NEKTAR THERAPEUTICS
Form 10-K
February 27, 2014
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UNITED STATES

SECURITIES AND EXCHANGE COMMISSION

Washington, DC 20549

Form 10-K

x **ANNUAL REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934.**
For the fiscal year ended December 31, 2013

or

¨ **TRANSITION REPORTS PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934.**
For the transition period from to

Commission File Number: 0-24006

NEKTAR THERAPEUTICS

(Exact name of registrant as specified in its charter)

Delaware	**94-3134940**
(State or other jurisdiction of incorporation or organization)	**(IRS Employer Identification No.)**

455 Mission Bay Boulevard South

San Francisco, California 94158

(Address of principal executive offices and zip code)

415-482-5300

(Registrant s telephone number, including area code)

Securities registered pursuant to Section 12(b) of the Act:

Title of Each Class	**Name of Each Exchange on Which Registered**
Common Stock, $0.0001 par value	NASDAQ Global Select Market

Securities registered pursuant to Section 12(g) of the Act:

None

Indicate by check mark if the registrant is a well-known seasoned issuer, as defined in Rule 405 of the Securities Act. Yes x No ¨

Indicate by check mark if the registrant is not required to file reports pursuant to Section 13 or Section 15(d) of the Act. Yes ¨ No x

Indicate by check mark whether the registrant (1) has filed all reports required to be filed by Section 13 or 15(d) of the Securities Exchange Act of 1934 during the preceding 12 months (or for such shorter period that the registrant was required to file such reports), and (2) has been subject to such filing requirements for the past 90 days) Yes x No ¨

Indicate by check mark whether the registrant has submitted electronically and posted on its corporate Web site, if any, every Interactive Data File required to be submitted and posted pursuant to Rule 405 of Regulation S-T (§ 232.405 of this chapter) during the preceding 12 months (or for such shorter period that the registrant was required to submit and post such files). Yes x No ¨

Indicate by check mark if disclosure of delinquent filers pursuant to Item 405 of Regulation S-K (§ 229.405) is not contained herein, and will not be contained, to the best of registrant s knowledge, in definitive proxy or information statements incorporated by reference in Part III of this Form 10-K or any amendment to this Form 10-K. x

Indicate by check mark whether the registrant is a large accelerated filer, an accelerated filer, a non-accelerated filer, or a smaller reporting company. See the definitions of large accelerated filer, accelerated filer and smaller reporting company in Rule 12b-2 of the Exchange Act. (Check one):

Large accelerated filer x	Accelerated filer ¨
Non-accelerated filer ¨ (Do not check if a smaller reporting company)	Smaller reporting company ¨

Indicate by check mark whether the registrant is a shell company (as defined in Exchange Act Rule 12b-2) Yes ¨ No x

The approximate aggregate market value of voting stock held by non-affiliates of the registrant, based upon the last sale price of the registrant s common stock on the last business day of the registrant s most recently completed second fiscal quarter, June 28, 2013, as reported on the NASDAQ Global Select Market, was approximately $1,330,867,461. This calculation excludes approximately 456,759 shares held by directors and executive officers of the registrant. Exclusion of these shares does not constitute a determination that each such person is an affiliate of the registrant.

As of February 20, 2014, the number of outstanding shares of the registrant s common stock was 126,645,285.

DOCUMENTS INCORPORATED BY REFERENCE

Portions of registrant s definitive Proxy Statement to be filed for its 2014 Annual Meeting of Stockholders are incorporated by reference into Part III hereof. Such Proxy Statement will be filed with the Securities and Exchange Commission within 120 days of the end of the fiscal year covered by this Annual Report on Form 10-K.

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2013 ANNUAL REPORT ON FORM 10-K

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Forward-Looking Statements

This report includes forward-looking statements within the meaning of Section 27A of the Securities Act of 1933, as amended, and Section 21E of the Securities Exchange Act of 1934, as amended. All statements other than statements of historical fact are forward-looking statements for purposes of this annual report on Form 10-K, including any projections of earnings, revenue, milestone payments, royalties, sales or other financial items, any statements of the plans and objectives of management for future operations (including, but not limited to, preclinical development, clinical trials and manufacturing), any statements related to our financial condition and future working capital needs, any statements regarding potential future financing alternatives, any statements concerning proposed drug candidates, any statements regarding the timing for the start or end of clinical trials or submission of regulatory approval filings, any statements regarding future economic conditions or performance, any statements regarding the success of our collaboration arrangements or future payments that may come due to us under these arrangements, any statements regarding our plans and objectives to initiate or continue clinical trials, and any statements of assumptions underlying any of the foregoing. In some cases, forward-looking statements can be identified by the use of terminology such as may, will, expects, plans, anticipates, estimates, potential or continue, or the negative thereof or other comparable terminology. Although we believe the expectations reflected in the forward-looking statements contained herein are reasonable, such expectations or any of the forward-looking statements may prove to be incorrect and actual results could differ materially from those projected or assumed in the forward-looking statements. Our future financial condition and results of operations, as well as any forward-looking statements, are subject to inherent risks and uncertainties, including, but not limited to, the risk factors set forth in Part I, Item 1A Risk Factors below and for the reasons described elsewhere in this annual report on Form 10-K. All forward-looking statements and reasons why results may differ included in this report are made as of the date hereof and we do not intend to update any forward-looking statements except as required by law or applicable regulations. Except where the context otherwise requires, in this annual report on Form 10-K, the Company, Nektar, we, us, and our refer to Nektar Therapeutics, a Delaware corporation, and, where appropriate, its subsidiaries.

Trademarks

The Nektar brand and product names, including but not limited to Nektar®, contained in this document are trademarks, registered trademarks or service marks of Nektar Therapeutics in the United States and certain other countries. This document also contains references to trademarks and service marks of other companies that are the property of their respective owners.

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PART I

Item 1. ***Business***

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

Our most-advanced proprietary drug candidate, naloxegol (formerly known as NKTR-118), is an oral peripherally-acting opioid antagonist, for the treatment of opioid-induced constipation, or OIC, in patients with non-cancer pain, the most common side effect caused by chronic administration of prescription opioid pain medicines. Naloxegol has been specifically designed as a once-daily tablet to block the binding of opioids to the opioid receptors in the gastrointestinal tract while not crossing the blood brain barrier and impacting the analgesic activity of opioids binding to opioid receptors in the brain. In November 2013, we reported that our collaboration partner AstraZeneca PLC announced that the United States Food and Drug Administration, or FDA, accepted the New Drug Application, or NDA, for naloxegol, with a Prescription Drug User Fee Act, or PDUFA, date of September 16, 2014. The NDA filing was based on comprehensive data from a Phase 3 clinical development program comprised of four clinical trials designed to investigate the safety and efficacy of naloxegol for the treatment of OIC. AstraZeneca has also filed marketing applications for naloxegol with health authorities in the European Union (E.U.) and Canada. The FDA is currently planning to hold an advisory committee meeting to review the cardiovascular safety and potential additional safety study requirements for peripheral mu-opioid receptor antagonist class of drugs, including naloxegol. The FDA advisory committee meeting, which had been originally scheduled for March 10-11, 2014, is being rescheduled due to scheduling conflicts.

