

NEKTAR THERAPEUTICS

Form 424B5

January 21, 2011

Filed Pursuant to Rule 424(b)5

A filing fee of \$30,948.78 calculated in accordance with Rule 457(r) has been transmitted to the SEC in connection with the offering of shares of common stock from the registration statement (File No. 333-171747) by means of this prospectus supplement and the accompanying prospectus. The proposed maximum aggregate offering price has been calculated as 21,850,000 shares (which includes shares of common stock that may be purchased by the underwriter pursuant to its overallotment option) multiplied by \$12.20 per share, the average of the high and low sale price of our common stock on The NASDAQ Global Select Market on January 18, 2011.

PROSPECTUS SUPPLEMENT

(To Prospectus dated January 18, 2011)

19,000,000 Shares

Common Stock

We are offering 19,000,000 shares of our common stock. Our common stock is quoted 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 January 18, 2011 was \$12.34 per share.

Investing in our common stock involves a high degree of risk. Please read Risk Factors beginning on page S-4 of this prospectus supplement and in the documents incorporated by reference in this prospectus supplement.

Neither the Securities and Exchange Commission nor any state securities commission has approved or disapproved of these securities or determined if this prospectus supplement or the accompanying prospectus is truthful or complete. Any representation to the contrary is a criminal offense.

	PER SHARE	TOTAL
Public Offering Price	\$ 11.85	\$ 225,150,000
Underwriting Discounts and Commissions	\$ 0.25	\$ 4,750,000
Proceeds to Nektar (Before Expenses)	\$ 11.60	\$ 220,400,000

Delivery of the shares of common stock is expected to be made on or about January 24, 2011. We have granted the underwriter an option for a period of 30 days to purchase up to an additional 2,850,000 shares of our common stock solely to cover overallotments. If the underwriter exercises the option in full, the total underwriting discounts and commissions payable by us will be \$5,462,500 and the total proceeds to us, before expenses, will be \$253,460,000.

Sole Book-Running Manager

Jefferies

Prospectus Supplement dated January 19, 2011

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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 have not, and the underwriter has 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 are not, and the underwriter is 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 entitled **Where You Can Find More Information** and **Incorporation of Certain Information by Reference**.

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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 18, 2011, 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 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 18, 2011 are part of a registration statement on Form S-3 (File No. 333-171747) 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 references 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.

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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-4.*

Company Overview

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 improve the benefits of drugs for patients. Our current proprietary product pipeline is comprised of drug candidates across a number of therapeutic areas including oncology, pain, anti-infectives, anti-viral and immunology. Our research and development activities involve small molecule drugs, peptides and other potential biologic drug candidates. We create our innovative drug candidates by using our proprietary advanced polymer conjugate technologies and expertise to modify the chemical structure of drugs by applying our proprietary. Polymer chemistry is a science focused on the synthesis or bonding of polymer architectures with drug molecules to alter the properties of the molecule when it is bonded with polymers. 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 pharmacokinetics, pharmacodynamics, half-life, bioavailability, metabolism or distribution of drugs and improve the overall benefits and use of a drug for the patient. Our objective is to apply our advanced polymer conjugate technology platform to create new drugs in multiple therapeutic areas.

Each of our drug candidates which we are currently developing internally is a proprietary new chemical or biological entity that addresses large potential markets. We are developing drug candidates that can be delivered by either oral or subcutaneous administration. Our most advanced proprietary product candidate, Oral NKTR-118, is a peripheral opioid antagonist that is currently being evaluated for the treatment of opioid-induced constipation. On September 20, 2009, we entered into a license agreement with AstraZeneca AB for the global development and commercialization of Oral NKTR-118 and NKTR-119. NKTR-119 is an early stage research and development program that combines various opioids with Oral NKTR-118. Under this agreement, AstraZeneca assumed all responsibility for development and commercialization of NKTR-118 and NKTR-119. Our other lead product candidate, NKTR-102, a topoisomerase I inhibitor-polymer conjugate, is currently being evaluated in three separate Phase 2 clinical trials for ovarian, breast and colorectal cancers. In addition, in 2009 we commenced a Phase 1 clinical trial for NKTR-105 (PEGylated docetaxel) for patients with refractory solid tumors. We also have a number of early stage programs in research and preclinical development.

In addition to our proprietary product candidate pipeline, we have a number of collaborations and license, manufacturing and supply agreements for our technology with leading biotechnology and pharmaceutical companies, including Affymax, Amgen Baxter, Roche, Merck (formerly Schering Plough), Pfizer and UCB Pharma. A total of seven products using our PEGylation technology platform have received regulatory approval in the U.S. or Europe,

and are currently marketed by our partners. There are also a number of other products in clinical development that use our technology platform.

On October 29, 2010, we entered into a supply, dedicated suite and manufacturing guarantee agreement with Amgen Inc. and Amgen Manufacturing. Under the terms of the agreement, we will receive manufacturing fees on future orders, if any, submitted by Amgen for polymer materials to be manufactured and supplied by us. Amgen has no minimum purchase commitment. If quantities of the polymer materials ordered by Amgen exceed specified quantities (with each specified quantity representing a small portion of the quantity that we

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have historically supplied to Amgen), significant additional payments become payable to us in return for our guarantee of the supply of additional quantities of the polymer materials.

We also have a collaboration with Bayer Healthcare LLC to develop BAY41-6551 (NKTR-061, Amikacin Inhale), which is an inhaled solution of amikacin, an aminoglycoside antibiotic. We originally developed the liquid aerosol inhalation platform and product and entered into a collaboration agreement with Bayer Healthcare LLC in August 2007 for its further development and commercialization. BAY41-6551 completed Phase 2 development and we and Bayer are currently preparing for the start of a Phase 3 clinical study. Bayer and Nektar have been working together to prepare for the pivotal studies of BAY41-6551 following the consummation of the collaboration in August 2007. The program is behind schedule. The reason for this is that Bayer and Nektar decided to finalize the design of the device for commercial manufacturing prior to initiating Phase 3 clinical development with the objective of commencing Phase 3 clinical trials as soon as possible following completion of this work.

On December 31, 2008, we completed the sale and transfer of certain pulmonary technology rights, certain pulmonary collaboration agreements and approximately 140 of our dedicated pulmonary personnel and operations to Novartis Pharma AG. We retained all of our rights to BAY41-6551 and certain rights to receive royalties on net sales of the Cipro Inhale (also known as Ciprofloxacin Inhaled Powder or CIP) program with Bayer Schering Pharma AG that we transferred to Novartis as part of the transaction. We also retained certain intellectual property rights to patents specific to inhaled insulin.

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*. The information contained in, or that can be accessed through, our website is not part of, and is not incorporated in, this prospectus supplement or the accompanying prospectus and should not be considered part of this prospectus supplement or the accompanying prospectus.

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The Offering

Common stock we are offering

19,000,000 shares

**Common stock to be outstanding
after this offering**

113,517,285 shares

Over-allotment Option

We have granted the underwriter an option to purchase 2,850,000 additional shares of our common stock to cover over-allotments, if any. This option is exercisable, in whole or in part, for a period of 30 days from the date of this prospectus supplement.

Use of Proceeds

We intend to use the net proceeds from this offering for general corporate purposes, which may include capital and operating expenditures, including drug research and development costs, working capital, repaying, redeeming or repurchasing debt, acquisitions, and share repurchases. Pending the application of the net proceeds, we may invest the net proceeds in short-term, interest-bearing instruments or other investment-grade securities. See Use of Proceeds on page S-20 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-4 of this prospectus supplement.

