALD™ filing, which provides for an accelerated marketing authorization application (MAA) review timeline. In June 2016, we also met with the European Medicines Agency (EMA) and filed an MAA for conditional approval of ONZEALD™ for adult patients with advanced breast cancer who have brain metastases. On July 14, 2016, we received a letter from the EMA notifying us that the ONZEALD™ application successfully passed validation to be accepted for review. As contemplated by our recently announced European commercialization collaboration with Daiichi and in connection with our MAA filing for ONZEALD™, in 2016 we plan to initiate a randomized Phase 3 confirmatory study to evaluate ONZEALD™ as compared to a single-agent chemotherapy of physician's choice in approximately 350 adult patients with advanced breast cancer who have brain metastases (Confirmatory Study). The primary endpoint of the Confirmatory Study will be overall survival and the Confirmatory Study will include a pre-specified interim analysis for overall survival which is to be conducted after 130 events have occurred in the study. In addition, based on our meetings with the FDA's Oncology Division, the FDA staff has indicated that positive results from the Confirmatory Study could also support an NDA filing in the U.S. where Nektar has retained all rights to ONZEALD™.

NKTR-181 for chronic pain

NKTR-181 is a novel mu-opioid analgesic drug candidate for chronic pain conditions and is currently in Phase 3 clinical development. We enrolled the first patient in the first Phase 3 efficacy study in February 2015 and we recently completed enrollment in the study. In this study, we are randomizing patients with chronic low back pain in an enriched enrollment randomized withdrawal design which will include a qualifying screening period, an open-label titration period where NKTR-181 is given to all patients, followed by a 12 week double-blind randomized period where subjects will be randomized on a 1:1 basis to receive either NKTR-181 or placebo. On February 29, 2016, we increased the sample size of this trial by 200 patients following a prespecified sample size assessment by an independent analysis center after approximately fifty percent of the initially planned 416 patients completed the study. We anticipate topline data from the Phase 3 efficacy portion of this trial in the first quarter of 2017.

Nektar 214 Immuno-oncology program

In December 2015, we dosed the first patient in a Phase 1/2 clinical study for NKTR-214, which is our engineered immunostimulatory CD122-biased cytokine designed to preferentially activate the beta and gamma sub-units of

Table of Contents

the IL-2 receptor with the objective to induce proliferation of tumor-killing T cells within the body (CD8-positive effector T cells and natural killer T cells) without stimulating regulatory T cells (CD4-positive T cells). The study is being conducted at two primary investigator sites: the University of Texas MD Anderson Cancer Center and Yale Cancer Center. The dose-escalation stage of the Phase 1/2 study is designed to evaluate safety and efficacy, and define the recommended Phase 2 dose of NKTR-214 in patients with solid tumors. In addition to a determination of the recommended Phase 2 dose, the study will assess preliminary anti-tumor activity, including objective response rate. The immunologic effect of NKTR-214 on tumor-infiltrating lymphocytes and other immune infiltrating cells in both blood and tumor tissue will also be assessed.

On September 27, 2016, we entered into a Clinical Trial Collaboration Agreement with Bristol-Myers Squibb Company (BMS) to conduct Phase 1/2 clinical trials evaluating NKTR-214, and BMS 's human monoclonal antibody that binds PD-1, known as Opdivo (nivolumab), as a potential combination treatment regimen in five tumor types and seven potential indications. Under the Agreement, BMS will be responsible for 50% of all out-of-pocket costs reasonably incurred in connection with third party contract research organizations, laboratories, clinical sites and institutional review boards. Each party will otherwise be responsible for its own internal costs.

Ownership of, and global commercial rights to, NKTR-214 remain solely with us under the Agreement. If we wish to license the right to commercialize NKTR-214 in one of certain major market territories prior to September 30, 2018 (the Exclusivity Expiration Date), we must first negotiate with BMS, for a period of three months (the Negotiation Period) to grant an exclusive license to develop and commercialize NKTR-214 in any of these major market territories. If BMS and we do not reach an agreement for an exclusive license within the Negotiation Period, we will be free to license any right to NKTR-214 to other parties in any territory worldwide except that in the event that we receive a license offer from a third party during a period of 90 calendar days after the end of the Negotiation Period, we will provide BMS ten business days to match the terms of such third-party offer. After the Exclusivity Expiration Date, we are free to license NKTR-214 without any further obligation to BMS.

NKTR-358 for autoimmune diseases

We are developing NKTR-358, a drug candidate currently being studied pre-clinically for use in autoimmune diseases. NKTR-358 is an immune-regulatory cytokine targeting the IL-2 pathway to stimulate growth of regulatory T cells (T-reg). In healthy people, T-regs regulate protective immune responses by suppressing auto-reactive effector T cells and engaging the natural capability of the immune system to return itself to homeostasis. In people with autoimmune diseases, T-regs fail to suppress auto-reactive T cells due to impaired function or low frequency and this imbalance can cause the immune system to attack healthy tissue. Current systemic treatments for autoimmune diseases, including corticosteroids and anti-TNF agents, suppress the immune system broadly and come with severe side effects. NKTR-358 is designed to selectively bind to the IL-2R α receptor to proliferate T-regs without stimulating effector T cells and restoring balance to the immune system. We currently plan to submit an Investigational New Drug application for NKTR-358 in the first quarter of 2017.

NKTR-255 Immuno-oncology program

We are developing NKTR-255, one of our immune-oncology product candidates that is currently being studied pre-clinically. NKTR-255 is a memory T cell stimulating cytokine designed to engage the IL-15 pathway to induce long-term T cell activation and improve the quality of T cell memory response to treat cancer. Through enhanced engagement of the IL-15R α /IL-2R β receptor complex, NKTR-255 stimulates proliferation and survival

Table of Contents

of CD8+ T cells, natural killer cells and enhances formation of long-term immunological memory which may lead to sustained anti-tumor immune response. Native rhIL-15 is rapidly cleared from the body and must be administered frequently and in high doses limiting its utility due to toxicity. NKTR-255 is designed with IL-15 receptor alpha specificity to enhance biological activity and improve safety profile.

Corporate information

We were incorporated in California in 1990 and reincorporated in Delaware in 1998. We maintain our executive offices at 455 Mission Bay Boulevard South, San Francisco, California 94158, and our main telephone number is (415) 482-5300. Our website is located at www.nektar.com. Information contained on our website is not a part of, and not incorporated into, this prospectus supplement or the accompanying prospectus.

Recent developments

Based upon preliminary estimates, as of September 30, 2016, we had cash and investments in marketable securities of approximately \$253.5 million. This financial information has been prepared by and is the responsibility of our management and has not been reviewed by our independent registered public accounting firm, and, accordingly, our independent registered public accounting firm does not express an opinion on, or provide any other form of assurance with respect to, this preliminary data. This financial information is subject to completion of our quarterly financial closing procedures, the preparation of our consolidated financial statements, and the performance of a review of our consolidated financial statements by our independent registered public accounting firm as of and for the three- and nine-month periods ended September 30, 2016. Our actual results may differ from these estimates.

Table of Contents

The offering

Common stock offered by us

shares

Common stock outstanding after this offering

shares

Option to purchase additional shares of common stock from us

shares

Use of proceeds

We intend to use the net proceeds from this offering for general corporate purposes including research and development funding and working capital. In particular, we intend to use the proceeds to fund the development of our drug candidates, including NKTR-181, Amikacin Inhale, NKTR-102 (also known as ONZEALD), NKTR-214, NKTR-358 and other preclinical programs. See Use of proceeds on page S-11 of this prospectus supplement.

NASDAQ Global Select Market listing

Our common stock is listed on The NASDAQ Global Select Market under the symbol NKTR.

Risk factors

Investing in our common stock involves a high degree of risk. See Risk factors on page S-7 of this prospectus supplement.

Outstanding shares

The number of shares of our common stock to be outstanding immediately after this offering is based on 136,602,488 shares outstanding as of June 30, 2016, and excludes as of such date:

18,311,876 shares of common stock issuable upon the exercise of outstanding options, at a weighted average exercise price of \$11.52 per share;

1,105,846 shares of common stock issuable upon the vesting of outstanding restricted stock units; and

7,015,200 shares of common stock available for future grant under our 2012 Performance Incentive Plan and our Employee Stock Purchase Plan, as amended and restated.

Except as otherwise indicated, all information in this prospectus supplement assumes:

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no exercise of the outstanding stock options described above; and

no exercise by the underwriters of their option to purchase additional shares.

S-6

Table of Contents

Risk factors

An investment in our common stock involves a high degree of risk. Before deciding whether to invest in our common stock, in addition to the risks described below, you should carefully consider those risk factors included in our most recent annual report on Form 10-K and our most recent quarterly report on Form 10-Q, which are incorporated herein by reference, together with the information in this prospectus supplement, the accompanying prospectus, the documents incorporated herein by reference and in any free writing prospectus that we have authorized for use in connection with this offering.

Risks related to our common stock and this offering

The price of our common stock is expected to remain volatile.

Our stock price is volatile. Based on closing bid prices on The NASDAQ Global Select Market, our stock price ranged from \$11.00 to \$19.68 during the period from January 1, 2016 through October 14, 2016. We expect our stock price to remain volatile. A variety of factors may have a significant effect on the market price of our common stock, including:

announcements of data from, or material developments in, our clinical studies and those of our collaboration partners, including data regarding efficacy and safety, delays in clinical development, regulatory approval or commercial launch;

announcements by collaboration partners as to their plans or expectations related to drug candidates and approved drugs in which we have a substantial economic interest;

announcements regarding terminations or disputes under our collaboration agreements;

fluctuations in our results of operations;

developments in patent or other proprietary rights, including intellectual property litigation or entering into intellectual property license agreements and the costs associated with those arrangements;

announcements of technological innovations or new therapeutic products that may compete with our approved products or products under development;

announcements of changes in governmental regulation affecting us or our competitors;

litigation brought against us or third parties to whom we have indemnification obligations;

public concern as to the safety of drug formulations developed by us or others;

our financing needs and activities; and

general market conditions.

Our stockholders may be diluted, and the price of our common stock may decrease, as a result of the exercise of outstanding stock options or the future issuances of securities.

We may issue additional common stock, preferred stock, restricted stock units or securities convertible into or exchangeable for our common stock, and these newly issued securities may have rights, preferences or privileges senior to those of our existing stockholders. Furthermore, substantially all shares of common stock for which our outstanding stock options are exercisable are, once they have been purchased, eligible for immediate sale in the public market. The issuance of additional common stock, preferred stock, restricted stock units or securities convertible into or exchangeable for our common stock or the exercise of stock options would dilute existing stockholders and could lower the price of our common stock.

S-7

Table of Contents

Our management will have broad discretion as to the use of the proceeds from this offering, and we may not use the proceeds effectively.