Our second-most-advanced drug candidate, etirinotecan pegol (also known as NKTR-102), is a next-generation topoisomerase I inhibitor, currently being evaluated in a Phase 3 clinical study as a single-agent therapy for women with metastatic breast cancer. This Phase 3 clinical study, which we call the BEACON study (BrEAst Cancer Outcomes with NKTR-102), was initiated by us in December 2011 and enrollment completed in July 2013. The BEACON study enrolled approximately 850 women with locally recurrent or metastatic breast cancer who have had prior treatment with anthracycline, taxane and capecitabine in either the adjuvant or metastatic setting. Patients in the BEACON study were randomized on a 1:1 basis to receive either single-agent etirinotecan pegol or a single agent of physician s choice. The primary endpoint of the BEACON study is overall survival, and secondary endpoints include progression-free survival and objective tumor response rate. On January 14, 2014, we announced that the Independent Data Monitoring Committee, or the DMC, created to provide safety oversight for the BEACON study recommended continuation of the Phase 3 BEACON study following an interim data analysis which was performed after reaching 50% of the events needed to achieve the primary endpoint of overall survival. In November 2012, the FDA designated etirinotecan pegol as a Fast Track development program for the treatment of patients with locally recurrent or metastatic breast cancer progressing after treatment with an anthracycline, a taxane, and capecitabine. We have also studied or provided support for ongoing studies being conducted for etirinotecan pegol in bevacizumab (Avastin)-resistant high-grade glioma, colorectal cancer, metastatic and recurrent non-small cell lung cancer, and ovarian cancer.

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Our third most advanced proprietary drug candidate, NKTR-181, is a novel mu-opioid analgesic drug candidate for chronic pain conditions. The molecule has been designed to have a slow rate of entry into the brain, which is expected to reduce the attractiveness of the molecule as a target of abuse and reduce other serious central nervous system-related side effects, such as sedation and respiratory depression, which are commonly associated with standard opioid therapies. Its potential differentiating properties are inherent to the design of the new molecule and, as a new molecular structure, NKTR-181 s abuse deterrent property does not rely on a formulation approach, a common method used with opioid drugs to reduce their ease of conversion into abusable forms of an opioid. In May 2012, the FDA designated NKTR-181 as a Fast Track development program for the treatment of moderate to severe chronic pain. In the first half of 2013, we conducted a human abuse liability study, or HAL study, for NKTR-181. On June 19, 2013, we announced results from that HAL study demonstrated that NKTR-181 was rated similar to placebo in drug liking and feeling high scores and had highly statistically significant lower drug liking scores and reduced feeling high scores as compared to oxycodone at all doses tested ($p < 0.0001$). On September 26, 2013, we announced preliminary topline results from a Phase 2 clinical study of NKTR-181 in patients with moderate to severe chronic pain from osteoarthritis of the knee. In this study, NKTR-181 performed as expected as an opioid analgesic throughout the study. However, patients who were randomized to the placebo arm following a drug titration phase did not show the expected increase in pain scores observed in similar enriched enrollment, randomized withdrawal studies. This lack of a placebo rebound in the maintenance phase of the trial caused the Phase 2 study to miss the primary endpoint, which was the average change in a patient s pain score from baseline to the end of the double-blind, randomized treatment period. In December 2013, we met with the FDA to discuss the results of the Phase 2 clinical study and certain preliminary considerations for the Phase 3 clinical study design. We are currently evaluating the appropriate Phase 3 clinical study design for NKTR-181 and expect to start a Phase 3 clinical study in mid-2014, following the completion of an end-of-Phase 2 meeting with the FDA planned to occur in the first half of 2014.

We also have additional proprietary preclinical and clinical drug candidates being developed for pain relief. On January 14, 2014, we announced that the first subjects were dosed in a Phase 1 clinical study for NKTR-171, a new sodium channel blocker being developed as an oral therapy for the treatment of peripheral neuropathic pain. This single-ascending dose Phase 1 clinical study of NKTR-171 will assess its pharmacokinetics, tolerability, and safety in up to 75 healthy subjects. NKTR-171 is a new molecular entity that is specifically designed to treat neuropathic pain by blocking hyperactive neuronal sodium channels associated with damaged nerves in the peripheral nervous system. NKTR-171 is designed to be a peripherally-restricted molecule, with the aim of not causing central nervous system (CNS) side effects that limit usage of existing therapies. In addition, we are also developing NKTR-192, a novel mu-opioid analgesic molecule with a short-acting profile designed to treat acute pain while addressing the serious CNS-related side effects associated with standard short-acting opioid therapies. In January 2014, we announced that we observed elevated liver enzymes in some patients at the highest dose in a Phase 1 clinical study for NKTR-192. As a result, NKTR-192 will no longer be developed as an oral formulation and has returned to preclinical development where we are exploring its potential as an injectable therapy to treat migraine and acute cancer pain. In addition, we are also advancing other acute pain drug candidates in preclinical development.

We have a significant collaboration with Baxter Healthcare (Baxter), to identify and develop PEGylated drug candidates with the objective of providing new long-acting therapies for hemophilia patients. Under the terms of this collaboration, we are providing our PEGylation technology and expertise and Baxter is responsible for all clinical development. The first drug candidate in this collaboration, BAX 855, is a longer-acting (PEGylated) form of a full-length recombinant factor VIII (rFVIII) protein which has completed Phase 1 clinical development in patients with hemophilia A. In February 2013, Baxter initiated a Phase 3 multi-center, open-label clinical study called PROLONG-ATE in previously treated adult patients with severe hemophilia A to assess the efficacy, safety and pharmacokinetics of BAX 855 for prophylaxis and on-demand treatment of bleeding. On November 13, 2013, Baxter announced that it had completed enrollment of 146 patients in the PROLONG-ATE clinical study.

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We also have a significant collaboration with Bayer Healthcare LLC (Bayer), to develop BAY41-6551 (Amikacin Inhale, formerly known as NKTR-061), which is an inhaled solution of amikacin, an aminoglycoside antibiotic. We originally developed the liquid aerosol inhalation platform and the NKTR-061 drug candidate and entered into a collaboration agreement with Bayer in August 2007 to further advance the drug candidate s development and potential commercialization. Bayer is currently enrolling patients in a Phase 3 clinical study for Amikacin Inhale that commenced in April 2013. Bayer is conducting this study under a Special Protocol Assessment process that was agreed to with the FDA in 2011.