Outstanding Shares

The number of shares of our common stock to be outstanding immediately after this offering is based on 94,517,285 shares outstanding as of December 31, 2010, and excludes as of such date:

16,898,992 shares of common stock issuable upon the exercise of outstanding options, at a weighted average exercise price of approximately \$9.40 per share, and 223,351 shares of common stock issuable upon the vesting of restricted stock units;

10,141,248 shares of common stock available for future grant under our 2000 Non-Officer Equity Incentive Plan, as amended, Employee Stock Purchase Plan, as amended and restated, and 2008 Equity Incentive Plan; and

9,989,539 shares of common stock issuable upon the conversion of our outstanding convertible subordinated notes at a conversion price of approximately \$21.52 per share.

Except as otherwise indicated, all information in the prospectus supplement assumes no exercise by the underwriter of its overallotment option.

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Risk Factors

An investment in our common stock involves a high degree of risk. Before deciding whether to invest in our common stock, you should consider carefully the risks discussed below, together with other information in this prospectus supplement, the accompanying prospectus, the information and documents incorporated by reference and in any free writing prospectus that we have authorized for use in connection with this offering. The risks described below may not be the only ones relating to our company. Additional risks that we currently believe are immaterial may also impair our business operations. Our business, results of operation, financial condition, cash flow and future prospects and the trading price of our common stock and our ability to repay our convertible notes could be harmed as a result of any of these risks, and investors may lose all or part of their investment.

Risks Related to Our Business

Drug development is an inherently uncertain process with a high risk of failure at every stage of development.

We have a number of proprietary product candidates and partnered product candidates in research and development ranging from the early discovery research phase through preclinical testing and clinical trials. Preclinical testing and clinical trials are long, expensive and highly uncertain processes. It will take us, or our collaborative partners, several years to complete clinical trials. Drug development is an uncertain scientific and medical endeavor, and failure can unexpectedly occur at any stage of clinical development even after early preclinical or mid-stage clinical results suggest that the drug candidate has potential as a new therapy that may benefit patients and that health authority approval would be anticipated. Typically, there is a high rate of attrition for product candidates in preclinical and clinical trials due to scientific feasibility, safety, efficacy, changing standards of medical care and other variables. We or our partners have a number of important product candidates in mid- to late-stage development, such as Bayer's Amikacin Inhale, Oral NKTR-118 (oral PEGylated naloxol) and NKTR-119, which we partnered with AstraZeneca, and NKTR-102 (PEGylated irinotecan). We also have an ongoing Phase 1 clinical trial for NKTR-105 (PEGylated docetaxel) for patients with refractory solid tumors. Any one of these trials could fail at any time, as clinical development of drug candidates presents numerous unpredictable and significant risks and is very uncertain at all times prior to regulatory approval by one or more health authorities in major markets.

Even with success in preclinical testing and clinical trials, the risk of clinical failure remains high prior to regulatory approval.

A number of companies in the pharmaceutical and biotechnology industries have suffered significant unforeseen setbacks in later stage clinical trials (i.e., Phase 2 or Phase 3 trials) due to factors such as inconclusive efficacy results and adverse medical events, even after achieving positive results in earlier trials that were satisfactory both to them and to reviewing regulatory agencies. Although we announced positive preliminary Phase 2 clinical results for Oral NKTR-118 (oral PEGylated naloxol) in 2009, there are still substantial risks and uncertainties associated with the future commencement and outcome of a Phase 3 clinical trial and the regulatory review process even following our partnership with AstraZeneca. While NKTR-102 (PEGylated irinotecan) continues in Phase 2 clinical development for multiple cancer indications, it is possible this product candidate could fail in one or all of the cancer indications in which it is currently being studied due to efficacy, safety or other commercial or regulatory factors. In 2010 and in January 2011, we announced preliminary positive results from our Phase 2 trials for NKTR-102 in ovarian and breast

cancer. These results were based on preliminary data only, and such results could change based on final audit and verification procedures. In addition, the preliminary results from the NKTR-102 clinical studies for ovarian and breast cancer are not necessarily indicative or predictive of the future results from the completed ovarian or breast cancer trials, anticipated Phase 3 trials in these indications or clinical trials in the other cancer indications for which we are studying NKTR-102. There remains a significant uncertainty as to the success or failure of NKTR-102 and whether this drug candidate will eventually receive regulatory approval or be a commercial success even if approved by one or more health authorities in any of the cancer indications for which it is being studied. The risk of failure is increased for our product candidates that are based on new technologies, such as the application of our advanced polymer conjugate technology to small molecules, including Oral NKTR-118, Oral NKTR-119, NKTR-102, NKTR-105 and other drug candidates currently in the discovery research or preclinical development phases.

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The results from the expanded Phase 2 clinical trial for NKTR-102 in women with platinum-resistant/refractory ovarian cancer are unlikely to result in submission of an NDA, and the future results from this trial are difficult to predict.

In 2010, we expanded the NKTR-102 Phase 2 study in women with platinum-resistant/refractory ovarian cancer with the potential for us to consider an NDA submission after we evaluate these expanded study results. The FDA almost always requires a sponsor to conduct Phase 3 clinical trials prior to consideration and approval of an NDA, and, as a result, review or approval of an NDA by the FDA based on the expanded Phase 2 study prior to completion of successful Phase 3 clinical studies, if such NDA is submitted, would be unusual and is highly unlikely. Further, this expansion study will necessarily change the final efficacy (e.g., overall response rates, progression-free survival, overall survival) and safety (i.e., frequency and severity of serious adverse events) results, and, accordingly, the final results in this study remain subject to substantial change and could be materially and adversely different from previously announced results. If the clinical studies for NKTR-102 in women with platinum-resistant/refractory ovarian cancer are not successful, it could significantly harm our business, results of operations and financial condition.

We may not be able to obtain intellectual property licenses related to the development of our technology on a commercially reasonable basis, if at all.

Numerous pending and issued U.S. and foreign patent rights and other proprietary rights owned by third parties relate to pharmaceutical compositions, medical devices and equipment and methods for preparation, packaging and delivery of pharmaceutical compositions. We cannot predict with any certainty which, if any, patent references will be considered relevant to our or our collaborative partners' technology or drug candidates by authorities in the various jurisdictions where such rights exist, nor can we predict with certainty which, if any, of these rights will or may be asserted against us by third parties. In certain cases, we have existing licenses or cross-licenses with third parties, however the scope and adequacy of these licenses is very uncertain and can change substantially during long development and commercialization cycles for biotechnology and pharmaceutical products. There can be no assurance that we can obtain a license to any technology that we determine we need on reasonable terms, if at all, or that we could develop or otherwise obtain alternate technology. If we are required to enter into a license with a third party, our potential economic benefit for the products subject to the license will be diminished. If a license is not available on commercially reasonable terms or at all, our business, results of operation, and financial condition could be significantly harmed and we may be prevented from developing and selling the product.

If any of our pending patent applications do not issue, or are deemed invalid following issuance, we may lose valuable intellectual property protection.