Our management will have broad discretion in the application of the net proceeds from this offering and could spend the proceeds in ways that do not improve our results of operations or enhance the value of our common stock. Our failure to apply these funds effectively could significantly harm our business or the development of our drug candidates and decrease the price of our common stock.

Investors in this offering will experience immediate and substantial dilution in the net tangible book value per share of the common stock they purchase.

Since the price per share of our common stock being offered is substantially higher than the net tangible book value per share of our common stock, you will suffer substantial dilution in the net tangible book value of the common stock you purchase in this offering. See the section titled

Dilution in this prospectus supplement for a more detailed discussion of the dilution you will incur if you purchase common stock in this offering.

Shares of common stock are equity securities and are subordinate to any preferred stock we may issue and to any existing or future indebtedness.

Shares of our common stock rank junior to our existing indebtedness, including our 7.75% senior secured notes due October 2020, or our senior secured notes, to any shares of preferred stock that we may issue in the future, to any future indebtedness we may incur and to all creditor claims and other non-equity claims against us and our assets available to satisfy claims on us, including claims in a bankruptcy or similar proceeding. Our senior secured notes restrict, and any future indebtedness and preferred stock may restrict, payment of dividends on our common stock.

Additionally, unlike indebtedness, where principal and interest customarily are payable on specified due dates, in the case of our common stock, (i) dividends are payable only when and if declared by our board of directors or a duly authorized committee of our board of directors, and (ii) as a corporation, we are restricted to making dividend payments and redemption payments out of legally available assets. We have never declared or paid any cash dividends on our common stock and do not currently anticipate declaring or paying cash dividends on our common stock in the foreseeable future. Furthermore, our common stock places no restrictions on our business or operations or on our ability to incur indebtedness or engage in any transactions, subject only to the voting rights available to shareholders generally.

We have implemented certain anti-takeover measures, which make it more difficult to acquire us, even though such acquisitions may be beneficial to our stockholders.

Provisions of our certificate of incorporation and bylaws, as well as provisions of Delaware law, could make it more difficult for a third party to acquire us, even though such acquisitions may be beneficial to our stockholders. These anti-takeover provisions include:

establishment of a classified board of directors such that not all members of the board may be elected at one time;

lack of a provision for cumulative voting in the election of directors, which would otherwise allow less than a majority of stockholders to elect director candidates;

the ability of our board to authorize the issuance of blank check preferred stock to increase the number of outstanding shares and thwart a takeover attempt;

prohibition on stockholder action by written consent, thereby requiring all stockholder actions to be taken at a meeting of stockholders;

Table of Contents

establishment of advance notice requirements for nominations for election to the board of directors or for proposing matters that can be acted upon by stockholders at stockholder meetings; and

limitations on who may call a special meeting of stockholders.

Further, provisions of Delaware law relating to business combinations with interested stockholders may discourage, delay or prevent a third party from acquiring us. These provisions may also discourage, delay or prevent a third party from acquiring a large portion of our securities or initiating a tender offer or proxy contest, even if our stockholders might receive a premium for their shares in the acquisition over the then current market prices. We also have a change of control severance benefit plan which provides for certain cash severance, stock award acceleration and other benefits in the event our employees are terminated (or, in some cases, resign for specified reasons) following an acquisition. This severance plan could discourage a third party from acquiring us.

Table of Contents

Special note regarding forward-looking statements

All statements included or incorporated by reference in this prospectus supplement and the accompanying prospectus, other than statements of historical facts, that address activities, events or developments that we intend, expect, project, believe or anticipate will or may occur in the future are forward-looking statements. This prospectus supplement and the accompanying prospectus contain forward-looking statements that are based on current expectations, estimates, forecasts and projections about us, our future performance, our business or the business of others on our behalf, our beliefs and our management's assumptions. In addition, we, or others on our behalf, may make forward-looking statements in press releases or written statements, or in our communications and discussions with investors and analysts in the normal course of business through meetings, webcasts, phone calls and conference calls. Words such as expect, anticipate, outlook, could, will, target, project, believe, seek, estimate, should, may, assume, or continue, and variations of such words and similar expressions are intended to identify forward-looking statements. These statements are not guarantees of future performance and involve certain risks, uncertainties and assumptions that are difficult to predict. We have based our forward-looking statements on our management's beliefs and assumptions based on information available to our management at the time the statements are made. We caution you that actual outcomes and results may differ materially from what is expressed, implied or forecast by our forward-looking statements. Reference is made in particular to forward-looking statements regarding projections of earnings, revenue, milestone payments, royalties, sales or other financial items, plans and objectives of management for future operations (including, but not limited to, preclinical research and development, clinical trials and manufacturing), financial condition, liquidity and future working capital needs, future financing alternatives, proposed drug candidates, the timing for the start or end of clinical trials or submission of regulatory approval filings, future economic conditions or performance, the success of our collaboration arrangements or future payments that may come due to us under these arrangements, plans and objectives to initiate or continue clinical trials and any assumptions underlying any of the foregoing. Except as required under the federal securities laws and the rules and regulations of the SEC, we do not have any intention or obligation to update publicly any forward looking statements after the distribution of this prospectus supplement and the accompanying prospectus, whether as a result of new information, future events, changes in assumptions or otherwise.

You are cautioned not to rely unduly on any forward-looking statements. These risks and uncertainties are discussed in more detail under Risk Factors, Business and Management's Discussion and Analysis of Financial Condition and Results of Operations in our periodic reports and other documents on file with the SEC. You may obtain copies of these documents as described under the section titled Where you can find more information below.

Table of Contents

Use of proceeds

We estimate that the net proceeds from the sale of shares of common stock that we are offering will be approximately \$163.9 million, or approximately \$188.6 million if the underwriters exercise in full their option to purchase \$26.3 million of additional shares of common stock, after deducting underwriting discounts and commissions and estimated offering expenses payable by us.

We intend to use the net proceeds from this offering for general corporate purposes including research and development funding and working capital. In particular, we intend to use the proceeds to fund the development of our drug candidates, including NKTR-181, Amikacin Inhale, NKTR-102 (also known as ONZEALD), NKTR-214, NKTR-358 and other preclinical programs.

The amounts and timing of these expenditures will depend on a number of factors, such as the timing, scope, progress and results of our research and development efforts, the timing and progress of any partnering efforts, the timing, progress, and results from our collaboration partners development and commercialization efforts, and the competitive environment for our drug candidates. As of the date of this prospectus supplement, we cannot specify with certainty all of the particular uses of the proceeds from this offering. Accordingly, we will retain broad discretion over the use of such proceeds.

S-11

Table of Contents**Dilution**

Our net tangible book deficit as of June 30, 2016 was approximately \$(115.8) million, or \$(0.85) per share. Net tangible book value per share is determined by dividing our total tangible assets, less total liabilities, by the number of shares of our common stock outstanding as of June 30, 2016. Dilution in net tangible book value per share represents the difference between the amount per share paid by purchasers of shares of common stock in this offering and the net tangible book value per share of our common stock immediately after this offering.

After giving effect to the sale of 11,013,215 shares of our common stock in this offering at an assumed public offering price of \$15.89 per share, the last reported sale price of our common stock on The NASDAQ Global Select Market on October 14, 2016, and after deducting underwriting discounts and commissions and estimated offering expenses payable by us, our as adjusted net tangible book value as of June 30, 2016 would have been approximately \$48.1 million, or \$0.33 per share. This represents an immediate increase in net tangible book value of \$1.18 per share to existing stockholders and immediate dilution in net tangible book value of \$15.56 per share to new investors purchasing our common stock in this offering. The following table illustrates this dilution on a per share basis:

Assumed public offering price per share	\$ 15.89
Net tangible book value (deficit) per share as of June 30, 2016	\$ (0.85)
Increase per share attributable to new investors	1.18
As adjusted net tangible book value per share as of June 30, 2016 after this offering	0.33
Dilution in net tangible book value per share to new investors	\$ 15.56

A \$1.00 increase (decrease) in the assumed public offering price of \$15.89 per share, the last reported sale price of our common stock on The NASDAQ Global Select Market on October 14, 2016, would (decrease) increase the number of shares of common stock to be issued by us in this offering by (652,055) and 739,639, respectively, assuming the aggregate dollar amount of shares offered by us, as set forth on the cover page of this prospectus supplement, remains the same. We may also increase or decrease the aggregate dollar amount of shares we are offering. An increase (decrease) of \$1.0 million of shares offered by us would increase (decrease) the net proceeds of this offering by approximately \$0.9 million, assuming that the assumed public offering price remains the same, and after deducting underwriting discounts and commissions and estimated offering expenses payable by us. The as adjusted information discussed above is illustrative only and will be adjusted based on the actual public offering price and other terms of this offering determined at pricing.

If the underwriters exercise in full their option to purchase 1,651,982 additional shares of common stock at an assumed public offering price of \$15.89 per share, the last reported sale price of our common stock on The NASDAQ Global Select Market on October 14, 2016, the as adjusted net tangible book value after this offering would be \$0.49 per share, representing an increase in net tangible book value of \$1.34 per share to existing stockholders and immediate dilution in net tangible book value of \$15.40 per share to new investors purchasing our common stock in this offering.

The above discussion and table are based on 136,602,488 shares outstanding as of June 30, 2016, and exclude as of such date:

18,311,876 shares of common stock issuable upon the exercise of outstanding options, at a weighted average exercise price of \$11.52 per share;

1,105,846 shares of common stock issuable upon the vesting of outstanding restricted stock units; and

7,015,200 shares of common stock available for future grant under our 2012 Performance Incentive Plan and our Employee Stock Purchase Plan, as amended and restated.

Table of Contents

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

S-13

Table of Contents

Underwriting

We are offering the shares of common stock described in this prospectus supplement through a number of underwriters. J.P. Morgan Securities LLC is acting as sole book-running manager of the offering and as representative of the underwriters. We have entered into an underwriting agreement with the underwriters. Subject to the terms and conditions of the underwriting agreement, we have agreed to sell to the underwriters, and each underwriter has severally agreed to purchase, at the public offering price less the underwriting discounts and commissions set forth on the cover page of this prospectus supplement, the number of shares of common stock listed next to its name in the following table:

Name	Number of shares
J.P. Morgan Securities LLC	

Total

The underwriters are committed to purchase all of the shares of common stock offered by us if they purchase any shares. The underwriting agreement also provides that if an underwriter defaults, the purchase commitment of the non-defaulting underwriters may also be increased or the offering may be terminated.

The underwriters propose to offer the shares directly to the public at the public offering price set forth on the cover page of this prospectus supplement and to certain dealers at that price less a concession not in excess of \$ per share. After the public offering of the shares, the offering price and other selling terms may be changed by the underwriters. Sales of shares made outside of the United States may be made by affiliates of the underwriters. The offering of the shares by the underwriters is subject to receipt and acceptance and subject to the underwriters right to reject any order in whole or in part.