We also have a number of license, manufacturing and supply agreements with leading biotechnology and pharmaceutical companies, including Amgen Inc., MAP Pharmaceuticals, Inc., Merck & Co., Inc., Ophthotech Corporation, Pfizer, Inc., F. Hoffmann-La Roche Ltd (Roche), Regado Biosciences, Inc., and UCB Pharma. A total of eight products using our PEGylation technology have received regulatory approval in the U.S. or E.U. There are also a number of other products in clinical development that incorporate our advanced PEGylation and advanced polymer conjugate technologies.

On December 31, 2008, we completed the sale and transfer of certain pulmonary technology rights, certain pulmonary collaboration agreements and approximately 140 dedicated pulmonary personnel and operations to Novartis Pharma AG. We retained all of our rights to Amikacin Inhale and our right to receive royalties on net sales of the Cipro DPI (Cipro Dry Powder Inhaler, previously called Cipro Inhale) program with Bayer Schering Pharma AG that we transferred to Novartis as part of the transaction. In August 2012, Bayer initiated a global Phase 3 program called RESPIRE for the Cipro DPI product candidate in patients with non-cystic fibrosis bronchiectasis. The two placebo-controlled trials, RESPIRE-1 and RESPIRE-2, are enrolling up to 600 patients and will evaluate Cipro DPI as a chronic, intermittent therapy over a period of 48 weeks.

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 Annual Report.

Our Technology Platform

As a leader in the PEGylation field, we have advanced our technology platform to include new advanced polymer conjugate chemistries and polymer technologies that can be tailored in specific and customized ways with the objective of optimizing and significantly improving the profile of a wide range of molecules including many classes of drugs targeting numerous disease areas. PEGylation has been a highly effective technology platform for the development of therapeutics with significant commercial success, such as Amgen s Neulasta® (pegfilgrastim) and Roche s PEGASYS® (PEG-interferon alfa-2a). Nearly all of the PEGylated drugs approved over the last fifteen years were enabled with our PEGylation technology through our collaborations and licensing partnerships with a number of well-known biotechnology and pharmaceutical companies. PEGylation is a versatile technology as a result of polyethylene glycol (PEG) being a water soluble, amphiphilic, non-toxic, non-immunogenic compound that has been shown to safely clear from the body. Its primary use to date has been in currently approved biologic drugs to favorably alter their pharmacokinetic or pharmacodynamic properties. However, in spite of its widespread success in commercial drugs, there are some limitations with the first-generation PEGylation approaches that have been used with biologics. These techniques cannot be used successfully to create small molecule drugs which could potentially benefit from the application of the technology. Other limitations of the early applications of PEGylation technology include sub-optimal bioavailability and bioactivity, and its limited ability to be used to fine-tune properties of the drug, as well as its inability to be used to create oral drugs.

With our expertise and proprietary technology in PEGylation, we have created the next generation of PEGylation technology. Our advanced polymer conjugate technology platform is designed to overcome the

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limitations of the first generation of the technology platform and to allow the platform to be utilized with a broader range of molecules across many therapeutic areas. We have also developed robust manufacturing processes for generating second generation PEGylation reagents that allow us to utilize the full potential of these newer approaches.

Both our PEGylation and advanced polymer conjugate technology platforms have the potential to offer one or more of the following benefits:

- improve efficacy or safety of a drug as a result of better pharmacokinetics, pharmacodynamics, longer half-life and sustained exposure of the drug;
- improve targeting or binding affinity of a drug to its target receptors with the potential to improve efficacy and reduce toxicity or drug resistance;
- improve solubility of a drug;
- enable oral administration of parenterally-administered drugs, or drugs that must be administered intravenously or subcutaneously, and increase oral bioavailability of small molecules;
- prevent drugs from crossing the blood-brain barrier, or reduce their rate of passage into the brain, thereby limiting undesirable central nervous system effects;
- reduce first-pass metabolism effects of certain drug classes with the potential to improve efficacy, which could reduce the need for other medicines and reduce toxicity;
- reduce the rates of drug absorption and of elimination or metabolism by improving stability of the drug in the body and providing it with more time to act on its target;
- differentially alter binding affinity of a drug for multiple receptors, improving its selectivity for one receptor over another; and
- reduce immune response to certain macromolecules with the potential to prolong their effectiveness with repeated doses.

We have a broad range of approaches that we may use when designing our own drug candidates, some of which are further described below.

Small Molecule Stable Polymer Conjugates

Our customized approach for small molecule polymer conjugates allows for the fine-tuning of the physicochemical and pharmacological properties of small molecule oral drugs to potentially increase their therapeutic benefit. In addition, this approach can enable oral administration of subcutaneously or intravenously delivered small molecule drugs that have low bioavailability when delivered orally. The benefits of this approach can also include: improved potency, modified biodistribution with enhanced pharmacodynamics, and reduced transport across specific membrane barriers in the body, such as the blood-brain barrier. Two primary examples of reducing transport across the blood-brain barrier are naloxegol, an orally-available peripherally-acting opioid antagonist that AstraZeneca has filed applications for marketing authorizations, and NKTR-171, a novel peripherally-acting sodium channel blocker that is currently in a Phase 1 clinical study for the treatment of neuropathic pain. An additional example of the application of membrane transport, specifically slowing transport across the blood-brain barrier is NKTR-181, an

orally-available mu-opioid analgesic molecule that we plan to initiate Phase 3 clinical studies starting in mid-2014, following the completion of an end-of-Phase 2 meeting with the FDA in the first half of 2014.

Small Molecule Pro-Drug Releasable Polymer Conjugates

The pro-drug polymer conjugation approach can be used to optimize the pharmacokinetics and pharmacodynamics of a small molecule drug to substantially increase its efficacy and improve its side effect profile. We are currently using this platform with oncolytics, which typically have sub-optimal half-lives that can

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limit their therapeutic efficacy. With our releasable polymer conjugate technology platform, we believe that these drugs can be modulated for programmed release within the body, optimized bioactivity and increased sustained exposure of active drug to tumor cells in the body. We are using this approach with our lead oncolytic drug candidate, etirinotecan pegol, a next-generation topoisomerase I-inhibitor currently in the Phase 3 BEACON clinical study for treatment of metastatic breast cancer.

Large Molecule Polymer Conjugates (Proteins and Peptides)

Our customized approaches with large molecule polymer conjugates have enabled numerous successful PEGylated biologics on the market today. Based on our knowledge of the technology and biologics, our scientists have designed novel hydrolyzable linkers that in many cases can be used to optimize bioactivity. Through rational drug design, a protein or peptide s pharmacokinetics and pharmacodynamics can be substantially improved and its half-life can be significantly extended. An example of this is BAX 855, a longer-acting (PEGylated) form of a full-length recombinant factor VIII (rFVIII) protein, which is currently being evaluated in Phase 3 clinical development in collaboration with Baxter for the treatment of hemophilia A.