The patent positions of pharmaceutical, medical device and biotechnology companies, such as ours, are uncertain and involve complex legal and factual issues. We own greater than 100 U.S. and 380 foreign patents and a number of pending patent applications that cover various aspects of our technologies. We have filed patent applications, and plan

The results from the expanded Phase 2 clinical trial for NKTR-102 in women with platinum-resistant/refractory ovarian

to file additional patent applications, covering various aspects of our PEGylation and advanced polymer conjugate technologies and our proprietary product candidates. There can be no assurance that patents that have issued will be valid and enforceable or that patents for which we apply will issue with broad coverage, if at all. The coverage claimed in a patent application can be significantly reduced before the patent is issued and, as a consequence, our patent applications may result in patents with narrow coverage that may not prevent competition from similar products or generics. Since publication of discoveries in scientific or patent literature often lags behind the date of such discoveries, we cannot be certain that we were the first inventor of inventions covered by our patents or patent applications. As part of the patent application process, we may have to participate in interference proceedings declared by the U.S. Patent and Trademark Office, which could result in substantial cost to us, even if the eventual outcome is favorable. Further, an issued patent may undergo further proceedings to limit its scope so as not to provide meaningful protection and any claims that have issued, or that eventually issue, may be circumvented or otherwise invalidated.

Any attempt to enforce our patents or patent application rights could be time consuming and costly. An adverse outcome could subject us to significant liabilities to third parties, require disputed rights to be licensed from or to third parties or require us to cease using the technology in dispute. Even if a patent is issued and enforceable, because development and commercialization of pharmaceutical

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products can be subject to substantial delays, patents may expire early and provide only a short period of protection, if any, following commercialization of related products.

There are many laws, regulations and judicial decisions that dictate and otherwise influence the manner in which patent applications are filed and prosecuted and in which patents are granted and enforced. Changes to these laws, regulations and judicial decisions are subject to influences outside of our control and may negatively affect our business, including our ability to obtain meaningful patent coverage or enforcement rights to any of our issued patents.

New laws, regulations and judicial decisions may be retroactive in effect, potentially reducing or eliminating our ability to implement our patent-related strategies. Changes to laws, regulations and judicial decisions that affect our business are often difficult or impossible to foresee, which limits our ability to adequately adapt our patent strategies to these changes.

If we or our partners are not able to manufacture drugs or drug substances in quantities and at costs that are commercially feasible, we may fail to meet our contractual obligations or our proprietary and partnered product candidates may experience clinical delays or constrained commercial supply which could significantly harm our business.

If we are not able to scale-up manufacturing to meet the drug quantities required to support large clinical trials or commercial manufacturing in a timely manner or at a commercially reasonable cost, we risk delaying our clinical trials or those of our partners and may breach contractual obligations and incur associated damages and costs, and reduce or even eliminate associated revenues. In some cases, we may subcontract manufacturing or other services. Pharmaceutical manufacturing involves significant risks and uncertainties related to the demonstration of adequate stability, sufficient purification of the drug substance and drug product, the identification and elimination of impurities, optimal formulations, process validation, and challenges in controlling for all of these factors during manufacturing scale-up for large clinical trials and commercial manufacturing and supply. In addition, we have faced and may in the future face significant difficulties, delays and unexpected expenses as we validate third party contract manufacturers required for scale-up to clinical or commercial quantities. Failure to manufacture products in quantities or at costs that are commercially feasible could cause us not to meet our supply requirements, contractual obligations or other requirements for our proprietary product candidates and, as a result, would significantly harm our business, results of operations and financial condition.

For instance, we entered a service agreement with Novartis pursuant to which we subcontract to Novartis certain important services to be performed in relation to our partnered program for Amikacin Inhale with Bayer Healthcare LLC. If our subcontractors do not dedicate adequate resources to our programs, we risk breach of our obligations to our partners. Building and validating large scale clinical or commercial-scale manufacturing facilities and processes, recruiting and training qualified personnel and obtaining necessary regulatory approvals is complex, expensive and time consuming. In the past we have encountered challenges in scaling up manufacturing to meet the requirements of large scale clinical trials without making modifications to the drug formulation, which may cause significant delays in clinical development. Further, our drug and device combination products, such as Amikacin Inhale and the Cipro Inhale program, require significant device design, formulation development work and manufacturing scale-up activities. Further, we have experienced significant delays in starting the Phase 3 clinical development program for Amikacin Inhale as we seek to finalize the device design with a demonstrated capability to be manufactured at

commercial scale. This work is ongoing and there remains significant risk in finalizing the device until those activities are completed. Drug/device combination products are particularly complex, expensive and time-consuming to develop due to the number of variables involved in the final product design, including ease of patient/doctor use, maintenance of clinical efficacy, reliability and cost of manufacturing, regulatory approval requirements and standards and other important factors. There continues to be substantial and unpredictable risk and uncertainty related to manufacturing and supply until such time as the commercial supply chain is validated and proven.

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We will need to restructure our convertible notes or raise substantial additional capital to repay the notes and fund operations, and we may be unable to restructure the notes or raise such capital when needed and on acceptable terms.

We have \$215.0 million in outstanding convertible subordinated notes due September 2012. We do not have sufficient resources to fund the development of the drug candidates in our current research and development pipeline, complete planned clinical development of NKTR-102 and NKTR-105 and repay these convertible notes. We have no material credit facility or other material committed sources of capital. We expect the Phase 3 clinical trials of NKTR-102 to require particularly significant resources because we anticipate bearing a majority or all of the development costs for that drug candidate. Prior to the maturity of the notes, we plan to explore a number of alternatives to provide for the repayment of the notes, including restructuring the notes. Despite these efforts, we may be unable to find a commercially acceptable alternative or any alternative to repaying the notes by September 2012. Our future capital requirements will depend upon numerous factors, including:

the progress, timing, cost and results of our clinical development programs, including our planned further clinical development of NKTR-102;

patient enrollment in our current and future clinical studies, including in particular our expected Phase 3 clinical development plans for NKTR-102;

whether and when we receive potential milestone payments and royalties, particularly from the product candidates that are subject to our collaboration agreements with AstraZeneca for NKTR-118 and Bayer for Amikacin Inhale;

the success, progress, timing and costs of our business development efforts to implement new business collaborations, licenses and other strategic transactions;

the cost, timing and outcomes of regulatory reviews of our product candidates (e.g., NKTR-102) and those of our collaboration partners (e.g., NKTR-118, Amikacin Inhale);

our general and administrative expenses, capital expenditures and other uses of cash;

disputes concerning patents, proprietary rights, or license and collaboration agreements;

the availability and scope of coverage from government and private insurance payment or reimbursement for our drug candidates partnered with collaboration partners and any future drug candidates that may receive regulatory approval in the future; and

the size, design (i.e., primary and secondary endpoints) and number of clinical studies required by the government health authorities in order to consider for approval our product candidates and those of our collaboration partners.

Although we believe that our cash, cash equivalents and short-term investments in marketable securities of \$303.3 million as of September 30, 2010 will be sufficient to meet our liquidity requirements through at least the next 12 months, we will need by September 2012 to restructure our notes or obtain additional funds through one or more financing or collaboration partnership transactions. If adequate funds are not available or are not available on acceptable terms when we need them, we may need to delay or reduce our Phase 3 clinical trials of NKTR-102 or otherwise make changes to our operations to cut costs.

If we are unable either to create sales, marketing and distribution capabilities or to enter into agreements with third parties to perform these functions, we will be unable to commercialize our products successfully.