The underwriters have an option to buy up to additional shares of common stock from us to cover sales of shares by the underwriters which exceed the number of shares specified in the table above. The underwriters have 30 days from the date of this prospectus supplement to exercise this option to purchase additional shares. If any shares are purchased with this option, the underwriters will purchase shares in approximately the same proportion as shown in the table above. If any additional shares of common stock are purchased, the underwriters will offer the additional shares on the same terms as those on which the shares are being offered.

The underwriting fee is equal to the public offering price per share of common stock less the amount paid by the underwriters to us per share of common stock. The following table shows the per share and total underwriting discounts and commissions to be paid to the underwriters assuming both no exercise and full exercise of the underwriters' option to purchase additional shares.

	Without option exercise	Per share With full option exercise	Without option exercise	Total With full option exercise
Underwriting discounts and commissions	\$	\$	\$	\$

We estimate that the total expenses of this offering incurred by us, including registration, filing and listing fees, printing fees and legal and accounting expenses, but excluding underwriting discounts and commissions, will be approximately \$600,000.

Table of Contents

A prospectus supplement in electronic format may be made available on the web sites maintained by one or more underwriters, or selling group members, if any, participating in the offering. The underwriters may agree to allocate a number of shares to underwriters and selling group members for sale to their online brokerage account holders. Internet distributions will be allocated by the representative to underwriters and selling group members that may make Internet distributions on the same basis as other allocations.

For a period of 90 days after the date of this prospectus supplement, we have agreed that we will not (i) offer, pledge, sell, contract to sell, sell any option or contract to purchase, purchase any option or contract to sell, grant any option, right or warrant to purchase, or otherwise transfer or dispose of, directly or indirectly, or file with the SEC a registration statement under the Securities Act (other than any registration statement on Form S-8 filed for the purpose of registering securities issuable pursuant to our existing stock incentive plans) relating to, any shares of our common stock or securities convertible into or exercisable or exchangeable for any shares of our common stock, or publicly disclose the intention to make any offer, sale, pledge, disposition or filing, or (ii) enter into any swap or other arrangement that transfers, in whole or in part, any of the economic consequences of ownership of any shares of common stock or any such other securities (regardless of whether any of these transactions are to be settled by the delivery of shares of common stock, or such other securities, in cash or otherwise), in each case without the prior written consent of J.P. Morgan Securities LLC, other than (a) the sale of securities in this offering, (b) any shares of our common stock issued pursuant to transactions relating to our existing stock incentive plans (including the issuance or grant of options, restricted stock or other equity-based awards thereunder and the issuance of shares of our common stock upon the exercise of options issued pursuant thereto), (c) shares of our common stock or other securities convertible into or exercisable for shares of our common stock issued in connection with a joint venture, collaboration agreement, license agreement, loan or any acquisition of assets or equity of another entity, provided that (x) the aggregate number of shares of our common stock or securities convertible into or exercisable for our common stock issued pursuant to this clause (c) shall not exceed 5.0% of the total number of shares of our common stock issued and outstanding immediately following the completion of this offering, and (y) the recipient of any such shares of our common stock and securities issued pursuant to clause (c) shall enter into a lock-up agreement.

Our directors and executive officers have entered into lock-up agreements with the underwriters prior to the commencement of this offering pursuant to which each of these persons or entities, with limited exceptions, for a period of 90 days after the date of this prospectus supplement, may not, without the prior written consent of J.P. Morgan Securities LLC, (i) offer, pledge, sell, contract to sell, sell any option or contract to purchase, purchase any option or contract to sell, grant any option, right or warrant to purchase, or otherwise transfer or dispose of, directly or indirectly, any shares of our common stock or any securities convertible into or exercisable or exchangeable for our common stock (including, without limitation, common stock or such other securities which may be deemed to be beneficially owned by such directors, executive officers and investors in accordance with the rules and regulations of the SEC and securities which may be issued upon exercise of a stock option or warrant), or publicly disclose the intention to make any offer, sale, pledge or disposition, (ii) enter into any swap or other agreement that transfers, in whole or in part, any of the economic consequences of ownership of the common stock or such other securities, whether any such transaction described in clause (i) or (ii) above is to be settled by delivery of common stock or such other securities, in cash or otherwise or (iii) make any demand for or exercise any right with respect to the registration of any shares of our common stock or any security convertible into or exercisable or exchangeable for our common stock.

Certain of our directors and executive officers have established trading plans pursuant to Rule 10b5-1 of the Exchange Act and may sell, pledge, transfer or otherwise dispose, directly or indirectly, shares of our common stock pursuant to such plans during the 90-day lock-up period. Should sales be made by such directors and executive officers pursuant to these trading plans, reports on Form 4 will be filed with the SEC, if required by

Table of Contents

law. In addition, the foregoing restrictions shall not apply to the sale of shares of our common stock to cover tax withholding obligations in connection with the settlement or release of restricted stock units.

J.P. Morgan Securities LLC, in its sole discretion, may release the common stock and other securities subject to the lock-up agreements described above in whole or in part at any time with or without notice.

We have agreed to indemnify the several underwriters and their controlling persons against certain liabilities, including liabilities under the Securities Act.

Our common stock is listed on The NASDAQ Global Select Market under the symbol NKTR.

In connection with this offering, the underwriters may engage in stabilizing transactions, which involve making bids for, purchasing and selling shares of common stock in the open market for the purpose of preventing or retarding a decline in the market price of the common stock while this offering is in progress. These stabilizing transactions may include making short sales of the common stock, which involve the sale by the underwriters of a greater number of shares of common stock than they are required to purchase in this offering, and purchasing shares of common stock on the open market to cover positions created by short sales. Short sales may be covered shorts, which are short positions in an amount not greater than the underwriters' option referred to above, or may be naked shorts, which are short positions in excess of that amount. The underwriters may close out any covered short position either by exercising their option to purchase additional shares, in whole or in part, or by purchasing shares in the open market. In making this determination, the underwriters will consider, among other things, the price of shares available for purchase in the open market compared to the price at which the underwriters may purchase shares through the option to purchase additional shares. A naked short position is more likely to be created if the underwriters are concerned that there may be downward pressure on the price of the common stock in the open market that could adversely affect investors who purchase in this offering. To the extent that the underwriters create a naked short position, they will purchase shares in the open market to cover the position.

The underwriters have advised us that, pursuant to Regulation M of the Securities Act, they may also engage in other activities that stabilize, maintain or otherwise affect the price of the common stock, including the imposition of penalty bids. This means that if the representative of the underwriters purchases common stock in the open market in stabilizing transactions or to cover short sales, the representative can require the underwriters that sold those shares as part of this offering to repay the underwriting discounts and commissions received by them.

These activities may have the effect of raising or maintaining the market price of the common stock or preventing or retarding a decline in the market price of the common stock, and, as a result, the price of the common stock may be higher than the price that otherwise might exist in the open market. If the underwriters commence these activities, they may discontinue them at any time. The underwriters may carry out these transactions on The NASDAQ Global Select Market, as applicable, in the over-the-counter market or otherwise.

Other relationships

The underwriters and their respective affiliates are full service financial institutions engaged in various activities, which may include securities trading, commercial and investment banking, financial advisory, investment management, investment research, principal investment, hedging, financing and brokerage activities. Certain of the underwriters and their respective affiliates have, from time to time, performed and may, from time to time, in the future provide us with investment banking, financial advisory or other services for which they may receive customary compensation.

In the ordinary course of their various business activities, the underwriters and their respective affiliates may make or hold a broad array of investments and actively trade debt and equity securities (or related derivative

Table of Contents

securities) and financial instruments (including bank loans) for their own account and for the accounts of their customers, and such investment and securities activities may involve our securities and/or instruments. The underwriters and their respective affiliates may also make investment recommendations and/or publish or express independent research views in respect of such securities or instruments and may at any time hold, or recommend to clients that they acquire, long and/or short positions in such securities and instruments.

Selling restrictions

Other than in the United States, no action has been taken by us or the underwriters that would permit a public offering of the securities offered by this prospectus supplement and accompanying prospectus in any jurisdiction where action for that purpose is required. The securities offered by this prospectus supplement and accompanying prospectus may not be offered or sold, directly or indirectly, nor may this prospectus supplement and accompanying prospectus or any other offering material or advertisements in connection with the offer and sale of any such securities be distributed or published in any jurisdiction, except under circumstances that will result in compliance with the applicable rules and regulations of that jurisdiction. Persons into whose possession this prospectus supplement and accompanying prospectus comes are advised to inform themselves about and to observe any restrictions relating to the offering and the distribution of this prospectus supplement and accompanying prospectus. This prospectus supplement and accompanying prospectus does not constitute an offer to sell or a solicitation of an offer to buy any securities referred to by this prospectus supplement and accompanying prospectus in any jurisdiction in which such an offer or solicitation is unlawful.

European Economic Area

In relation to each Member State of the European Economic Area which has implemented the Prospectus Directive (each, a Relevant Member State), from and including the date on which the European Union Prospectus Directive (the EU Prospectus Directive) was implemented in that Relevant Member State (the Relevant Implementation Date) an offer of securities described in this prospectus supplement may not be made to the public in that Relevant Member State prior to the publication of a prospectus in relation to the shares which has been approved by the competent authority in that Relevant Member State or, where appropriate, approved in another Relevant Member State and notified to the competent authority in that Relevant Member State, all in accordance with the EU Prospectus Directive, except that, with effect from and including the Relevant Implementation Date, an offer of securities described in this prospectus supplement may be made to the public in that Relevant Member State at any time:

- A. to any legal entity which is a qualified investor as defined under the EU Prospectus Directive;
- B. to fewer than 100 or, if the Relevant Member State has implemented the relevant provision of the 2010 PD Amending Directive, 150, natural or legal persons (other than qualified investors as defined in the EU Prospectus Directive); or
- C. in any other circumstances falling within Article 3(2) of the EU Prospectus Directive, provided that no such offer of securities described in this prospectus supplement shall result in a requirement for the publication by us of a prospectus pursuant to Article 3 of the EU Prospectus Directive.

For the purposes of this provision, the expression an offer of securities to the public in relation to any securities in any Relevant Member State means the communication in any form and by any means of sufficient information on the terms of the offer and the securities to be offered so as to enable an investor to decide to purchase or subscribe for the securities, as the same may be varied in the Relevant Member State by any measure implementing the EU Prospectus Directive in the Relevant Member State and the expression EU Prospectus Directive means Directive 2003/71/EC (and any amendments thereto, including the 2010 PD

Table of Contents

Amending Directive, to the extent implemented in the Relevant Member State) and includes any relevant implementing measure in each Relevant Member State, and the expression "2010 PD Amending Directive" means Directive 2010/73/EU.