Antibody Fragment Polymer Conjugates

This approach uses a large molecular weight PEG conjugated to antibody fragments in order to potentially improve their toxicity profile, extend their half-life and allow for ease of synthesis with the antibody. The specially designed PEG replaces the function of the fragment crystallizable (Fc) domain of full length antibodies with a branched architecture PEG with either stable or degradable linkage. This approach can be used to reduce antigenicity, reduce glomerular filtration rate, enhance uptake by inflamed tissues, and retain antigen-binding affinity and recognition. There is currently one approved product on the market that utilizes our technology with an antibody fragment, CIMZIA® (certoluzimab pegol), which was developed by our partner UCB Pharma and is approved for the treatment of Crohn s Disease, psoriatic arthritis and ankylosing spondylitis in the U.S. and rheumatoid arthritis in the U.S. and E.U.

Our Strategy

The key elements of our business strategy are described below:

Advance Our Proprietary Clinical Pipeline of Drug Candidates that Leverage Our PEGylation and Advanced Polymer Conjugate Platform

Our objective is to create value by advancing our lead drug candidates through various stages of clinical development. To support this strategy, we have significantly expanded and added expertise to our internal preclinical, clinical development and regulatory departments. A key component of our development strategy is to potentially reduce the risks and time associated with drug development by capitalizing on the known safety and efficacy of approved drugs as well as established pharmacologic targets and drugs directed to those targets. For many of our novel drug candidates, we may seek to study the drug candidates in indications for which the parent drugs have not been studied or approved. We believe that the improved characteristics of our drug candidates will provide meaningful benefit to patients compared to the existing therapies. In addition, in certain instances we have the opportunity to develop new treatments for patients for which the parent drugs are not currently approved.

Ensure Future Growth of our Proprietary Pipeline through Internal Research Efforts and Advancement of our Preclinical Drug Candidates into Clinical Trials

We believe it is important to maintain a diverse pipeline of new drug candidates to continue to build on the value of our business. Our discovery research organization is continuing to identify new drug candidates by applying our technology platform to a wide range of molecule classes, including small molecules and large proteins, peptides and antibodies, across multiple therapeutic areas. We continue to advance our most promising research drug candidates into preclinical development with the objective of advancing these early stage research programs to human clinical studies over the next several years.

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Enter into Strategic and High-Value Partnerships to Bring Certain of Our Drug Candidates to Market

We decide on a drug candidate-by-drug candidate basis how far to advance clinical development (e.g. Phase 1, 2 or 3) and whether to commercialize products on our own, or seek a partner, or pursue a combination of these approaches. For example, in December 2010, we decided that we would move etirinotecan pegol (also known as NKTR-102) into Phase 3 clinical development in metastatic breast cancer prior to completing a collaboration partnership for this drug candidate. When we determine to seek a partner, our strategy is to enter into collaborations with leading pharmaceutical and biotechnology companies to fund further clinical development, manage the global regulatory filing process, and market and sell drugs in one or more geographies. The options for future collaboration arrangements range from comprehensive licensing and commercialization arrangements to co-promotion and co-development agreements with the structure of the collaboration depending on factors such as the structure of economic risk sharing, the cost and complexity of development, marketing and commercialization needs, therapeutic area and geographic capabilities.

Continue to Build a Leading Intellectual Property Estate in the Field of PEGylation and Polymer Conjugate Chemistry across Therapeutic Modalities

We are committed to continuing to build on our intellectual property position in the field of PEGylation and polymer conjugate chemistry. To that end, we have a comprehensive patent strategy with the objective of developing a patent estate covering a wide range of novel inventions including among others, polymer materials, conjugates, formulations, synthesis, therapeutic areas, methods of treatment and methods of manufacture.

Nektar Proprietary Drug Candidates in Clinical Development

The following table summarizes our proprietary drug candidates that are being developed by us or in collaboration with other pharmaceutical companies or independent investigators. The table includes the type of molecule or drug, the target indications for the drug candidate, and the status of the clinical development program.

Drug Candidate	Target Indication	Status(1)
Naloxegol (orally available peripherally-acting mu-opioid receptor antagonist)	Opioid-induced constipation	Filed in U.S., E.U., and Canada (Partnered with AstraZeneca AB)
Etirinotecan pegol (next-generation topoisomerase I inhibitor)	Locally recurrent or metastatic breast cancer	Phase 3
BAY41-6551 (Amikacin Inhale, formerly NKTR-061)	Gram-negative pneumonias	Phase 3 (Partnered with Bayer Healthcare LLC)*
NKTR-181 (orally-available mu-opioid analgesic molecule)	Moderate to severe chronic pain	Completed Phase 2
Etirinotecan pegol	Platinum-resistant/refractory ovarian cancer	Completed Phase 2
Etirinotecan pegol	Non-small cell lung cancer	ISS Phase 2
Etirinotecan pegol	Bevacizumab-resistant high-grade glioma	ISS Phase 2
Etirinotecan pegol	Small cell lung cancer	ISS Phase 2
Etirinotecan pegol	Second-line metastatic colorectal cancer in patients with the KRAS gene mutation	Phase 2

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Drug Candidate	Target Indication	Status(1)
Etirinotecan pegol (in combination with 5-Fluorouracil/leucovorin)	Gastrointestinal-related solid tumors	Completed Phase 1
NKTR-171 (orally-available peripherally-acting sodium channel blocker)	Neuropathic pain	Phase 1
Naloxegol fixed-dose combinations (opioid/NKTR-118 combinations)	Chronic pain without constipation	Research/Preclinical (Partnered with AstraZeneca AB)
NKTR-192 (mu-opioid analgesic molecule)	Migraine and acute cancer pain	Research/Preclinical
NKTR-214 (cytokine immunostimulatory therapy)	Oncology	Research/Preclinical

(1) Status definitions are:
Filed an application for approval and marketing has been filed with the applicable government health authority.

Phase 3 or Pivotal product in large-scale clinical trials conducted to obtain regulatory approval to market and sell the drug (these trials are typically initiated following encouraging Phase 2 trial results).

Phase 2 a drug candidate in clinical trials to establish dosing and efficacy in patients.

Phase 1 a drug candidate in clinical trials, typically in healthy subjects, to test safety.

Research/Preclinical a drug candidate is being studied in research by way of in vitro studies and/or animal studies

ISS Investigator sponsored study for which the Company is providing support.

* This drug candidate uses, in part, a liquid aerosol technology platform that was transferred to Novartis by us in the pulmonary asset sale transaction that was completed on December 31, 2008. As part of that transaction, we retained an exclusive license to this technology for the development and commercialization of this drug candidate originally developed by us.