We will need to restructure our convertible notes or raise substantial additional capital to repay the notes and fund

We currently have no sales, marketing or distribution capabilities. To commercialize any of our products that receive regulatory approval for commercialization, we must either develop internal sales, marketing and distribution capabilities, which will be expensive and time consuming, or enter into collaboration arrangements with third parties to perform these services. If we decide to market our products directly, we must commit significant financial and managerial resources to develop a marketing and sales force with

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technical expertise and with supporting distribution, administration and compliance capabilities. Factors that may inhibit our efforts to commercialize our products directly or indirectly with our partners include:

our inability to recruit and retain adequate numbers of effective sales and marketing personnel; the inability of sales personnel to obtain access to or persuade adequate numbers of physicians to use or prescribe our products; the lack of complementary products or multiple product pricing arrangements may put us at a competitive disadvantage relative to companies with more extensive product lines; and unforeseen costs and expenses associated with creating and sustaining an independent sales and marketing organization.

If we, or our partners through our collaboration, are not successful in recruiting sales and marketing personnel or in building a sales and marketing infrastructure, we will have difficulty commercializing our products, which would adversely affect our business, results of operations and financial condition. To the extent we rely on other pharmaceutical or biotechnology companies with established sales, marketing and distribution systems to market our products, we will need to establish and maintain partnership arrangements, and we may not be able to enter into these arrangements on acceptable terms or at all. To the extent that we enter into co-promotion or other arrangements, any revenues we receive will depend upon the efforts of third parties, which may not be successful and are only partially in our control. In that event, our product revenues would likely be lower than if we marketed and sold our products directly.

If we are unable to establish and maintain collaboration partnerships on attractive commercial terms, our business, results of operations and financial condition could suffer.

We intend to continue to seek partnerships with pharmaceutical and biotechnology partners to fund a portion of our research and development expenses and develop and commercialize our product candidates. In September 2009, we entered into a license agreement with AstraZeneca for NKTR-118 and NKTR-119 which included an upfront payment of \$125.0 million. The completion of the AstraZeneca transaction was critical to our financial results and financial condition for the year ended December 31, 2009. The timing of new collaboration partnerships is difficult to predict due to availability of clinical data, the number of potential partners that need to complete due diligence and approval processes, the definitive agreement negotiation process and numerous other unpredictable factors that can delay, impede or prevent significant transactions. If we are unable to find suitable partners or to negotiate collaborative arrangements with favorable commercial terms with respect to our existing and future product candidates or the licensing of our technology, or if any arrangements we negotiate, or have negotiated, are terminated, our business, results of operations and financial condition could suffer.

The commercial potential of a drug candidate in development is difficult to predict and if the market size for a new drug is significantly smaller than we anticipated, it could significantly and negatively impact our revenue, results of operations and financial condition.

It is very difficult to estimate the commercial potential of product candidates due to factors such as safety and efficacy

If we are unable to establish and maintain collaboration partnerships on attractive commercial terms, our business,

compared to other available treatments, including potential generic drug alternatives with similar efficacy profiles, changing standards of care, third party payer reimbursement, patient and physician preferences, the availability of competitive alternatives that may emerge either during the long drug development process or after commercial introduction, and the availability of generic versions of our successful product candidates following approval by health authorities based on the expiration of regulatory exclusivity or our inability to prevent generic versions from coming to market in one or more geographies by the assertion of one or more patents covering such approved drug. If due to one or more of these risks the market potential for a product candidate is lower than we anticipated, it could significantly and negatively impact the commercial terms of any collaboration partnership potential for such product candidate or, if we have already entered into a collaboration for such drug candidate, the revenue potential from royalty and milestone payments could be significantly diminished and would negatively impact our revenue, results of operations and financial condition.

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Our revenue is exclusively derived from our collaboration agreements, which can result in significant fluctuation in our revenue from period to period, and our past revenue is therefore not necessarily indicative of our future revenue.

Our revenue is derived from our collaboration agreements with partners, under which we may receive contract research payments, milestone payments based on clinical progress, regulatory progress or net sales achievements, royalties or manufacturing revenue. Significant variations in the timing of receipt of cash payments and our recognition of revenue can result from the nature of significant milestone payments based on the execution of new collaboration agreements, the timing of clinical, regulatory or sales events which result in single milestone payments and the timing and success of the commercial launch of new drugs by our collaboration partners. The amount of our revenue derived from collaboration agreements in any given period will depend on a number of unpredictable factors, including our ability to find and maintain suitable collaboration partners, the timing of the negotiation and conclusion of collaboration agreements with such partners, whether and when we or our partner achieve clinical and sales milestones, whether the partnership is exclusive or whether we can seek other partners, the timing of regulatory approvals in one or more major markets and the market introduction of new drugs or generic versions of the approved drug, as well as other factors.

If our partners, on which we depend to obtain regulatory approvals for and to commercialize our partnered products, are not successful, or if such collaborations fail, the development or commercialization of our partnered products may be delayed or unsuccessful.

When we sign a collaborative development agreement or license agreement to develop a product candidate with a pharmaceutical or biotechnology company, the pharmaceutical or biotechnology company is generally expected to:

design and conduct large scale clinical studies;
prepare and file documents necessary to obtain government approvals to sell a given product candidate; and/or
market and sell our products when and if they are approved.

Our reliance on collaboration partners poses a number of risks to our business, including risks that:

we may be unable to control whether, and the extent to which, our partners devote sufficient resources to the development programs or commercial marketing and sales efforts;
disputes may arise or escalate in the future with respect to the ownership of rights to technology or intellectual property developed with partners;
disagreements with partners could lead to delays in, or termination of, the research, development or commercialization of product candidates or to litigation or arbitration proceedings;
contracts with our partners may fail to provide us with significant protection, or to be effectively enforced, in the event one of our partners fails to perform;
partners have considerable discretion in electing whether to pursue the development of any additional product candidates and may pursue alternative technologies or products either on their own or in collaboration with our competitors;

Our revenue is exclusively derived from our collaboration agreements, which can result in significant fluctuation in o

partners with marketing rights may choose to devote fewer resources to the marketing of our partnered products than they do to products of their own development or products in-licensed from other third parties; the timing and level of resources that our partners dedicate to the development program will affect the timing and amount of revenue we receive;

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we do not have the ability to unilaterally terminate agreements (or partners may have extension or renewal rights) that we believe are not on commercially reasonable terms or consistent with our current business strategy;

partners may be unable to pay us as expected; and

partners may terminate their agreements with us unilaterally for any or no reason, in some cases with the payment of a termination fee penalty and in other cases with no termination fee penalty.

Given these risks, the success of our current and future partnerships is highly unpredictable and can have a substantial negative or positive impact on our business. We have entered into collaborations in the past that have been subsequently terminated, such as our collaboration with Pfizer for the development and commercialization of inhaled insulin that was terminated by Pfizer in November 2007. If other collaborations are suspended or terminated, our ability to commercialize certain other proposed product candidates could also be negatively impacted. If our collaborations fail, our product development or commercialization of product candidates could be delayed or cancelled, which would negatively impact our business, results of operations and financial condition.

If we or our partners do not obtain regulatory approval for our product candidates on a timely basis, or at all, or if the terms of any approval impose significant restrictions or limitations on use, our business, results of operations and financial condition will be negatively affected.