Canada

The common stock may be sold only to purchasers purchasing, or deemed to be purchasing, as principal that are accredited investors, as defined in National Instrument 45-106 *Prospectus Exemptions* or subsection 73.3(1) of the *Securities Act* (Ontario), and are permitted clients, as defined in National Instrument 31-103 *Registration Requirements, Exemptions and Ongoing Registrant Obligations*. Any resale of the common stock must be made in accordance with an exemption from, or in a transaction not subject to, the prospectus requirements of applicable securities laws.

Securities legislation in certain provinces or territories of Canada may provide a purchaser with remedies for rescission or damages if this prospectus supplement (including any amendment thereto) contains a misrepresentation, provided that the remedies for rescission or damages are exercised by the purchaser within the time limit prescribed by the securities legislation of the purchaser's province or territory. The purchaser should refer to any applicable provisions of the securities legislation of the purchaser's province or territory for particulars of these rights or consult with a legal advisor.

Pursuant to section 3A.3 of National Instrument 33-105 *Underwriting Conflicts* (NI 33-105), the underwriters are not required to comply with the disclosure requirements of NI 33-105 regarding underwriter conflicts of interest in connection with this offering.

United Kingdom

In the United Kingdom, this document is only being distributed to and is only directed at (i) persons who are outside the United Kingdom or (ii) to investment professionals falling within Article 19(5) of the Financial Services and Markets Act 2000 (Financial Promotion) Order 2005 (the "Order") or (iii) high net worth entities, and other persons to whom it may lawfully be communicated, falling within Article 49(2)(a) to (d) of the Order (all such persons together being referred to as "relevant persons"). The securities are only available to, and any invitation, offer or agreement to subscribe for, purchase or otherwise acquire such securities will be engaged in only with, relevant persons. Any person who is not a relevant person should not act or rely on this document or any of its contents.

Switzerland

The securities offered by this prospectus supplement may not be publicly offered in Switzerland and will not be listed on the SIX Swiss Exchange ("SIX") or on any other stock exchange or regulated trading facility in Switzerland. This document does not constitute a prospectus within the meaning of, and has been prepared without regard to the disclosure standards for issuance prospectuses under art. 652a or art. 1156 of the Swiss Code of Obligations or the disclosure standards for listing prospectuses under art. 27 ff. of the SIX Listing Rules or the listing rules of any other stock exchange or regulated trading facility in Switzerland. Neither this document nor any other offering or marketing material relating to the securities or the offering may be publicly distributed or otherwise made publicly available in Switzerland.

Neither this document nor any other offering or marketing material relating to the offering, us, the securities have been or will be filed with or approved by any Swiss regulatory authority. In particular, this document will not be filed with, and the offer of securities will not be supervised by, the Swiss Financial Market Supervisory Authority FINMA ("FINMA"), and the offer of securities has not been and will not be authorized under the Swiss

Table of Contents

Federal Act on Collective Investment Schemes (CISA). The investor protection afforded to acquirers of interests in collective investment schemes under the CISA does not extend to acquirers of securities.

Dubai International Financial Centre (DIFC)

This document relates to an Exempt Offer in accordance with the Markets Rules 2012 of the Dubai Financial Services Authority (DFSA). This document is intended for distribution only to persons of a type specified in the Markets Rules 2012 of the DFSA. It must not be delivered to, or relied on by, any other person. The DFSA has no responsibility for reviewing or verifying any documents in connection with Exempt Offers. The DFSA has not approved this prospectus supplement nor taken steps to verify the information set forth herein and has no responsibility for this document. The securities to which this document relates may be illiquid and/or subject to restrictions on their resale. Prospective purchasers of the securities offered should conduct their own due diligence on the securities. If you do not understand the contents of this document you should consult an authorized financial advisor.

In relation to its use in the DIFC, this document is strictly private and confidential and is being distributed to a limited number of investors and must not be provided to any person other than the original recipient, and may not be reproduced or used for any other purpose. The interests in the securities may not be offered or sold directly or indirectly to the public in the DIFC.

United Arab Emirates

The securities offered by this prospectus supplement have not been, and are not being, publicly offered, sold, promoted or advertised in the United Arab Emirates (including the Dubai International Financial Centre) other than in compliance with the laws of the United Arab Emirates (and the Dubai International Financial Centre) governing the issue, offering and sale of securities. Further, this prospectus supplement does not constitute a public offer of securities in the United Arab Emirates (including the Dubai International Financial Centre) and is not intended to be a public offer. This prospectus supplement has not been approved by or filed with the Central Bank of the United Arab Emirates, the Securities and Commodities Authority or the Dubai Financial Services Authority.

Australia

This prospectus supplement:

does not constitute a disclosure document under Chapter 6D.2 of the Corporations Act 2001 (Cth) (the Corporations Act);

has not been, and will not be, lodged with the Australian Securities and Investments Commission (ASIC), as a disclosure document for the purposes of the Corporations Act and does not purport to include the information required of a disclosure document under Chapter 6D.2 of the Corporations Act; and

may only be provided in Australia to select investors who are able to demonstrate that they fall within one or more of the categories of investors, or Exempt Investors, available under section 708 of the Corporations Act.

The securities offered by this prospectus supplement may not be directly or indirectly offered for subscription or purchased or sold, and no invitations to subscribe for or buy the securities may be issued, and no draft or definitive offering memorandum, advertisement or other offering material relating to any securities may be distributed in Australia, except where disclosure to investors is not required under Chapter 6D of the Corporations Act or is otherwise in compliance with all applicable Australian laws and regulations. By submitting an application for the securities, you represent and warrant to us that you are an Exempt Investor.

Table of Contents

As any offer of securities under this document will be made without disclosure in Australia under Chapter 6D.2 of the Corporations Act, the offer of those securities for resale in Australia within 12 months may, under section 707 of the Corporations Act, require disclosure to investors under Chapter 6D.2 if none of the exemptions in section 708 applies to that resale. By applying for the securities you undertake to us that you will not, for a period of 12 months from the date of issue of the securities, offer, transfer, assign or otherwise alienate those securities to investors in Australia except in circumstances where disclosure to investors is not required under Chapter 6D.2 of the Corporations Act or where a compliant disclosure document is prepared and lodged with ASIC.

Hong Kong

The securities offered by this prospectus supplement have not been offered or sold and will not be offered or sold in Hong Kong, by means of any document, other than (a) to professional investors as defined in the Securities and Futures Ordinance (Cap. 571) of Hong Kong and any rules made under that Ordinance; or (b) in other circumstances which do not result in the document being a prospectus as defined in the Companies Ordinance (Cap. 32) of Hong Kong or which do not constitute an offer to the public within the meaning of that Ordinance. No advertisement, invitation or document relating to the securities has been or may be issued or has been or may be in the possession of any person for the purposes of issue, whether in Hong Kong or elsewhere, which is directed at, or the contents of which are likely to be accessed or read by, the public of Hong Kong (except if permitted to do so under the securities laws of Hong Kong) other than with respect to securities which are or are intended to be disposed of only to persons outside Hong Kong or only to professional investors as defined in the Securities and Futures Ordinance and any rules made under that Ordinance.

Warning

The contents of this document have not been reviewed by any regulatory authority in Hong Kong. You are advised to exercise caution in relation to the offer. If you are in any doubt about any of the contents of this document, you should obtain independent professional advice.

Japan

The securities offered by this prospectus supplement have not been and will not be registered under the Financial Instruments and Exchange Act. Accordingly, the securities may not be offered or sold, directly or indirectly, in Japan or to, or for the benefit of, any resident of Japan (which term as used herein means any person resident in Japan, including any corporation or other entity organized under the laws of Japan), or to others for re-offering or resale, directly or indirectly, in Japan or to or for the benefit of a resident of Japan, except pursuant to an exemption from the registration requirements of, and otherwise in compliance with, the Financial Instruments and Exchange Act and any other applicable laws, regulations and ministerial guidelines of Japan.

Singapore

This prospectus supplement has not been registered as a prospectus with the Monetary Authority of Singapore. Accordingly, this prospectus supplement and any other document or material in connection with the offer or sale, or invitation for subscription or purchase, of securities may not be circulated or distributed, nor may the securities be offered or sold, or be made the subject of an invitation for subscription or purchase, whether directly or indirectly, to persons in Singapore other than:

to an institutional investor under Section 274 of the Securities and Futures Act, Chapter 289 of Singapore (the SFA);

Table of Contents

to a relevant person pursuant to Section 275(1), or any person pursuant to Section 275(1A), and in accordance with the conditions specified in Section 275, of the SFA; or

otherwise pursuant to, and in accordance with the conditions of, any other applicable provision of the SFA.

Where the securities are subscribed or purchased under Section 275 of the SFA by a relevant person which is:

a corporation (which is not an accredited investor (as defined in Section 4A of the SFA)) the sole business of which is to hold investments and the entire share capital of which is owned by one or more individuals, each of whom is an accredited investor; or

a trust (where the trustee is not an accredited investor) whose sole purpose is to hold investments and each beneficiary of the trust is an individual who is an accredited investor, securities (as defined in Section 239(1) of the SFA) of that corporation or the beneficiaries' rights and interest (howsoever described) in that trust shall not be transferred within six months after that corporation or that trust has acquired the securities pursuant to an offer made under Section 275 of the SFA except:

to an institutional investor or to a relevant person defined in Section 275(2) of the SFA, or to any person arising from an offer referred to in Section 275(1A) or Section 276(4)(i)(B) of the SFA;

where no consideration is or will be given for the transfer;

where the transfer is by operation of law;

as specified in Section 276(7) of the SFA; or

as specified in Regulation 32 of the Securities and Futures (Offers of Investments) (Shares and Debentures) Regulations 2005 of Singapore.

Bermuda

The securities offered by this prospectus supplement may be offered or sold in Bermuda only in compliance with the provisions of the Investment Business Act of 2003 of Bermuda which regulates the sale of securities in Bermuda. Additionally, non-Bermudian persons (including companies) may not carry on or engage in any trade or business in Bermuda unless such persons are permitted to do so under applicable Bermuda legislation.

Saudi Arabia

This prospectus supplement may not be distributed in the Kingdom of Saudi Arabia except to such persons as are permitted under the Offers of Securities Regulations as issued by the board of the Saudi Arabian Capital Market Authority (CMA) pursuant to resolution number 2-11-2004 dated 4 October 2004 as amended by resolution number 1-28-2008, as amended (the CMA Regulations). The CMA does not make any representation as to the accuracy or completeness of this document and expressly disclaims any liability whatsoever for any loss arising from, or incurred in reliance upon, any part of this document. Prospective purchasers of the securities offered hereby should conduct their own due diligence on the accuracy of the information relating to the securities. If you do not understand the contents of this document, you should consult an authorized financial adviser.