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Approved Drugs and Drug Candidates Enabled By Our Technology through Licensing Collaborations

The following table outlines our collaborations with a number of pharmaceutical companies that license our intellectual property and, in some cases, purchase our proprietary PEGylation materials for their drug products. A total of eight products using our PEGylation technology have received regulatory approval in the U.S. or Europe. There are also a number of other candidates that have been filed for approval or are in various stages of clinical development. These collaborations generally contain one or more elements including a license to our intellectual property rights and manufacturing and supply agreements under which we may receive manufacturing revenue, milestone payments, and/or royalties on commercial sales of drug products.

Drug	Primary or Target Indications	Drug Marketer/Partner	Status(1)
Neulasta® (pegfilgrastim)	Neutropenia	Amgen Inc.	Approved
PEGASYS® (peginterferon alfa-2a)	Hepatitis-C	F. Hoffmann-La Roche Ltd	Approved
Somavert® (pegvisomant)	Acromegaly	Pfizer Inc.	Approved
PEG-INTRON® (peginterferon alfa-2b)	Hepatitis-C	Merck (through its acquisition of Schering-Plough Corporation)	Approved
Macugen® (pegaptanib sodium injection)	Age-related macular degeneration	Valeant Pharmaceuticals International, Inc.	Approved
CIMZIA® (certolizumab pegol)	Rheumatoid arthritis	UCB Pharma	Approved*
CIMZIA® (certolizumab pegol)	Crohn s disease	UCB Pharma	Approved*
CIMZIA® (certoluzimab pegol)	Psoriasis/Ankylosing Spondylitis	UCB Pharma	Approved*
MIRCERA® (C.E.R.A.) (Continuous Erythropoietin Receptor Activator)	Anemia associated with chronic kidney disease in patients on dialysis and patients not on dialysis	F. Hoffmann-La Roche Ltd	Approved**
OMONTYS® (peginesatide)	Anemia associated with chronic kidney disease (CKD) in adult patients on dialysis	Affymax, Inc.	Approved (currently withdrawn from market)
LEVADEX®	Migraine	Allergan, Inc.	Filed for approval in U.S.
BAX 855 (PEGylated rFVIII)	Hemophilia A	Baxter Healthcare	Phase 3
FOVISTA	Neovascular age-related macular degeneration	Ophthotech Corporation	Phase 3
Cipro Dry Powder Inhaler (Cipro DPI)	Cystic fibrosis lung infections	Bayer Schering Pharma AG	Phase 3***
REG1 Anticoagulation System	Acute coronary syndrome	Regado Biosciences, Inc.	Phase 3
Longer-acting blood clotting proteins	Hemophilia	Baxter Healthcare	Research/Preclinical

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(1) Status definitions are:
Approved regulatory approval to market and sell product obtained in one or more of the U.S., E.U. or other countries.

Filed an application for approval and marketing has been filed with the applicable government health authority.

Phase 3 or Pivotal product in large-scale clinical trials conducted to obtain regulatory approval to market and sell the drug (these trials are typically initiated following encouraging Phase 2 trial results).

Research/Preclinical a drug candidate is being studied in research by way of in vitro studies and/or animal studies

* In February 2012, we sold our rights to receive royalties on future worldwide net sales of CIMZIA® effective as of January 1, 2012.
** Amgen Inc. prevailed in a patent lawsuit against F. Hoffmann-La Roche Ltd (Roche) and as a result of this legal ruling Roche is currently prevented from marketing MIRCERA® in the U.S. until July 2014. In February 2012, we sold our rights to receive royalties on future worldwide net sales of MIRCERA® effective as of January 1, 2012 until the agreement with Roche is terminated or expires.
*** This drug candidate was developed using our proprietary pulmonary delivery technology that was transferred by us to Novartis in an asset sale transaction that closed on December 31, 2008. As part of the transaction, Novartis assumed our rights and obligations for Cipro DPI (formerly known as Cipro Inhale) under our agreements with Bayer Schering Pharma AG; however, we maintained the rights to receive royalties on commercial sales of Cipro DPI if the drug candidate is approved.

With respect to all of our collaboration and license agreements with third parties, please refer to Item 1A, Risk Factors, including without limitation, 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 liability that could adversely affect our business, results of operations and financial condition.

Overview of Selected Nektar Proprietary Drug Development Programs and Significant Partnered Drug Development Programs

Naloxegol and Naloxegol Fixed-Dose Combination Products (formerly NKTR-118 and NKTR-119), License Agreement with AstraZeneca AB

In September 2009, we entered into a global license agreement with AstraZeneca AB (AstraZeneca) pursuant to which we granted AstraZeneca a worldwide, exclusive, perpetual, royalty-bearing license under our patents and other intellectual property to develop, market and sell naloxegol and naloxegol fixed-dose combination products. Naloxegol is an orally-available peripherally-acting mu-opioid antagonist being investigated for the treatment of opioid-induced constipation (OIC) which is a common side effect of prescription opioid medications. Opioids attach to specific proteins called opioid receptors. When the opioids attach to certain opioid receptors in the gastrointestinal tract, constipation may occur. OIC is a result of decreased fluid absorption and lower gastrointestinal motility due to opioid receptor binding in the gastrointestinal tract. Globally, approximately 40 50% (28-35 million) of patients taking opioids for long-term pain develop constipation. It is estimated that approximately 40 50% (11-18 million) of those OIC sufferers achieve the desired treatment outcomes with current options that include over-the-counter and prescription laxatives.

AstraZeneca has completed a Phase 3 clinical development program for naloxegol, which AstraZeneca calls the KODIAC studies. The KODIAC studies (KODIAC-04, KODIAC-05, KODIAC-07 and KODIAC-08) evaluated the efficacy and safety of naloxegol for treating OIC in patients with non-cancer pain. KODIAC-04 and KODIAC-05 were replicate, multicenter- randomized, double-blind, placebo-controlled pivotal trials of 12 weeks duration that evaluated 12.5 mg and 25 mg naloxegol administered once-daily. The primary endpoint in both trials was percentage of OIC responders versus placebo over 12 weeks of treatment. The studies enrolled approximately 630 patients each. KODIAC-07 was a three-month safety extension of KODIAC-04. All three studies were conducted in patients with non-cancer pain and documented OIC, who required daily opioid therapy.