We or our partners may not obtain regulatory approval for product candidates on a timely basis, or at all, or the terms of any approval (which in some countries includes pricing approval) may impose significant restrictions or limitations on use. Product candidates must undergo rigorous animal and human testing and an extensive FDA mandated or equivalent foreign authorities review process for safety and efficacy. This process generally takes a number of years and requires the expenditure of substantial resources. The time required for completing testing and obtaining approvals is uncertain, and the FDA and other U.S. and foreign regulatory agencies have substantial discretion to terminate clinical trials, require additional clinical development or other testing at any phase of development, delay or withhold registration and marketing approval and mandate product withdrawals, including recalls. In addition, undesirable side effects caused by our product candidates could cause us or regulatory authorities to interrupt, delay or halt clinical trials and could result in a more restricted label or the delay or denial of regulatory approval by regulatory authorities.

Even if we or our partners receive regulatory approval of a product, the approval may limit the indicated uses for which the product may be marketed. Our partnered products that have obtained regulatory approval, and the manufacturing processes for these products, are subject to continued review and periodic inspections by the FDA and other regulatory authorities. Discovery from such review and inspection of previously unknown problems may result in restrictions on marketed products or on us, including withdrawal or recall of such products from the market, suspension of related manufacturing operations or a more restricted label. The failure to obtain timely regulatory approval of product candidates, any product marketing limitations or a product withdrawal would negatively impact our business, results of operations and financial condition.

We are a party to numerous collaboration agreements and other significant agreements which contain complex commercial terms that could result in disputes, litigation or indemnification

If we or our partners do not obtain regulatory approval for our product candidates on a timely basis, or at all, or if the

liability that could adversely affect our business, results of operations and financial condition.

We currently derive, and expect to derive in the foreseeable future, all of our revenue from collaboration agreements with biotechnology and pharmaceutical companies. These collaboration agreements contain complex commercial terms, including:

clinical development and commercialization obligations that are based on certain commercial reasonableness performance standards that can often be difficult to enforce if disputes arise as to adequacy of performance; research and development performance and reimbursement obligations for our personnel and other resources allocated to partnered product development programs;

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clinical and commercial manufacturing agreements, some of which are priced on an actual cost basis for products supplied by us to our partners with complicated cost allocation formulas and methodologies;
intellectual property ownership allocation between us and our partners for improvements and new inventions developed during the course of the partnership;
royalties on end product sales based on a number of complex variables, including net sales calculations, geography, patent life, generic competitors, and other factors; and
indemnity obligations for third-party intellectual property infringement, product liability and certain other claims.

On September 20, 2009, we entered into a worldwide exclusive license agreement with AstraZeneca for the further development and commercialization of NKTR-118 and NKTR-119. In addition, we have also entered into complex commercial agreements with Novartis in connection with the sale of certain assets related to our pulmonary business, associated technology and intellectual property to Novartis (the Novartis Pulmonary Asset Sale), which was completed on December 31, 2008. Our agreements with AstraZeneca and Novartis contain complex representations and warranties, covenants and indemnification obligations that could result in substantial future liability and harm our financial condition if we breach any of our agreements with AstraZeneca or Novartis or any third party agreements impacted by these complex transactions. As part of the Novartis Pulmonary Asset Sale, we entered an exclusive license agreement with Novartis Pharma pursuant to which Novartis Pharma grants back to us an exclusive, irrevocable, perpetual, royalty-free and worldwide license under certain specific patent rights and other related intellectual property rights necessary for us to satisfy certain continuing contractual obligations to third parties, including in connection with development, manufacture, sale and commercialization activities related to our partnered program for Amikacin Inhale with Bayer Healthcare LLC. We also entered into a service agreement pursuant to which we have subcontracted to Novartis certain services to be performed related to our partner program for Amikacin Inhale.

From time to time, we have informal dispute resolution discussions with third parties regarding the appropriate interpretation of the complex commercial terms contained in our agreements. One or more disputes may arise or escalate in the future regarding our collaboration agreements, transaction documents, or third-party license agreements that may ultimately result in costly litigation and unfavorable interpretation of contract terms, which would have a material adverse impact on our business, results of operations or financial condition.

We purchase some of the starting material for drugs and drug candidates from a single source or a limited number of suppliers, and the partial or complete loss of one of these suppliers could cause production delays, clinical trial delays, substantial loss of revenue and contract liability to third parties.

We often face very limited supply of a critical raw material that can only be obtained from a single, or a limited number of, suppliers, which could cause production delays, clinical trial delays, substantial lost revenue opportunity or contract liability to third parties. For example, there are only a limited number of qualified suppliers, and in some cases single source suppliers, for the raw materials included in our PEGylation and advanced polymer conjugate drug formulations, and any interruption in supply or failure to procure such raw materials on commercially feasible terms could harm our business by delaying our clinical trials, impeding commercialization of approved drugs or increasing operating loss to the extent we cannot pass on increased costs to a manufacturing customer.

We purchase some of the starting material for drugs and drug candidates from a single source or a limited number of

We rely on trade secret protection and other unpatented proprietary rights for important proprietary technologies, and any loss of such rights could harm our business, results of operations and financial condition.

We rely on trade secret protection for our confidential and proprietary information. No assurance can be given that others will not independently develop substantially equivalent confidential and proprietary information or otherwise gain access to our trade secrets or disclose such technology, or that we can meaningfully protect our trade secrets. In addition, unpatented proprietary rights, including trade secrets and know-how, can be

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difficult to protect and may lose their value if they are independently developed by a third party or if their secrecy is lost. Any loss of trade secret protection or other unpatented proprietary rights could harm our business, results of operations and financial condition.

We expect to continue to incur substantial losses and negative cash flow from operations and may not achieve or sustain profitability in the future.

For the three and nine months ended September 30, 2010, we reported a net loss of \$8.7 million and \$15.4 million, respectively. If and when we achieve profitability depends upon a number of factors, including the timing and recognition of milestone payments and royalties received, the timing of revenue under our collaboration agreements, the amount of investments we make in our proprietary product candidates and the regulatory approval and market success of our product candidates. We may not be able to achieve and sustain profitability.

Other factors that will affect whether we achieve and sustain profitability include our ability, alone or together with our partners, to:

develop products utilizing our technologies, either independently or in collaboration with other pharmaceutical or biotech companies;

effectively estimate and manage clinical development costs, particularly the cost of NKTR-102 since we expect to bear a majority or all of such costs;

receive necessary regulatory and marketing approvals;

maintain or expand manufacturing at necessary levels;

achieve market acceptance of our partnered products;

receive royalties on products that have been approved, marketed or submitted for marketing approval with regulatory authorities; and

maintain sufficient funds to finance our activities.

If we do not generate sufficient cash through restructuring our convertible notes or raising additional capital, we may be unable to meet our substantial debt obligations.

As of September 30, 2010, we had cash, cash equivalents, and short-term investments in marketable securities valued at approximately \$303.3 million and approximately \$240.0 million of indebtedness, including approximately \$215.0 million in convertible subordinated notes due September 2012, \$19.2 million in capital lease obligations, and \$5.8 million of other liabilities.

Our substantial indebtedness has and will continue to impact us by:

making it more difficult to obtain additional financing;

constraining our ability to react quickly in an unfavorable economic climate;

constraining our stock price; and

constraining our ability to invest in our proprietary product development programs.