British Virgin Islands

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The securities are not being, and may not be offered to the public or to any person in the British Virgin Islands for purchase or subscription by or on behalf of us. The securities may be offered to companies incorporated

S-21

Table of Contents

under the BVI Business Companies Act, 2004 (British Virgin Islands), BVI Companies), but only where the offer will be made to, and received by, the relevant BVI Company entirely outside of the British Virgin Islands.

This prospectus supplement has not been, and will not be, registered with the Financial Services Commission of the British Virgin Islands. No registered prospectus has been or will be prepared in respect of the securities for the purposes of the Securities and Investment Business Act, 2010 (SIBA) or the Public Issuers Code of the British Virgin Islands.

The securities may be offered to persons located in the British Virgin Islands who are qualified investors for the purposes of SIBA. Qualified investors include (i) certain entities which are regulated by the Financial Services Commission in the British Virgin Islands, including banks, insurance companies, licensees under SIBA and public, professional and private mutual funds; (ii) a company, any securities of which are listed on a recognised exchange; and (iii) persons defined as professional investors under SIBA, which is any person (a) whose ordinary business involves, whether for that person's own account or the account of others, the acquisition or disposal of property of the same kind as the property, or a substantial part of our property; or (b) who has signed a declaration that he, whether individually or jointly with his spouse, has net worth in excess of US\$1,000,000 and that he consents to being treated as a professional investor.

China

This prospectus supplement does not constitute a public offer of the securities offered by this prospectus supplement, whether by sale or subscription, in the People's Republic of China (the PRC). The securities are not being offered or sold directly or indirectly in the PRC to or for the benefit of, legal or natural persons of the PRC.

Further, no legal or natural persons of the PRC may directly or indirectly purchase any of the securities without obtaining all prior PRC's governmental approvals that are required, whether statutorily or otherwise. Persons who come into possession of this document are required by the issuer and its representatives to observe these restrictions.

Korea

The securities have not been and will not be registered under the Financial Investments Services and Capital Markets Act of Korea and the decrees and regulations thereunder (the FSCMA), and the securities have been and will be offered in Korea as a private placement under the FSCMA. None of the securities may be offered, sold or delivered directly or indirectly, or offered or sold to any person for re-offering or resale, directly or indirectly, in Korea or to any resident of Korea except pursuant to the applicable laws and regulations of Korea, including the FSCMA and the Foreign Exchange Transaction Law of Korea and the decrees and regulations thereunder (the FETL). The securities have not been listed on any of securities exchanges in the world including, without limitation, the Korea Exchange in Korea. Furthermore, the purchaser of the securities shall comply with all applicable regulatory requirements (including but not limited to requirements under the FETL) in connection with the purchase of the securities. By the purchase of the securities, the relevant holder thereof will be deemed to represent and warrant that if it is in Korea or is a resident of Korea, it purchased the securities pursuant to the applicable laws and regulations of Korea.

Malaysia

No prospectus or other offering material or document in connection with the offer and sale of the securities has been or will be registered with the Securities Commission of Malaysia (Commission) for the Commission's approval pursuant to the Capital Markets and Services Act 2007. Accordingly, this prospectus supplement and

Table of Contents

any other document or material in connection with the offer or sale, or invitation for subscription or purchase, of the securities may not be circulated or distributed, nor may the securities be offered or sold, or be made the subject of an invitation for subscription or purchase, whether directly or indirectly, to persons in Malaysia other than (i) a closed end fund approved by the Commission; (ii) a holder of a Capital Markets Services Licence; (iii) a person who acquires the securities, as principal, if the offer is on terms that the securities may only be acquired at a consideration of not less than RM250,000 (or its equivalent in foreign currencies) for each transaction; (iv) an individual whose total net personal assets or total net joint assets with his or her spouse exceeds RM3 million (or its equivalent in foreign currencies), excluding the value of the primary residence of the individual; (v) an individual who has a gross annual income exceeding RM300,000 (or its equivalent in foreign currencies) per annum in the preceding twelve months; (vi) an individual who, jointly with his or her spouse, has a gross annual income of RM400,000 (or its equivalent in foreign currencies), per annum in the preceding twelve months; (vii) a corporation with total net assets exceeding RM10 million (or its equivalent in foreign currencies) based on the last audited accounts; (viii) a partnership with total net assets exceeding RM10 million (or its equivalent in foreign currencies); (ix) a bank licensee or insurance licensee as defined in the Labuan Financial Services and Securities Act 2010; (x) an Islamic bank licensee or takaful licensee as defined in the Labuan Financial Services and Securities Act 2010; and (xi) any other person as may be specified by the Commission; provided that, in the each of the preceding categories (i) to (xi), the distribution of the securities is made by a holder of a Capital Markets Services Licence who carries on the business of dealing in securities. The distribution in Malaysia of this prospectus supplement is subject to Malaysian laws. This prospectus supplement does not constitute and may not be used for the purpose of public offering or an issue, offer for subscription or purchase, invitation to subscribe for or purchase any securities requiring the registration of a prospectus with the Commission under the Capital Markets and Services Act 2007.

Taiwan

The securities have not been and will not be registered with the Financial Supervisory Commission of Taiwan pursuant to relevant securities laws and regulations and may not be sold, issued or offered within Taiwan through a public offering or in circumstances which constitutes an offer within the meaning of the Securities and Exchange Act of Taiwan that requires a registration or approval of the Financial Supervisory Commission of Taiwan. No person or entity in Taiwan has been authorized to offer, sell, give advice regarding or otherwise intermediate the offering and sale of the securities in Taiwan.

South Africa

Due to restrictions under the securities laws of South Africa, the securities are not offered, and the Offer shall not be transferred, sold, renounced or delivered, in South Africa or to a person with an address in South Africa, unless one or other of the following exemptions applies:

the offer, transfer, sale, renunciation or delivery is to duly registered banks, mutual banks, financial services provider, financial institution, the Public Investment Corporation (in each case registered as such in South Africa), a person who deals with securities in their ordinary course of business, or a wholly owned subsidiary of a bank, mutual bank, authorized services provider or financial institution, acting as agent in the capacity of an authorized portfolio manager for a pension fund (duly registered in South Africa), or as manager for a collective investment scheme (registered in South Africa); or

the contemplated acquisition cost of the securities, for any single addressee acting as principal is equal to or greater than R1,000,000. This document does not, nor is it intended to, constitute an *offer to the public* (as that term is defined in the South African Companies Act, 2008 (the SA Companies Act)) and does not, nor is it intended to, constitute a

Table of Contents

prospectus prepared and registered under the SA Companies Act. This document is not an *offer to the public* and must not be acted on or relied on by persons who do not fall within Section 96(1)(a) of the SA Companies Act (such persons being referred to as *relevant persons*). Any investment or investment activity to which this document relates is available only to relevant persons and will be engaged in only with relevant persons.

A South African resident person or company or any non-South African company which is a subsidiary of a South African company is not permitted to acquire the securities unless such person has obtained exchange control approval to do so.

S-24

Table of Contents

Legal matters

The validity of the common stock offered by this prospectus supplement and the accompanying prospectus will be passed upon for us by Sidley Austin LLP, Palo Alto, California. Cooley LLP is counsel for the underwriters in connection with this offering.

Experts

Ernst & Young LLP, independent registered public accounting firm, has audited our consolidated financial statements included in our Annual Report on Form 10-K for the year ended December 31, 2015, and the effectiveness of our internal control over financial reporting as of December 31, 2015, as set forth in their reports, which are incorporated by reference in this prospectus supplement and elsewhere in the registration statement. Our financial statements are incorporated by reference in reliance on Ernst & Young LLP's reports, given on their authority as experts in accounting and auditing.

Where you can find more information

This prospectus supplement and the accompanying prospectus are part of the registration statement on Form S-3 we filed with the SEC under the Securities Act and do not contain all the information set forth in the registration statement. Whenever a reference is made in this prospectus supplement or the accompanying prospectus to any of our contracts, agreements or other documents, the reference may not be complete and you should refer to the exhibits that are a part of the registration statement or the exhibits to the reports or other documents incorporated by reference in this prospectus supplement and the accompanying prospectus for a copy of such contract, agreement or other document. Because we are subject to the information and reporting requirements of the Exchange Act, we file annual, quarterly and current reports, proxy statements and other information with the SEC. Such reports, proxy statements and other information filed by us are available free of charge on our web site, www.nektar.com, and may be inspected and copied at the public reference facilities maintained by the SEC at 100 F Street, N.E., Washington, D.C. 20549. You may obtain information on the operation of the public reference facilities by calling the SEC at 1-800-SEC-0330. The SEC maintains an Internet site at www.sec.gov that contains reports, proxy and information statements and other information regarding registrants that file electronically with the SEC.

We maintain a website at www.nektar.com. The information contained on our website is not incorporated by reference in this prospectus supplement or the accompanying prospectus and you should not consider it a part of this prospectus supplement or the accompanying prospectus.

Table of Contents

Incorporation of certain information by reference

The SEC allows us to incorporate by reference information that we file with them. Incorporation by reference allows us to disclose important information to you by referring you to those other documents. The information incorporated by reference is an important part of this prospectus supplement, and information that we file later with the SEC will automatically update and supersede this information. This prospectus supplement may contain information that updates, modifies or is contrary to information in one or more previously filed documents incorporated by reference in this prospectus supplement. In the event of a conflict or inconsistency between information contained in this prospectus supplement and information later filed, you should rely on information contained in the document that was later filed. You should not assume that the information contained or incorporated by reference in this prospectus supplement is accurate as of any date other than the date of this prospectus supplement or the date of the document incorporated by reference in this prospectus supplement. We filed a registration statement on Form S-3 under the Securities Act with the SEC with respect to the securities being offered pursuant to this prospectus supplement. This prospectus supplement omits certain information contained in the registration statement, as permitted by the SEC. You should refer to the registration statement, including the exhibits, for further information about us and the securities being offered pursuant to this prospectus supplement. Statements in this prospectus supplement regarding the provisions of certain documents filed with, or incorporated by reference in, the registration statement are not necessarily complete and each statement is qualified in all respects by that reference. Copies of all or any part of the registration statement, including the documents incorporated by reference or the exhibits, may be obtained upon payment of the prescribed rates at the offices of the SEC listed above in [Where you can find more information](#).