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On November 12, 2012, AstraZeneca reported top-line efficacy and safety results from KODIAC-04, -05 and -07. For both KODIAC-04 and -05, the 25 mg dose of naloxegol demonstrated statistically significant results for the primary endpoint. In KODIAC-04, the 12.5 mg dose of naloxegol demonstrated statistically significant results for the primary endpoint and in KODIAC-05 the 12.5 mg dose did not meet statistical significance for the primary endpoint. The safety analyses also showed no clinically relevant imbalances in serious adverse events (SAEs), including externally adjudicated major cardiovascular events, across the three treatment arms in KODIAC-04, -05 and -07. The most common adverse events (AEs) in the naloxegol treatment arms in both trials were abdominal pain, diarrhea and nausea. In KODIAC-07, the safety extension of KODIAC-04, the occurrence of AEs and SAEs was lower than in KODIAC-04 and -05. All other common AEs were distributed similarly across the three treatment arms. In KODIAC-04 and -05 for either naloxegol dose, compared to placebo, there were no significant differences in change from baseline in mean daily pain scores or mean total daily opioid dose.

KODIAC-08 was an open-label, randomized, 52-week, long-term safety trial of naloxegol versus usual care (UC) in patients with non-cancer related pain and OIC. This trial was designed to evaluate the long-term safety and adverse event profile of naloxegol in patients taking 25 mg of naloxegol once daily, as compared to UC. In the trial, a total of 534 patients received naloxegol once daily for up to 52 weeks, while 270 patients received UC for OIC during the same treatment period. UC was defined as the investigator s choice of an existing laxative treatment regimen for OIC. On February 26, 2013, AstraZeneca announced positive top-line results from KODIAC-08. The trial reported no imbalances in SAEs. In addition, there were a low number of major adverse cardiovascular events, as adjudicated by an independent external committee, and there was no imbalance of these events across naloxegol and UC arms. There were no increases from baseline levels in mean daily pain scores or mean total daily opioid dose in either the naloxegol or the UC arm. Additionally, there were no reports of opioid withdrawal AEs which could be attributed to naloxegol. The most commonly reported AEs occurring more frequently on naloxegol than on UC included abdominal pain, diarrhea, nausea and headache.

AstraZeneca submitted an NDA filing in the U.S. on September 25, 2013 and a Marketing Authorization Application (MAA) filing in the E.U. in August 2013. The PDUFA date for the naloxegol NDA in the US is September 16, 2014. The FDA is currently planning to hold an advisory committee meeting to discuss the cardiovascular safety and potential additional safety study requirements for the peripheral mu-opioid receptor antagonist class of drugs, including naloxegol. The advisory committee meeting, which had been originally scheduled for March 10-11, 2014, is being rescheduled due to scheduling conflicts. Naloxegol is currently considered a Schedule II controlled substance by the U.S. Drug Enforcement Administration (DEA) based on structural relatedness to noroxymorphone. AstraZeneca has conducted the studies necessary to evaluate the abuse potential and dependence-producing properties of naloxegol in support of obtaining decontrol. A petition for the decontrol of naloxegol was submitted to the DEA in March 2012 and subsequently accepted for review. Commercialization and launch in the U.S. will be subject to both FDA approval and DEA schedule determination. Please refer to Item 1A, Risk Factors, including without limitation, If we or our partners do not obtain regulatory approval for our drug 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.

Under the terms of our license agreement, AstraZeneca made an initial license payment to us of $125.0 million and AstraZeneca has responsibility for all activities and bears all costs associated with research, development and commercialization for naloxegol and naloxegol fixed-dose combination products. For naloxegol, we have received $70.0 million and $25.0 million upon the acceptance for review of naloxegol regulatory approval applications filed by AstraZeneca with the FDA and European Medicines Agency (EMA), respectively, in 2013 and are also entitled to up to an additional $175.0 million upon certain regulatory approval and commercial launch milestones, and $375.0 million in sales milestones if the product achieves certain annual commercial sales levels.

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If the FDA does not require a future clinical trial or other significant studies to assess the cardiovascular safety (CV Safety Study) of naloxegol prior to an approval decision, AstraZeneca is required to pay us a $35.0 million milestone. If the FDA does require a CV Safety Study, AstraZeneca may terminate the license agreement with us in its entirety or only with respect to its rights in the United States. If AstraZeneca elects to terminate the license agreement in its entirety due to a CV Safety Study, we would be required to repay them the $70.0 million payment noted above plus accrued interest at 4.5% compounded annually in four installments in accordance with the following payment schedule: $10.0 million plus accrued interest on January 15, 2015, $10.0 million plus accrued interest on January 15, 2016, $20.0 million plus accrued interest on January 15, 2017 and $30.0 million plus accrued interest on January 15, 2018. If AstraZeneca elects to terminate the license agreement only with respect to its rights in the U.S., then such repayment amount would be funded through a 50% reduction of non-U.S. royalty amounts otherwise payable to us until the aggregate amount of such royalty reduction equals the total principal amount of $70.0 million plus accumulated interest at 4.5% compounded annually. If the FDA requires a post-approval cardiovascular safety study as a condition to approval of the naloxegol NDA, then the royalty rate payable to us from net sales of naloxegol in the U.S. by AstraZeneca would be reduced by two percentage points until the aggregate accumulated amount of such royalty payment reduction is equal to a maximum of $35.0 million.

The remaining $140.0 million of milestone payments are due upon the commercial launches of naloxegol in the U.S. and in the E.U. For the naloxegol fixed-dose combination products, we are also eligible to receive significant development milestones as well as significant sales milestone payments if the program achieves certain annual commercial sales levels. For both naloxegol and the fixed-dose combination products, we are also entitled to significant double-digit royalty payments, varying by country of sale and level of annual net sales. Our right to receive royalties (subject to certain adjustments) in any particular country will expire upon the later of (a) a specified period of time after the first commercial sale of the product in that country or (b) the expiration of patent rights in that particular country. AstraZeneca has agreed to use commercially reasonable efforts to develop one naloxegol fixed-dose combination product and has the right to develop multiple products which combine naloxegol with other opioids.

Etirinotecan pegol (NKTR-102, next generation, long-acting topoisomerase I inhibitor)

We are developing etirinotecan pegol (also known as NKTR-102), a next generation topoisomerase I (topo I) inhibitor which was designed using our PEGylation technology. Etirinotecan pegol is a novel macromolecular chemotherapeutic designed to enhance the anti-cancer effects of topo I inhibition while minimizing its toxicities. Unlike irinotecan, which is a first generation topo I inhibitor that exhibits a high initial peak concentration and short half-life, etirinotecan pegol s pro-drug design results in a lower initial peak concentration of active topo I inhibitor in the blood. The large etirinotecan pegol molecule is inactive when administered. Over time, the body s natural enzymatic processes slowly metabolize the linkers within the molecule, continuously freeing active drug that then can work to stop tumor cell division through topo I inhibition. In preclinical models, etirinotecan pegol achieved a 300-fold increase in tumor concentration as compared to irinotecan. Because etirinotecan pegol is a large molecule, based on preclinical studies we believe that it may penetrate the leaky vasculature within the tumor environment more readily than normal vasculature, concentrating and trapping etirinotecan pegol in tumor tissue. Clinical studies have shown that etirinotecan pegol has an extended pharmacokinetic profile and remains in circulation throughout the entire chemotherapy cycle, providing sustained exposure to topo I inhibition.