Currently, we are not generating positive cash flow. If we are unable to satisfy our debt service requirements, substantial liquidity problems could result. In relation to our convertible notes, since the market price of our common

We expect to continue to incur substantial losses and negative cash flow from operations and may not achieve or s

stock is significantly below the conversion price, the holders of our outstanding convertible notes are unlikely to convert the notes to common stock in accordance with the existing terms of the notes. If we do not generate sufficient cash from operations to repay principal or interest on our remaining convertible notes, or satisfy any of our other debt obligations, when due, we may have to raise additional funds from the issuance

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of equity or debt securities or entry into collaboration partnerships or otherwise restructure our obligations. Any such financing or restructuring may not be available to us on commercially acceptable terms, if at all.

If government and private insurance programs do not provide payment or reimbursement for our partnered products or proprietary products, those products will not be widely accepted, which would have a negative impact on our business, results of operations and financial condition.

In both domestic and foreign markets, sales of our partnered and proprietary products that have received regulatory approval will depend in part on market acceptance among physicians and patients, pricing approvals by government authorities and the availability of payment or reimbursement from third-party payers, such as government health administration authorities, managed care providers, private health insurers and other organizations. Such third-party payers are increasingly challenging the price and cost effectiveness of medical products and services. Therefore, significant uncertainty exists as to the pricing approvals for, and the payment or reimbursement status of, newly approved healthcare products. Moreover, legislation and regulations affecting the pricing of pharmaceuticals may change before regulatory agencies approve our proposed products for marketing and could further limit pricing approvals for, and reimbursement of, our products from government authorities and third-party payers. A government or third-party payer decision not to approve pricing for, or provide adequate coverage and reimbursements of, our products would limit market acceptance of such products.

We depend on third parties to conduct the clinical trials for our proprietary product candidates and any failure of those parties to fulfill their obligations could harm our development and commercialization plans.

We depend on independent clinical investigators, contract research organizations and other third-party service providers to conduct clinical trials for our proprietary product candidates. Though we rely heavily on these parties for successful execution of our clinical trials and are ultimately responsible for the results of their activities, many aspects of their activities are beyond our control. For example, we are responsible for ensuring that each of our clinical trials is conducted in accordance with the general investigational plan and protocols for the trial, but the independent clinical investigators may prioritize other projects over ours or communicate issues regarding our products to us in an untimely manner. Third parties may not complete activities on schedule or may not conduct our clinical trials in accordance with regulatory requirements or our stated protocols. The early termination of any of our clinical trial arrangements, the failure of third parties to comply with the regulations and requirements governing clinical trials or our reliance on results of trials that we have not directly conducted or monitored could hinder or delay the development, approval and commercialization of our product candidates and would adversely affect our business, results of operations and financial condition.

Our manufacturing operations and those of our contract manufacturers are subject to governmental regulatory

If government and private insurance programs do not provide payment or reimbursement for our partnered products

requirements, which, if not met, would have a material adverse effect on our business, results of operations and financial condition.

We and our contract manufacturers are required in certain cases to maintain compliance with current good manufacturing practices (cGMP), including cGMP guidelines applicable to active pharmaceutical ingredients, and are subject to inspections by the FDA or comparable agencies in other jurisdictions to confirm such compliance. We anticipate periodic regulatory inspections of our drug manufacturing facilities and the manufacturing facilities of our contract manufacturers for compliance with applicable regulatory requirements. Any failure to follow and document our or our contract manufacturers' adherence to such cGMP regulations or satisfy other manufacturing and product release regulatory requirements may disrupt our ability to meet our manufacturing obligations to our customers, lead to significant delays in the availability of products for commercial use or clinical study, result in the termination or hold on a clinical study or delay or prevent filing or approval of marketing applications for our products. Failure to comply with applicable regulations may also result in sanctions being imposed on us, including fines, injunctions, civil penalties, failure of regulatory authorities to grant marketing approval of our products, delays, suspension or withdrawal of approvals, license revocation, seizures or recalls of products, operating restrictions and criminal prosecutions, any of which could harm our business. The results of these inspections could result in costly manufacturing changes or facility or capital equipment upgrades to satisfy the FDA that our manufacturing

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and quality control procedures are in substantial compliance with cGMP. Manufacturing delays, for us or our contract manufacturers, pending resolution of regulatory deficiencies or suspensions would have a material adverse effect on our business, results of operations and financial condition.

Significant competition for our polymer conjugate chemistry technology platforms and our partnered and proprietary products and product candidates could make our technologies, products or product candidates obsolete or uncompetitive, which would negatively impact our business, results of operations and financial condition.

Our PEGylation and advanced polymer conjugate chemistry platforms and our partnered and proprietary products and product candidates compete with various pharmaceutical and biotechnology companies. Competitors of our PEGylation and polymer conjugate chemistry technologies include The Dow Chemical Company, Enzon Pharmaceuticals, Inc., SunBio Corporation, Mountain View Pharmaceuticals, Inc., Novo Nordisk A/S (formerly assets held by Neose Technologies, Inc.), and NOF Corporation. Several other chemical, biotechnology and pharmaceutical companies may also be developing PEGylation technologies or technologies that have similar impact on target drug molecules. Some of these companies license or provide the technology to other companies, while others are developing the technology for internal use.

There are several competitors for our proprietary product candidates currently in development. For Amikacin Inhale, the current standard of care includes several approved intravenous antibiotics for the treatment of either hospital-acquired pneumonia or ventilator-associated pneumonia in patients on mechanical ventilators. For Oral NKTR-118 (oral PEGylated naloxol), there are currently several alternative therapies used to address opioid-induced constipation (OIC) and opioid-induced bowel dysfunction (OBD), including subcutaneous Relistor® (methylnaltrexone bromide) and oral and rectal over-the-counter laxatives and stool softeners such as docusate sodium, senna and milk of magnesia. In addition, there are a number of companies developing potential products which are in various stages of clinical development and are being evaluated for the treatment of OIC and OBD in different patient populations, including Adolor Corporation, GlaxoSmithKline plc, Progenics Pharmaceuticals, Inc., Pfizer (via Wyeth acquisition completed in 2009), Mundipharma Int. Limited, Sucampo Pharmaceuticals and Takeda Pharmaceutical Company Limited. For NKTR-102 (PEGylated-irinotecan), there are a number of chemotherapies and cancer therapies approved today and in various stages of clinical development for ovarian and breast cancers including but not limited to: Avastin® (bevacizumab), Camptosar® (irinotecan), Doxil® (doxorubicin HCl), Ellence® (epirubicin), Gemzar® (gemcitabine), Herceptin® (trastuzumab), Hycamtin® (topotecan), Iniparib, Paraplatin® (carboplatin), and Taxol® (paclitaxel). Major pharmaceutical or biotechnology companies with approved drugs or drugs in development for these cancers include Bristol-Meyers Squibb, Eli Lilly & Co., Genentech, Inc., GlaxoSmithKline plc, Johnson and Johnson, Pfizer, Inc., Sanofi Aventis, and many others. There are also approved therapies for the treatment of colorectal cancer, including Eloxatin, Camptosar, Avastin, Erbitux, Vectibux, Xeloda, Adrucil and Wellcovorin. In addition, there are a number of drugs in various stages of preclinical and clinical development from companies exploring cancer therapies or improved chemotherapeutic agents to potentially treat colorectal cancer, including, but not limited to, products in development from Bristol-Myers Squibb Company, Pfizer, Inc., GlaxoSmithKline plc, Antigenics, Inc., F. Hoffmann-La Roche Ltd, Novartis AG, Cell Therapeutics, Inc., Neopharm Inc., Meditech Research Ltd, Alchemia Limited, Enzon Pharmaceuticals, Inc. and others.