We incorporate by reference the documents listed below and any documents that we file in the future with the SEC under Section 13(a), 13(c), 14 or 15(d) of the Exchange Act (excluding, in the case of any subsequent filings, any information furnished under Item 2.02 or 7.01 in any Current Report on Form 8-K and corresponding information furnished under Item 9.01 as an exhibit thereto) after the date of this prospectus supplement and before the completion of this offering:

our Annual Report on Form 10-K for the fiscal year ended December 31, 2015, filed with the SEC on February 29, 2016;

the information specifically incorporated by reference into our Annual Report on Form 10-K for the fiscal year ended December 31, 2015 from our definitive proxy statement on Schedule 14A for our 2016 Annual Meeting of Stockholders, filed with the SEC on April 29, 2016;

our Quarterly Report on Form 10-Q for the fiscal quarter ended March 31, 2016, filed with the SEC on May 4, 2016;

our Quarterly Report on Form 10-Q for the fiscal quarter ended June 30, 2016, filed with the SEC on August 4, 2016;

our Current Reports on Form 8-K filed with the SEC on June 1, 2016, June 2, 2016, June 27, 2016, September 27, 2016 (excluding the portions furnished under Item 7.01) and October 17, 2016 (excluding the portions furnished under Items 2.02 and 7.01); and

the description of our common stock set forth in our registration statement on Form 8-A, as amended.

It is specifically noted that any information that is deemed to be furnished, rather than filed, with the SEC is not incorporated by reference into this prospectus supplement, except as expressly incorporated herein.

We will provide without charge to each person to whom this prospectus supplement is delivered, including any beneficial owner of the securities, upon written or oral request, a copy of any and all of the documents that

Table of Contents

have been incorporated by reference in this prospectus supplement but not delivered with this prospectus supplement (without exhibits, unless the exhibits are specifically incorporated by reference but not delivered with this prospectus supplement). Requests should be directed to:

Nektar Therapeutics

455 Mission Bay Boulevard South

San Francisco, California 94158

(415) 482-5300

Attention: Secretary

S-27

Table of Contents

PROSPECTUS

NEKTAR THERAPEUTICS

Common Stock

Preferred Stock

Debt Securities

Warrants

This prospectus provides you with a general description of the securities we may offer and sell from time to time. In addition, selling security holders to be named in a prospectus supplement may offer and sell from time to time securities in such amounts as are set forth in such prospectus supplement. Unless otherwise set forth in a prospectus supplement, we will not receive any proceeds from the sale of securities by any selling security holder.

Each time we sell securities, we will provide you with a supplement to this prospectus that contains specific information about the offering and the amounts, prices and terms of the securities. The supplement may also add, update or change information contained in this prospectus. You should carefully read this prospectus and the accompanying prospectus supplement, together with the documents we incorporate therein by reference, before you invest in any of our securities.

We may, or the selling security holders may, from time to time offer or sell together or separately the following securities in one or more transactions:

common stock;

preferred stock;

debt securities, which may be senior, subordinated or junior subordinated and convertible or non-convertible; and

warrants to purchase common stock, preferred stock or debt securities.

The shares of our common stock may be sold at fixed prices, prevailing market prices at the time of sale, prices related to the prevailing market prices, varying prices determined at the times of sale or negotiated prices. The securities may be offered by us directly to purchasers or by any selling security holder directly to purchasers, through one or more agents designated from time to time by us or to or through one or more underwriters or dealers. If any agent, dealer or underwriter is involved in the sale of any of the securities, its name and any applicable purchase price, fee,

commission or discount arrangement between or among them will be set forth, or will be calculable from the information set forth, in the applicable prospectus supplement. See the sections titled "About this Prospectus" and "Plan of Distribution" for more information. No securities may be sold without delivery of this prospectus and the applicable prospectus supplement describing the method and terms of the offering of such securities. The last reported sale price of our common stock on the NASDAQ Global Select Market on January 17, 2014 was \$13.06 per share. You are urged to obtain current market quotations for our common stock.

Our common stock is listed on The NASDAQ Global Select Market under the symbol "NKTR".

Investing in our securities involves a high degree of risk. You should carefully consider the risk factors incorporated in this prospectus by reference and described under the heading "Risk Factors" beginning on page 5 of this prospectus.

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

The date of this prospectus is January 21, 2014.

Table of Contents

TABLE OF CONTENTS

	Page
<u>ABOUT THIS PROSPECTUS</u>	1
<u>ABOUT OUR COMPANY</u>	2
<u>RATIO OF EARNINGS TO FIXED CHARGES</u>	3
<u>FORWARD-LOOKING STATEMENTS</u>	4
<u>RISK FACTORS</u>	5
<u>USE OF PROCEEDS</u>	6
<u>DIVIDEND POLICY</u>	7
<u>GENERAL DESCRIPTION OF SECURITIES</u>	8
<u>DESCRIPTION OF CAPITAL STOCK</u>	10
<u>DESCRIPTION OF DEBT SECURITIES</u>	14
<u>DESCRIPTION OF WARRANTS</u>	23
<u>LEGAL OWNERSHIP OF SECURITIES</u>	26
<u>PLAN OF DISTRIBUTION</u>	30
<u>LEGAL MATTERS</u>	32
<u>EXPERTS</u>	33
<u>WHERE YOU CAN FIND MORE INFORMATION</u>	34
<u>INCORPORATION OF DOCUMENTS BY REFERENCE</u>	34

You should rely only on the information contained or incorporated by reference in this prospectus and in any applicable supplement to this prospectus. We have not authorized any other person to provide you with different information. If anyone provides you with different or inconsistent information, you should not rely on it. We are not making an offer to sell these securities in any jurisdiction where the offer or sale is not permitted. You should assume that the information appearing in this prospectus, the accompanying prospectus supplement and any free writing prospectus prepared by or on behalf of us is accurate only as of the date on their respective covers. Additionally, any information we have incorporated by reference in this prospectus or in any applicable prospectus supplement is accurate only as of the date of the document incorporated by reference, regardless of the time of delivery of this prospectus, any applicable prospectus supplement or any sale of securities. Our business, financial condition, results of operations and prospects may have changed since that date.

This prospectus and any applicable prospectus supplement contain and incorporate by reference market data, industry statistics and other data that have been obtained or compiled from information made available by third parties. We have not independently verified such data. This prospectus, any applicable prospectus supplement and the information incorporated herein or therein by reference include trademarks, service marks and trade names owned by us or other companies. All trademarks, service marks and trade names included or incorporated by reference in this prospectus, any applicable prospectus supplement or any related free writing prospectus are the property of their respective owners.

When used in this prospectus, the terms Nektar, we, our and us refer to Nektar Therapeutics, a Delaware corporation, and its consolidated subsidiaries, unless otherwise specified.

Table of Contents

ABOUT THIS PROSPECTUS

This prospectus is part of an automatic shelf registration statement that we filed with the Securities and Exchange Commission (SEC) as a well-known seasoned issuer as defined in Rule 405 under the Securities Act of 1933, as amended (Securities Act), using a shelf registration process. Under this process, we, or certain of our security holders, may sell any combination of common stock, preferred stock, debt securities or warrants in one or more offerings. This prospectus only provides you with a general description of the securities we, or a selling security holder, may offer. Each time we or, under certain circumstances, our security holders, sell any securities under this prospectus, we will provide you with a prospectus supplement that will contain more specific information about the terms of those securities. We may also add, update or change in the prospectus supplement any of the information contained in this prospectus. Before purchasing any securities, you should carefully read both this prospectus, the accompanying prospectus supplement and any free writing prospectus prepared by or on behalf of us, together with the additional information described under the heading **Where You Can Find More Information** and **Incorporation of Documents by Reference** in this prospectus and the prospectus supplement.

Table of Contents

ABOUT OUR COMPANY

We are a clinical-stage biopharmaceutical company developing a pipeline of drug candidates that utilize our PEGylation and advanced polymer conjugate technology platforms, which are designed to enable the development of new molecular entities that target known mechanisms of action. Our current proprietary pipeline is comprised of drug candidates across a number of therapeutic areas including oncology, pain, anti-infectives and immunology. Our research and development activities involve small molecule drugs, peptides and other biologic drug candidates. We create innovative drug candidates by using our proprietary advanced polymer conjugate technologies and expertise to modify the chemical structure of pharmacophores to create new molecular entities. Additionally, we may utilize established pharmacologic targets to engineer a new drug candidate relying on a combination of the known properties of these targets and our proprietary polymer chemistry technology and expertise. Our drug candidates are designed to improve the overall benefits and use of a drug for patients by improving the metabolism, distribution, pharmacokinetics, pharmacodynamics, half-life and/or bioavailability of drugs. Our objective is to apply our advanced polymer conjugate technology platform to create new drug candidates in multiple therapeutic areas that address large potential markets.

We were incorporated in California in 1990 and reincorporated in Delaware in 1998. We maintain our executive offices at 455 Mission Bay Boulevard South, San Francisco, California 94158, and our main telephone number is (415) 482-5300. Our website is located at www.nektar.com. Information contained on our website is not a part of, and not incorporated into, this prospectus or any accompanying prospectus supplement.

Table of Contents**RATIO OF EARNINGS TO FIXED CHARGES****(in thousands)**

Set forth below is information concerning our ratio of earnings to fixed charges on a consolidated basis for the periods indicated. For purposes of calculating this ratio, earnings consist of net loss from continuing operations before income taxes, fixed charges, amortization of capitalized interest and distributions from minority investments, less capitalized interest, preferred dividend requirements of consolidated subsidiaries and non-controlling interest in pretax income of subsidiaries that have not incurred fixed charges. Fixed charges consist of interest expense, amortization of deferred financing expense, estimated interest portion of rentals and preferred dividends of consolidated subsidiaries. Our net losses were inadequate to cover fixed charges for each of the periods presented.

For the periods indicated below, we had no outstanding shares of preferred stock with required dividend payments. Therefore, the ratios of earnings to combined fixed charges and preferred stock dividends are identical to the ratios presented in the table below.