Etirinotecan pegol is currently being evaluated as a single-agent therapy (145 mg/m2 every 21 days) in a Phase 3 open-label, randomized, multicenter clinical study in patients with metastatic breast cancer. This Phase 3 clinical study, which we call the BEACON study (BrEAst Cancer Outcomes with NKTR-102), was initiated in December 2011. The BEACON study enrolled approximately 850 patients with metastatic breast cancer who have had prior treatment with anthracycline, taxane and capecitabine in either the adjuvant or metastatic setting. We completed enrollment in the BEACON study in late July 2013. This study randomized patients on a 1:1 basis to receive single-agent etirinotecan pegol or a single agent chosen from a defined set of physician s choice

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alternatives. The physician s choice single agents include the following: ixabepilone, vinorelbine, gemcitabine, eribulin, or a taxane. Randomization was stratified by geographic region, prior treatment with eribulin and whether or not the patient has triple negative breast cancer. The primary endpoint of the BEACON study is overall survival, and secondary endpoints include progression-free survival and objective tumor response rate. Secondary endpoints and objectives also include clinical benefit rate, duration of response, pharmacokinetic data, safety profiles, quality-of-life measurements, and pharmacoeconomic implications. Exploratory objectives of the study include collecting specific biomarker data to correlate with objective tumor response rate, progression-free survival, overall survival and selected toxicities. In November 2012, the FDA designated etirinotecan pegol as a Fast Track development program for the treatment of patients with locally recurrent or metastatic breast cancer progressing after treatment with an anthracycline, a taxane, and capecitabine. On January 14, 2014, we announced that the Independent Data Monitoring Committee, or the DMC, created to provide safety oversight for the BEACON study recommended continuation of the Phase 3 BEACON study following an interim data analysis which was performed after reaching 50% of the events needed to achieve the primary endpoint of overall survival.

According to the American Cancer Society and World Health Organization, more than 1.4 million women worldwide are diagnosed with breast cancer globally every year. The chance of developing invasive breast cancer at some time in a woman s life is a little less than one in eight (12%). In 2014, the American Cancer Society estimates there will be 235,030 new cases of breast cancer in the United States. Metastatic breast cancer refers to cancer that has spread from the breast to distant sites in the body. Anthracyclines and taxanes are the among the most active and widely used chemotherapeutic agents for breast cancer, but the increased use of these agents at an early stage of disease often renders tumors resistant to these drugs by the time the disease recurs, thereby reducing the number of treatment options for metastatic disease. There are currently no FDA-approved topoisomerase I inhibitors to treat breast cancer.

Etirinotecan pegol has also completed a Phase 2 clinical study in approximately 170 patients with platinum-resistant/refractory ovarian cancer. The Phase 2 clinical study included two phases. The first phase was an open-label, randomized, study evaluating two treatment schedules of single-agent etirinotecan pegol (145 mg/m2 every 14 days or every 21 days). Each schedule originally followed a two-stage Simon design and a total of 71 patients were initially included in the study that was completed in the first half of 2010. The second phase was an expansion of patients in the every 21 day dosing schedule in women with platinum-resistant/refractory ovarian cancer who had previously received Doxil therapy. In September 2013, the FDA advised us that a Phase 3 clinical study would be required in order to support an NDA filing for etirinotecan pegol in ovarian cancer; however the FDA also indicated that a positive interim over-all survival analysis in a Phase 3 clinical study could potentially support an accelerated NDA filing prior to completing a Phase 3 clinical study. In December 2013, we also received scientific advice and protocol assistance from the EMA indicating that a Phase 3 clinical study would be required to support a marketing application for etirinotecan pegol in ovarian cancer. The EMA also indicated that a positive interim over-all survival analysis in a Phase 3 clinical study could potentially support a conditional approval of etirinotecan pegol for ovarian cancer. We do not plan to make a decision on future development for etirinotecan pegol in ovarian cancer until we review the top-line data from the BEACON study.

Ovarian cancer is a significant health problem for women worldwide. According to the American Cancer Society, in 2014, there will be an estimated 21,980 new cases of ovarian cancer diagnosed and an estimated 14,270 deaths from ovarian cancer in the United States. Ovarian cancer is the ninth most common cancer among women, excluding non-melanoma skin cancers. It ranks fifth in cancer deaths among women, accounting for more deaths than any other cancer of the female reproductive system. Historically, less than 40% of women with ovarian cancer are cured. According to the World Health Organization, about 230,000 women globally are diagnosed each year with ovarian cancer.

An etirinotecan pegol Phase 2 clinical study was initiated in June 2008 to evaluate the efficacy and safety of etirinotecan pegol monotherapy versus irinotecan in second-line metastatic colorectal cancer patients with the KRAS mutant gene. The Phase 2 clinical study was designed to enroll 174 patients with metastatic colorectal

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cancer. In February 2014, we decided to close enrollment in this study after 80 patients were randomized due to challenges in recruiting new patients because the comparator arm of this study, single-agent irinotecan, is not the common standard of care for second line metastatic colorectal therapy in the U.S. or E.U. Based on preliminary data we have collected to date from this study, etirinotecan pegol resulted in numerically improved overall survival, progression-free survival, objective response rate, and duration of response compared to that observed in the irinotecan comparator arm. However, due to the low number of patients enrolled in this study, we do not expect the results from this study to be statistically significant. Further, there are currently patients continuing in the study either on drug or in follow-up. Therefore, the data may change based on future additional data as well as verification and audit procedures that will be performed on the final completed study data. Following the conclusion of the study and completion of data verification and audit procedures, we currently plan to publish the results from this study at a scientific meeting.

We also conducted a Phase 1 dose-escalation clinical study which enrolled 26 patients to evaluate etirinotecan pegol in combination with 5-Fluorouracil (5-FU)/leucovorin in refractory solid tumor cancers. The chemotherapy agent 5-FU is currently used as a part of a combination treatment regimen for colorectal cancer in combination with irinotecan, which is also known as the FOLFIRI regimen. On January 18, 2014, we presented data from this study at the 2014 Gastrointestinal Cancers Symposium in San Francisco, California. Results from this Phase 1 clinical study include establishing a dose of 75 mg/m2 of etirinotecan pegol in combination with a standard dose of 5-FU/leucovorin and demonstrating clinical activity of etirinotecan pegol in combination with a standard dose of 5-FU/leucovorin clinical activity.