There can be no assurance that we or our partners will successfully develop, obtain regulatory approvals for and commercialize next-generation or new products that will successfully compete with those of our competitors. Many of our competitors have greater financial, research and development, marketing and sales, manufacturing and managerial capabilities. We face competition from these companies not just in product development but also in areas such as recruiting employees, acquiring technologies that might enhance our ability to commercialize products, establishing relationships with certain research and academic institutions, enrolling patients in clinical trials and seeking program partnerships and collaborations with larger pharmaceutical companies. As a result, our competitors may succeed in developing competing technologies, obtaining regulatory approval or gaining market acceptance for products before we do. These developments could make our products or technologies uncompetitive or obsolete.

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We could be involved in legal proceedings and may incur substantial litigation costs and liabilities that will adversely affect our business, results of operations and financial condition.

From time to time, third parties have asserted, and may in the future assert, that we or our partners infringe their proprietary rights, such as patents and trade secrets, or have otherwise breached our obligations to them. The third party often bases its assertions on a claim that its patents cover our technology or that we have misappropriated its confidential or proprietary information. Similar assertions of infringement could be based on future patents that may issue to third parties. In certain of our agreements with our partners, we are obligated to indemnify and hold harmless our partners from intellectual property infringement, product liability and certain other claims, which could cause us to incur substantial costs if we are called upon to defend ourselves and our partners against any claims. If a third party obtains injunctive or other equitable relief against us or our partners, they could effectively prevent us, or our partners, from developing or commercializing, or deriving revenue from, certain products or product candidates in the U.S. and abroad. For instance, F. Hoffmann-La Roche Ltd, to which we license our proprietary PEGylation reagent for use in the MIRCERA product, was a party to a significant patent infringement lawsuit brought by Amgen Inc. related to Roche's proposed marketing and sale of MIRCERA to treat chemotherapy anemia in the U.S. In October 2008, a federal court ruled in favor of Amgen, issuing a permanent injunction preventing Roche from marketing or selling MIRCERA in the U.S. In December 2009, the U.S. District court for the District of Massachusetts entered a final judgment and permanent injunction, and Roche and Amgen entered into a settlement and limited license agreement which allows Roche to begin selling MIRCERA in the U.S. in July 2014.

Third-party claims involving proprietary rights or other matters could also result in the award of substantial damages to be paid by us or a settlement resulting in significant payments to be made by us. For instance, a settlement might require us to enter a license agreement under which we pay substantial royalties or other compensation to a third party, diminishing our future economic returns from the related product. In 2006, we entered into a litigation settlement related to an intellectual property dispute with the University of Alabama in Huntsville pursuant to which we paid \$11.0 million and agreed to pay an additional \$10.0 million in equal \$1.0 million installments over ten years ending with the last payment due on July 1, 2016. We cannot predict with certainty the eventual outcome of any pending or future litigation. Costs associated with such litigation, substantial damage claims, indemnification claims or royalties paid for licenses from third parties could have a material adverse effect on our business, results of operations and financial condition.

If product liability lawsuits are brought against us, we may incur substantial liabilities.

The manufacture, clinical testing, marketing and sale of medical products involve inherent product liability risks. If product liability costs exceed our product liability insurance coverage, we may incur substantial liabilities that could have a severe negative impact on our financial position. Whether or not we are ultimately successful in any product liability litigation, such litigation would consume substantial amounts of our financial and managerial resources and might result in adverse publicity, all of which would impair our business. Additionally, we may not be able to maintain our clinical trial insurance or product liability insurance at an acceptable cost, if at all, and this insurance may not provide adequate coverage against potential claims or losses.

Our future depends on the proper management of our current and future business operations and their associated expenses.

Our business strategy requires us to manage our business to provide for the continued development and potential commercialization of our proprietary and partnered product candidates. Our strategy also calls for us to undertake increased research and development activities and to manage an increasing number of relationships with partners and other third parties, while simultaneously managing the expenses generated by these activities. Our decision to bring NKTR-102 into Phase 3 trials and to bear a majority or all of the clinical development costs substantially increases our expenses. If we are unable to manage effectively our current operations and any growth we may experience, our business, financial condition and results of operations may be adversely affected. If we are unable to effectively manage our expenses, we may find it necessary to reduce our personnel-related costs through further reductions in our workforce, which could

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harm our operations, employee morale and impair our ability to retain and recruit talent. Furthermore, if adequate funds are not available, we may be required to obtain funds through arrangements with partners or other sources that may require us to relinquish rights to certain of our technologies, products or future economic rights that we would not otherwise relinquish or require us to enter into other financing arrangements on unfavorable terms.

We are dependent on our management team and key technical personnel, and the loss of any key manager or employee may impair our ability to develop our products effectively and may harm our business, operating results and financial condition.

Our success largely depends on the continued services of our executive officers and other key personnel. The loss of one or more members of our management team or other key employees could seriously harm our business, operating results and financial condition. The relationships that our key managers have cultivated within our industry make us particularly dependent upon their continued employment with us. We are also dependent on the continued services of our technical personnel because of the highly technical nature of our products and the regulatory approval process. Because our executive officers and key employees are not obligated to provide us with continued services, they could terminate their employment with us at any time without penalty. We do not have any post-employment noncompetition agreements with any of our employees and do not maintain key person life insurance policies on any of our executive officers or key employees.

Because competition for highly qualified technical personnel is intense, we may not be able to attract and retain the personnel we need to support our operations and growth.

We must attract and retain experts in the areas of clinical testing, manufacturing, regulatory, finance, marketing and distribution and develop additional expertise in our existing personnel. In particular, as we plan to advance NKTR-102 into late stage development, additional highly qualified personnel will be required. We face intense competition from other biopharmaceutical companies, research and academic institutions and other organizations for qualified personnel. Many of the organizations with which we compete for qualified personnel have greater resources than we have. Because competition for skilled personnel in our industry is intense, companies such as ours sometimes experience high attrition rates with regard to their skilled employees. Further, in making employment decisions, job candidates often consider the value of the stock options they are to receive in connection with their employment. Our equity incentive plan and employee benefit plans may not be effective in motivating or retaining our employees or attracting new employees, and significant volatility in the price of our stock may adversely affect our ability to attract or retain qualified personnel. If we fail to attract new personnel or to retain and motivate our current personnel, our business and future growth prospects could be severely harmed.

If earthquakes and other catastrophic events strike, our business may be harmed.

Our corporate headquarters, including a substantial portion of our research and development operations, are located in the San Francisco Bay Area, a region known for seismic activity and a potential terrorist target. In addition, we own facilities for the manufacture of products using our PEGylation and advanced polymer conjugate technologies in

We are dependent on our management team and key technical personnel, and the loss of any key manager or employee

Huntsville, Alabama and own and lease offices in Hyderabad, India. There are no backup facilities for our manufacturing operations located in Huntsville, Alabama. In the event of an earthquake or other natural disaster, political instability, or terrorist event in any of these locations, our ability to manufacture and supply materials for drug candidates in development and our ability to meet our manufacturing obligations to our customers would be significantly disrupted and our business, results of operations and financial condition would be harmed. Our collaborative partners may also be subject to catastrophic events, such as hurricanes and tornadoes, any of which could harm our business, results of operations and financial condition. We have not undertaken a systematic analysis of the potential consequences to our business, results of operations and financial condition from a major earthquake or other catastrophic event, such as a fire, sustained loss of power, terrorist activity or other disaster, and do not have a recovery plan for such disasters. In addition, our insurance coverage may not be sufficient to compensate us for actual losses from any interruption of our business that may occur.