	Nine Months Ended September 30,		Year Ended December 31,			
	2013	2012	2011	2010	2009	2008
Ratio of earnings to fixed charges	N/A	N/A	N/A	N/A	N/A	N/A
Deficiency of earnings available to cover fixed charges	\$ (113,744)	\$ (171,449)	\$ (132,960)	\$ (37,057)	\$ (102,772)	\$ (35,142)

Table of Contents

FORWARD-LOOKING STATEMENTS

All statements included or incorporated by reference in this prospectus and any accompanying prospectus supplement, other than statements of historical facts, that address activities, events or developments that we intend, expect, project, believe or anticipate will or may occur in the future are forward-looking statements. This prospectus and any accompanying prospectus supplement contain forward-looking statements that are based on current expectations, estimates, forecasts and projections about us, our future performance, our business or the business of others on our behalf, our beliefs and our management's assumptions. In addition, we, or others on our behalf, may make forward-looking statements in press releases or written statements, or in our communications and discussions with investors and analysts in the normal course of business through meetings, webcasts, phone calls and conference calls. Words such as expect, anticipate, outlook, could, will, target, project, intend, plan, believe, seek, may, assume, or continue, and variations of such words and similar expressions are intended to identify such forward-looking statements. These statements are not guarantees of future performance and involve certain risks, uncertainties and assumptions that are difficult to predict. We have based our forward-looking statements on our management's beliefs and assumptions based on information available to our management at the time the statements are made. We caution you that actual outcomes and results may differ materially from what is expressed, implied or forecast by our forward-looking statements. Reference is made in particular to forward-looking statements regarding projections of earnings, revenue, milestone payments, royalties, sales or other financial items, plans and objectives of management for future operations (including, but not limited to, preclinical research and development, clinical trials and manufacturing), financial condition, liquidity and future working capital needs, future financing alternatives, proposed drug candidates, the timing for the start or end of clinical trials or submission of regulatory approval filings, future economic conditions or performance, the success of our collaboration arrangements or future payments that may come due to us under these arrangements, plans and objectives to initiate or continue clinical trials and any assumptions underlying any of the foregoing. Except as required under the federal securities laws and the rules and regulations of the Securities and Exchange Commission (SEC), we do not have any intention or obligation to update publicly any forward looking statements after the distribution of this prospectus and any accompanying prospectus supplement, whether as a result of new information, future events, changes in assumptions or otherwise.

You are cautioned not to rely unduly on any forward-looking statements. These risks and uncertainties are discussed in more detail under Risk Factors, Business and Management's Discussion and Analysis of Financial Condition and Results of Operations in our periodic reports and other documents on file with the SEC. You may obtain copies of these documents as described under the section titled Where You Can Find More Information below.

Table of Contents

RISK FACTORS

Investment in any securities offered pursuant to this prospectus involves risks. You should carefully consider the risk factors incorporated by reference to our most recent Annual Report on Form 10-K, our Quarterly Report for the three months ended September 30, 2013, any subsequent Annual Reports on Form 10-K, Quarterly Reports on Form 10-Q or Current Reports on Form 8-K we file after the date of this prospectus, and all other information contained or incorporated by reference into this prospectus, as updated by our subsequent filings under the Securities Exchange Act of 1934, as amended, and the risk factors and other information contained in the applicable prospectus supplement before acquiring any of such securities. The occurrence of any of these risks might cause you to lose all or part of your investment in the offered securities.

Table of Contents

USE OF PROCEEDS

Unless otherwise indicated in a prospectus supplement, we intend to use the net proceeds from the sale of the securities offered by us under this prospectus for general corporate purposes including research and development funding and working capital. When a particular series of securities is offered, the prospectus supplement relating thereto will set forth our intended use for the net proceeds we receive from the sale of the securities. Pending the application of the net proceeds, we may invest the proceeds in short-term, interest-bearing instruments or other investment-grade securities. Unless otherwise set forth in a prospectus supplement, we will not receive any proceeds from the sale of the securities by any selling security holder to be named in a prospectus supplement.

Table of Contents

DIVIDEND POLICY

We have never declared or paid any cash dividends on our common stock and do not currently anticipate declaring or paying cash dividends on our common stock in the foreseeable future. We currently intend to retain all of our future earnings, if any, to finance operations. Any future determination relating to our dividend policy will be made at the discretion of our board of directors and will depend on a number of factors, including future earnings, capital requirements, financial conditions, future prospects, contractual restrictions and other factors that our board of directors may deem relevant.

The indenture governing our 12% Senior Secured Notes due 2017 contains covenants that restrict our and our subsidiaries' ability to, among other things, pay dividends or distributions, including dividends or distributions on our common stock.

Table of Contents

GENERAL DESCRIPTION OF SECURITIES

We may offer shares of our common stock, preferred stock and various series of debt securities and warrants to purchase securities from time to time under this prospectus, together with any applicable prospectus supplement, at prices and on terms to be determined by market conditions at the time of offering. This prospectus provides you with a general description of the securities we may offer. Each time we offer a type or series of securities, we will provide a prospectus supplement that will describe the specific amounts, prices and other important terms of the securities, including, to the extent applicable:

designation or classification;

aggregate principal amount or aggregate offering price;

maturity;

original issue discount;

rates and times of payment of interest, dividends or other payments;

redemption, conversion, exercise, exchange, settlement or sinking fund terms;

conversion, exchange or settlement prices or rates and any provisions for changes to or adjustments in the conversion, exchange or settlement prices or rates and in the securities or other property receivable upon conversion, exchange or settlement;

ranking;

restrictive covenants;

voting or other rights; and

important federal income tax considerations.

The prospectus supplement also may add, update or change information contained in this prospectus or in documents we have incorporated by reference in this prospectus.

This prospectus may not be used to offer or sell securities unless accompanied by a prospectus supplement.

We may sell the securities directly to or through underwriters, dealers or agents. We, and our underwriters, dealers or agents, reserve the right to accept or reject all or part of any proposed purchase of securities. If we do offer securities through underwriters or agents, we will include in the applicable prospectus supplement:

the names of those underwriters or agents;

applicable fees, discounts and commissions to be paid to them;

details regarding over-allotment options, if any; and

the net proceeds to us.

Common Stock. We may issue shares of our common stock from time to time. The holders of common stock are entitled to one vote for each share held of record on all matters submitted to a vote of the stockholders. Directors are elected by a plurality vote, and the holders of common stock are not entitled to cumulative voting rights with respect to the election of directors. As a consequence, minority stockholders are not able to elect directors on the basis of their votes alone. Subject to preferences that may be applicable to any shares of preferred stock currently outstanding or issued in the future, holders of common stock are entitled to receive ratably such dividends as may be declared by our board of directors out of funds legally available therefor. In the event of our liquidation, dissolution or winding up, holders of our common stock are entitled to share ratably in all assets remaining after payment of liabilities and the liquidation preference of any then outstanding preferred stock. Holders of common stock have no preemptive rights and no right to convert their common stock into any other securities. There are no redemption or sinking fund provisions applicable to the common stock. We urge you to read the prospectus supplement related to the common stock being offered.

Table of Contents

Preferred Stock. We may issue shares of our preferred stock from time to time. Our board of directors has the authority, without further vote or action by the stockholders, to designate and issue shares of preferred stock in one or more series and to designate the rights, preferences and privileges of each series, which may be greater than the rights of the common stock. We will fix the rights, preferences and privileges, including any dividend rights, conversion rights, voting rights, terms of redemption, liquidation preferences, sinking fund terms and the number of shares constituting any series or the designation of any series, of the preferred stock of each series that we sell under this prospectus and applicable prospectus supplements in the certificate of designation relating to that series. We will incorporate by reference into the registration statement of which this prospectus is a part the form of any certificate of designation that describes the terms of the series of preferred stock that we are offering before the issuance of the related series of preferred stock. We urge you to read the prospectus supplements related to the series of preferred stock being offered, as well as the complete certificate of designation that contains the terms of the applicable series of preferred stock.

Debt Securities. We may issue debt securities from time to time, in one or more series, as either senior subordinated or junior subordinated debt, as convertible or non-convertible debt and as secured or unsecured debt. The senior debt securities will rank equally with any unsubordinated debt. The subordinated debt securities will rank equally with our other subordinated debt. Convertible debt securities will be convertible into or exchangeable for our common stock or our other securities at predetermined conversion rates. We may prescribe that conversion of such securities shall be mandatory or at your option. The debt securities will be issued under one or more indentures, which are contracts between us and a national banking association or other eligible party, as trustee. In this prospectus, we have summarized certain general features of the debt securities. We urge you, however, to read the applicable prospectus supplement (and any free writing prospectus that we may authorize to be provided to you) related to the series of debt securities being offered, as well as the complete indentures, any supplemental indentures and forms of debt securities containing the terms of the debt securities being offered which will be filed as exhibits to the registration statement of which this prospectus is a part or will be incorporated by reference from reports that we file with the Securities and Exchange Commission (SEC).

Warrants. We may issue warrants, in one or more series, for the purchase of common stock, preferred stock or debt securities from time to time. We may issue warrants independently or together with common stock, preferred stock or debt securities, and the warrants may be attached to or separate from those securities. The warrants will be evidenced by a warrant certificate issued under one or more warrant agreements, which are contracts between us and an agent for the holders of the warrants. In this prospectus, we have summarized certain general features of the warrants. The description in this prospectus and the applicable prospectus supplement of any warrants we offer will not necessarily be complete and will be qualified in its entirety by reference to the applicable warrant agreement and warrant certificate. We urge you to read the applicable warrant prospectus supplements, warrant agreements and warrant certificates that contain the terms of the warrants in their entirety.

Table of Contents

DESCRIPTION OF CAPITAL STOCK

The following description of our capital stock is not complete and may not contain all the information you should consider before investing in our securities. This description is summarized from, and qualified in its entirety by reference to, our certificate of incorporation, as amended and currently in effect (certificate of incorporation), and our amended and restated bylaws, as currently in effect (bylaws), all of which are publicly filed with the SEC. See [Where You Can Find More Information](#) and [Incorporation of Documents by Reference](#).

Our authorized capital stock consists of 300,000,000 shares of common stock, par value \$0.0001 per share, and 10,000,000 shares of preferred stock, par value \$0.0001 per share. As of December 31, 2013, there were 116,493,560 shares of common stock outstanding and no shares of preferred stock outstanding.

Common Stock

The holders of common stock are entitled to one vote for each share held of record on all matters submitted to a vote of the stockholders. Directors are elected by a plurality vote and the holders of common stock are not entitled to cumulative voting rights with respect to the election of directors. Accordingly, holders of a majority of the voting shares are able to elect all of the directors. Subject to preferences that may be applicable to any shares of preferred stock currently outstanding or issued in the future, holders of common stock are entitled to receive ratably such dividends as may be declared by our board of directors out of funds legally available therefor. In the event of our liquidation, dissolution or winding up, holders of our common stock are entitled to share ratably in all assets remaining after payment of liabilities and the liquidation preference of any then outstanding preferred stock. Holders of common stock have no preemptive rights and no right to convert their common stock into any other securities. There are no redemption or sinking fund provisions applicable to the common stock. The rights, preferences and privileges of holders of common stock are subject to, and may be adversely affected by, the rights of the holders of shares of any series of preferred stock that we may designate and issue in the future. All outstanding shares of common stock are, and all shares of common stock that may be issued upon conversion of our outstanding convertible subordinated notes discussed below will be, fully paid and non-assessable.