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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;
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, we have in place a preferred share purchase rights plan, commonly known as a poison pill. The provisions described above, our poison pill and 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 benefits 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.

Risks Related to Our Securities

The price of our common stock and convertible debt are expected to remain volatile.

Our stock price is volatile. During the year ended December 31, 2010, based on closing bid prices on The NASDAQ Global Select Market, our stock price ranged from \$9.39 to \$15.88 per share. We expect our stock price to remain volatile. In addition, as our convertible notes are convertible into shares of our common stock, volatility or depressed prices of our common stock could have a similar effect on the trading price of our notes. Also, interest rate fluctuations can affect the price of our convertible notes. A variety of factors may have a significant effect on the market price of our common stock or notes, including:

announcements of data from, or material developments in, our clinical trials or those of our competitors, including delays in clinical development, approval or launch;
announcements by collaboration partners as to their plans or expectations related to products using our technologies;
announcements or terminations of collaboration agreements by us or our competitors;
fluctuations in our results of operations;

We have implemented certain anti-takeover measures, which make it more difficult to acquire us, even though such

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;
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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;

hedging activities by purchasers of our convertible notes;

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; 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 and warrants, the restructuring of our convertible notes, or the future issuances of securities.

We may restructure our convertible notes or issue additional common stock, preferred stock, restricted stock units or securities convertible into or exchangeable for our common stock. Furthermore, substantially all shares of common stock for which our outstanding stock options or warrants 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 or warrants would dilute existing investors and could lower the price of our common stock.

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

Restructuring of our convertible notes or raising additional funds by issuing equity securities could cause significant dilution to existing stockholders; restructured or additional debt

Our stockholders may be diluted, and the price of our common stock may decrease, as a result of the exercise of o

financing may restrict our operations.

If we raise additional funds through the restructuring of our convertible notes or issuance of equity or convertible debt securities, the percentage ownership of our stockholders could be diluted significantly, and these restructured or newly issued securities may have rights, preferences or privileges senior to those of our existing stockholders. If we restructure our notes or incur additional debt financing, the payment of principal and interest on such indebtedness may limit funds available for our business activities, and we could be subject to covenants that restrict our ability to operate our business and make distributions to our stockholders. These restrictive covenants may include limitations on additional borrowing and specific restrictions on the use of our assets, as well as prohibitions on the ability of us to create liens, pay dividends, redeem our stock or make investments.

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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, intend, plan, believe, seek, estimate, 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 product sales, regulatory activities, clinical trial results, reimbursement, expenses, earnings per share, liquidity and capital resources, and trends. 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 reports and other documents on file with the SEC. You may obtain copies of these documents as described under Where You Can Find More Information below.

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Use of Proceeds

We estimate that the net proceeds from the sale of the 19,000,000 shares of common stock that we are offering will be approximately \$219.8 million, or approximately \$252.9 million if the underwriter exercises in full its option to purchase 2,850,000 additional shares of common stock, based on the public offering price of \$11.85 per share and after deducting the 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, which may include capital and operating expenditures, including drug research and development costs, working capital, repaying, redeeming or repurchasing debt, acquisitions, and share repurchases.

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, and the competitive environment for our product 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. Pending the application of the net proceeds as described above, we may invest the net proceeds in short-term, interest-bearing instruments or other investment-grade securities.

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Our net tangible book value as of September 30, 2010 was approximately \$30.4 million, or \$0.32 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 September 30, 2010. 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 19,000,000 shares of our common stock in this offering at the public offering price of \$11.85 per share and after deducting the underwriting discounts and commissions and estimated offering expenses payable by us, our as adjusted net tangible book value as of September 30, 2010 would have been approximately \$250.2 million, or \$2.21 per share. This represents an immediate increase in net tangible book value of \$1.89 per share to existing stockholders and immediate dilution in net tangible book value of \$9.64 per share to new investors purchasing our common stock in this offering. The following table illustrates this dilution on a per share basis:

Public offering price per share	\$ 11.85
Net tangible book value per share as of September 30, 2010	\$ 0.32
Increase per share attributable to new investors	\$ 1.89
As adjusted net tangible book value per share as of September 30, 2010 after this offering	\$ 2.21
Dilution in net tangible book value per share to new investors	\$ 9.64

If the underwriter exercises in full its option to purchase 2,850,000 additional shares of common stock at the public offering price of \$11.85 per share, the as adjusted net tangible book value after this offering would be \$2.44 per share, representing an increase in net tangible book value of \$2.12 per share to existing stockholders and immediate dilution in net tangible book value of \$9.41 per share to new investors purchasing our common stock in this offering.

The above discussion and table are based on 94,273,434 shares outstanding as of September 30, 2010, and exclude as of such date:

16,898,098 shares of common stock issuable upon the exercise of outstanding options, at a weighted average exercise price of approximately \$9.33 per share, and 227,495 shares of common stock issuable upon the vesting of restricted stock units;

9,681,615 shares of common stock available for future grant under our 2000 Non-Officer Equity Incentive Plan, as amended, Employee Stock Purchase Plan, as amended and restated, and 2008 Equity Incentive Plan; and 9,989,539 shares of common stock issuable upon the conversion of our outstanding convertible subordinated notes at a conversion price of approximately \$21.52 per share.

To the extent that outstanding options or warrants 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.

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Underwriting

Subject to the terms and conditions set forth in the underwriting agreement dated January 19, 2011, between us and Jefferies & Company, Inc., as underwriter, we have agreed to sell to the underwriter and the underwriter has agreed to purchase from us the entire 19,000,000 shares of our common stock offered by this prospectus supplement.

The underwriting agreement provides that the obligations of the underwriter are subject to certain conditions precedent such as the receipt by the underwriter of officers' certificates and legal opinions and approval of certain legal matters by its counsel. The underwriting agreement provides that the underwriter will purchase all of the shares, other than those shares covered by the overallotment option described below, if any of them are purchased. We have agreed to indemnify the underwriter and certain of its controlling persons against certain liabilities, including liabilities under the Securities Act, and to contribute to payments that the underwriter may be required to make in respect of those liabilities.

The underwriter has advised us that it currently intends to make a market in our common stock. However, the underwriter is not obligated to do so and may discontinue any market-making activities at any time without notice. No assurance can be given as to the liquidity of the trading market for our common stock.

The underwriter is offering the shares of our common stock subject to its acceptance of the shares from us and subject to prior sale. The underwriter reserves the right to withdraw, cancel or modify offers to the public and to reject orders in whole or in part. In addition, the underwriter has advised us that it does not intend to confirm sales to any account over which it exercises discretionary authority.

Commission and Expenses

The underwriter has advised us that it proposes to offer the shares of our common stock 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 \$0.15 per share. After the offering, the public offering price, concession and reallowance to dealers may be reduced by the underwriter. No such reduction will change the amount of proceeds to be received by us as set forth on the cover page of this prospectus supplement.

The following table shows the public offering price, the underwriting discounts and commissions that we are to pay the underwriter and the proceeds, before expenses, to us in connection with this offering. Such amounts are shown assuming both no exercise and full exercise of the underwriter's option to purchase additional shares.