Preferred Stock

Our board of directors has the authority, without further vote or action by the stockholders, to issue up to 10,000,000 shares of preferred stock in one or more series and to fix, by filing a certificate of designation pursuant to the Delaware General Corporation Law, the rights, preferences, privileges and restrictions thereof, including dividend rights, conversion rights, voting rights, terms of redemption, liquidation preferences, sinking fund terms and the number of shares constituting any series or the designation of such series. The issuance of preferred stock could adversely affect the voting power or other rights of holders of common stock and the likelihood that such holders will receive dividend payments and payments upon liquidation and could have the effect of delaying, deferring or preventing a change in control. We will incorporate by reference any certificate of designation that describes the terms of any authorized series of preferred stock before the issuance of the series of preferred stock. A prospectus supplement relating to such series will describe the terms of the preferred stock of the series, including the following, to the extent applicable:

the title and stated value;

the number of shares we are offering;

the liquidation preference per share;

the purchase price;

the dividend rate, period and payment date and method of calculation for dividends;

whether dividends will be cumulative or non-cumulative and, if cumulative, the date from which dividends will accumulate;

Table of Contents

the procedures for any auction and remarketing;

the provisions for any sinking fund;

any provisions for redemption or repurchase and any restrictions on our ability to exercise those redemption and repurchase rights;

any listing of the preferred stock on any securities exchange or market;

whether the preferred stock will be convertible into our common stock and any conversion price, or other means of calculation, and any conversion period;

whether the preferred stock will be exchangeable into debt securities and any exchange price, or other means of calculation, and any exchange period;

any voting rights of the preferred stock;

any preemptive rights;

any restrictions on transfer, sale or other assignment;

whether interests in the preferred stock will be represented by depositary shares;

a discussion of any material or special U.S. federal income tax considerations applicable to the preferred stock;

the relative ranking and preferences of the preferred stock as to dividend rights and rights upon liquidation, dissolution or winding up;

any limitations on issuance of any class or series of preferred stock ranking senior to or on a parity with the series of preferred stock as to dividend rights and rights upon liquidation, dissolution or winding up; and

any other specific terms, preferences, rights or limitations of or restrictions on the preferred stock.

The Delaware General Corporation Law provides that the holders of preferred stock will have the right to vote separately as a class on a proposed amendment to our certificate of incorporation involving certain fundamental

changes in the rights of holders of that preferred stock. This right is in addition to any voting rights that may be provided in the applicable certificate of designation. The issuance of preferred stock could adversely affect the voting power, conversion or other rights of holders of common stock and reduce the likelihood that holders of common stock will receive dividend payments and payments upon liquidation. Preferred stock could be issued quickly with terms calculated to delay or prevent a change in control of our company or make removal of management more difficult. Additionally, the issuance of preferred stock could have the effect of decreasing the market price of our common stock.

Anti-Takeover Effects of Provisions of Delaware Law and Our Charter Documents

Certificate of Incorporation and Bylaws

Our certificate of incorporation provides for our board of directors to be divided into three classes, with staggered three-year terms. As a result, only one class of directors will be elected at each annual meeting of stockholders, with the other classes continuing for the remainder of their respective three-year terms. Stockholders have no cumulative voting rights. Subject to the rights of the holders of any outstanding series of preferred stock, directors may not be removed without cause. Any vacancies on the board of directors shall be filled by the affirmative vote of a majority of the directors then in office, unless the board of directors otherwise determines that the vacancy shall be filled by stockholders entitled to vote for directors.

Our certificate of incorporation also requires that any action required or permitted to be taken by our stockholders must be effected at a duly called annual or special meeting of the stockholders and may not be

Table of Contents

effected by a consent in writing. A special meeting of the stockholders may be called by the chairman of our board of directors, our chief executive officer, a resolution adopted by a majority of the total number of authorized directors or by stockholders owning 10 percent or more of the outstanding voting capital stock. The stockholders may amend, or adopt new, bylaws and amend certain provisions of our certificate of incorporation, including the provisions related to stockholder actions and the calling of special meetings of stockholders, only by the affirmative vote of the holders of 66 2/3 percent of the voting power of all of the outstanding shares of the voting stock of the Company entitled to vote at an election of directors. These provisions may have the effect of delaying, deferring or preventing a change in control.

The classification of our board of directors and lack of cumulative voting will make it more difficult for our existing stockholders to replace our board of directors as well as for another party to obtain control of us by replacing our board of directors. Since our board of directors has the power to retain and discharge our officers, these provisions could also make it more difficult for existing stockholders or another party to effect a change in management. These and other provisions may have the effect of deterring hostile takeovers or delaying changes in control or management. These provisions are intended to enhance the likelihood of continued stability in the composition of our board of directors and in the policies of our board of directors and to discourage certain types of transactions that may involve an actual or threatened change in control. These provisions are designed to reduce our vulnerability to an unsolicited acquisition proposal. The provisions also are intended to discourage certain tactics that may be used in proxy fights. However, such provisions could have the effect of discouraging others from making tender offers for our shares and, as a consequence, such provisions also may inhibit increases in the market price of our shares that could result from actual or rumored takeover attempts. Such provisions also may have the effect of preventing changes in our management.

Our bylaws establish advance notice procedures with regard to stockholder proposals relating to the nomination of candidates for election as directors or new business to be brought before meetings of our stockholders. These procedures provide that notice of stockholder proposals must be timely given in writing to our secretary prior to the meeting at which the action is to be taken. Generally, to be timely, notice must be received at our principal executive offices not less than the close of business on the sixtieth (60th) day nor earlier than the close of business on the ninetieth (90th) day prior to the first anniversary of the annual meeting for the preceding year. The notice must contain certain information specified in the bylaws. These provisions may have the effect of precluding the conduct of

our
investment
in
BlackRock
on
the
equity
method.
We
believe
that
providing
amounts
adjusted
as
if

we
had
recorded
our
investment
in
BlackRock
on
the
equity
method
for
all
periods
presented
helps
provide

a basis of comparability for the impact of the BlackRock deconsolidation given the magnitude of the impact on various components of our consolidated income statement.

2006 to 2007 Change

September 30, 2007

September 30, 2006

Non-GAAP to GAAP
Reconciliation
Income Statement Summary
2004 to 2006
Appendix
BlackRock
For the year ended December 31, 2006

PNC
 Deconsolidation and
 BlackRock
 PNC
 In millions
 As Reported
 Adjustments (a)
 Other Adjustments
 Equity Method
 As Adjusted
 Net interest income
 \$2,245
 \$(10)
 \$2,235
 Provision for credit losses
 124
 124
 Noninterest income
 6,327
 \$(1,812)
 (1,087)
 \$144
 3,572
 Noninterest expense
 4,443
 (91)
 (765)
 3,587
 Income before minority interest and income taxes
 4,005
 (1,721)
 (332)
 144
 2,096
 Minority interest in income of BlackRock
 47
 18
 (65)
 Income taxes
 1,363
 (658)
 (130)
 7
 582
 Net income
 \$2,595
 \$(1,081)
 \$(137)
 \$137
 \$1,514

For the year ended December 31, 2005

BlackRock

PNC

Deconsolidation and

BlackRock

PNC

In millions

As Reported

Other Adjustments

Equity Method

As Adjusted

Net interest income

\$2,154

\$(12)

\$2,142

Provision for credit losses

21

21

Noninterest income

4,173

(1,214)

\$163

3,122

Noninterest expense

4,306

(853)

3,453

Income before minority interest and income taxes

2,000

(373)

163

1,790

Minority interest in income of BlackRock

71

(71)

Income taxes

604

(150)

11

465

Net income

\$1,325

\$(152)

\$152

\$1,325

(a)

Includes

the

impact

of

the
following
items,
all
on
a
pretax
basis,
and
adjustment
for
the
tax
impact
thereof:
\$2,078
million
gain
on
BlackRock/MLIM
transaction,
\$196
million
securities
portfolio
rebalancing
loss,
\$101
million
of
BlackRock/MLIM
transaction
integration
costs,
\$48
million
mortgage
loan
portfolio
repositioning
loss,
and
\$12 million net loss related to our BlackRock LTIP shares obligation.

Non-GAAP to GAAP
Reconciliation
Income Statement Summary
2004 to 2006 (continued)
Appendix
For the year ended December 31, 2004
BlackRock

PNC
 Deconsolidation and
 BlackRock
 PNC
 In millions
 As Reported
 Other Adjustments
 Equity Method
 As Adjusted
 Net interest income
 \$1,969
 \$(14)
 \$1,955
 Provision for credit losses
 52
 52
 Noninterest income
 3,572
 (745)
 \$101
 2,928
 Noninterest expense
 3,712
 (564)
 3,148
 Income before minority interest and income taxes
 1,777
 (195)
 101
 1,683
 Minority interest in income of BlackRock
 42
 (42)
 Income taxes
 538
 (59)
 7
 486
 Net income
 \$1,197
 \$(94)
 \$94
 \$1,197
 In millions
 2004
 2005
 2006
 CAGR
 Adjusted net interest income
 \$1,955

\$2,142
 \$2,235
 Adjusted noninterest income
 2,928
 3,122
 3,572
 Adjusted total revenue
 4,883
 5,264
 5,807
 9%
 Adjusted noninterest expense
 3,148
 3,453
 3,587
 7%
 Adjusted net income
 \$1,197
 \$1,325
 \$1,514
 12%
 In millions
 2004
 2005
 2006
 CAGR
 Net interest income, as reported
 \$1,969
 \$2,154
 \$2,245
 Noninterest income, as reported
 3,572
 4,173
 6,327
 Total revenue, as reported
 5,541
 6,327
 8,572
 24%
 Noninterest expense, as reported
 3,712
 4,306
 4,443
 9%
 Net income, as reported
 \$1,197
 \$1,325
 \$2,595
 47%

Non-GAAP to GAAP
Reconcilement
Noninterest Income/Total Revenue
Appendix
Nine Months Ending September 30, 2007
Dollars in millions
Retail

Banking
 Corporate &
 Institutional
 Banking
 Other
 Banking and
 Other
 BlackRock
 PFPC
 Total
 Net interest income (expense)
 \$1,517
 \$571
 \$48
 \$2,136
 (\$14)
 \$2,122
 Noninterest income
 1,280

 558

 260

 2,098

 \$227
 631

 2,956

 Total Revenue
 \$2,797
 \$1,129
 \$308
 \$4,234
 \$227
 \$617
 \$5,078
 Noninterest income as a % of
 total revenue
 46%
 49%
 84%
 50%
 100%
 102%
 58%

The PNC Financial Services Group, Inc.
PNC
BB&T Corporation
BBT
Comerica
CMA
Fifth Third Bancorp

FITB
KeyCorp
KEY
National City Corporation
NCC
Regions Financial
RF
SunTrust Banks, Inc.
STI
U.S. Bancorp
USB
Wachovia Corporation
WB
Wells Fargo & Company
WFC
Ticker
Peer Group of
Super-Regional Banks
Appendix