Colorectal cancer is the third most commonly diagnosed cancer and the third leading cause of cancer death in the U.S. According to the American Cancer Society, nearly 137,000 new cases of colon and rectal cancer will be diagnosed in the U.S. in 2014, and about 51,000 people will die annually of the disease. Worldwide, over 1.2 million people are diagnosed annually with colorectal cancer and, according to the World Health Organization, there are 690,000 deaths annually from colorectal cancers. Most metastatic colorectal cancer patients have recurrence within two years and require retreatment with chemotherapy regimens.

In addition to the clinical studies being conducted by us, there are also three investigator-initiated Phase 2 studies being conducted for etirinotecan pegol. On August 7, 2012, we announced a Phase 2 investigator-initiated clinical study of etirinotecan pegol in patients with bevacizumab (Avastin)-resistant high-grade glioma being conducted at the Stanford Cancer Institute. In May 2013, the study completed enrollment of 20 patients with high-grade glioma who had received a median of three prior lines of therapy before enrolling in the study. On February 5, 2013, we announced a Phase 2 investigator-initiated clinical study of etirinotecan pegol in patients with metastatic and recurrent non-small cell lung cancer being conducted at the Abramson Cancer Center of the University of Pennsylvania. On October 24, 2013, we announced a Phase 2 investigator-initiated clinical study of etirinotecan pegol in patients with relapsed or refractory small-cell lung cancer at the Roswell Park Cancer Institute.

BAY41-6551 (Amikacin Inhale, formerly NKTR-061), Agreement with Bayer Healthcare LLC

In August 2007, we entered into a co-development, license and co-promotion agreement with Bayer Healthcare LLC (Bayer) to develop a specially-formulated Amikacin (BAY41-6551, Amikacin Inhale, formerly called NKTR-061) for the treatment of gram negative pneumonias. Under the terms of the agreement, Bayer is responsible for most future clinical development and commercialization costs, all activities to support worldwide regulatory filings, approvals and related activities, further development of formulated Amikacin and final product packaging for Amikacin Inhale. We are responsible for all future development, manufacturing and supply of the nebulizer device for clinical and commercial use. We have engaged third party contract manufacturers to perform our device manufacturing obligations for this program. We are entitled to up to $50.0 million in development milestone payments as well as sales milestone payments upon achievement of certain annual sales targets. We are also entitled to royalties based on annual worldwide net sales of Amikacin Inhale. Our right to receive these royalties in any particular country will expire upon the later of ten years after the first commercial sale of the

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product in that country or the expiration of certain patent rights in that particular country, subject to certain exceptions. We share a portion of these royalties with the Research Foundation of the State University of New York under a license agreement. The agreement expires in relation to a particular country upon the expiration of all royalty and payment obligations between the parties related to such country. Subject to termination fee payment obligations in certain circumstances, Bayer also has the right to terminate the agreement for convenience. In addition, the agreement may also be terminated by either party for certain product safety concerns, the product s failure to meet certain minimum commercial profile requirements or uncured material breaches by the other party.

Gram-negative pneumonias are often the result of complications of other patient conditions or surgeries. Gram-negative pneumonias carry a mortality risk that can exceed 50% in mechanically-ventilated patients and accounts for a substantial proportion of the pneumonias in intensive care units today. Amikacin Inhale is designed to be an adjunctive therapy to the current antibiotic therapies administered intravenously as standard of care. The aerosol generator within the nebulizer for Amikacin Inhale delivers a fine aerosol of the antimicrobial agent directly to the site of infection in the lungs. This drug candidate can be integrated with conventional mechanical ventilators or used as a hand-held off-vent device for patients no longer requiring breathing assistance.

In April 2013, Bayer initiated enrollment in a global Phase 3 clinical study, which it calls INHALE, to evaluate the efficacy and safety of Amikacin Inhale versus aerosolized placebo in the treatment of intubated and mechanically ventilated patients with Gram-negative pneumonia receiving standard of care intravenous antibiotics. The global INHALE development program is comprised of two prospective, randomized, double-blind, placebo-controlled, large multi-center global programs involving centers in North America, South America, Europe, Japan, Australia and Asia. The INHALE development program is being conducted by Bayer under a Special Protocol Assessment agreement with the FDA that is intended to support the submission of an NDA if the INHALE clinical studies are successful.

NKTR-181 (mu-opioid analgesic molecule for chronic pain)

NKTR-181 is an orally-available mu-opioid drug candidate in development as a long-acting analgesic to treat chronic pain. NKTR-181 is designed with the objective to address the abuse liability and serious central nervous system (CNS) side effects associated with current opioid therapies. NKTR-181 is a novel mu-opioid analgesic molecule created using Nektar s proprietary polymer conjugate technology, which provides it with a long-acting profile and slows its entry into the CNS. Its potential differentiating properties are inherent to the design of the new molecule and as a new molecular structure. NKTR-181 s abuse deterrent property does not rely on a formulation approach to prevent its conversion into a more abusable form of an opioid. In May 2012, the FDA granted Fast Track designation for the NKTR-181 development program.

In 2011, we completed two separate Phase 1 clinical studies of NKTR-181. The first study, a single-ascending dose study of NKTR-181 evaluated the pharmacokinetics and pharmacodynamics of a 50-fold range of single oral doses of NKTR-181 in 84 healthy subjects at up to 500 mg dose levels. The second study, a multiple-ascending dose study of NKTR-181 evaluated the pharmacokinetics and pharmacodynamics of four separate dose cohorts of NKTR-181 (100 mg 400 mg) administered orally twice- daily. The study enrolled a total of 60 healthy subjects over an eight-day treatment period, and included a placebo arm (n=3) for each dose cohort. Measurements in the study included plasma concentrations-time profiles, reductions in pupil diameter, and a cold pressor test, a model of pain used in healthy subjects to measure central analgesic activity. In this multiple dose Phase 1 clinical study, NKTR-181 exhibited a sustained analgesic response. Pupillometry data from the study demonstrated that NKTR-181 s centrally-mediated opioid effects are dose-dependent and indicates that the molecule enters the brain slowly, which has the potential to reduce the euphoria and other CNS side effects that are associated with current opioids. NKTR-181 was also well-tolerated at all doses evaluated in both studies.

In June 2012, we initiated a Phase 2 clinical study to evaluate the efficacy, safety and tolerability of NKTR-181 in patients with moderate to severe chronic pain from osteoarthritis of the knee. The Phase 2 clinical study utilized a double-blind, placebo-controlled, randomized withdrawal, enriched enrollment study design. The study

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enrolled 213 opioid-naïve patients with osteoarthritis of the knee who were not getting adequate pain relief from their current non-opioid pain medication. Patients who qualified during the baseline period entered a titration phase, during which they were titrated on NKTR-181 tablets administered orally twice-daily until a dose was reached that provided a reduction of at least 20% in the patient s pain score as compared to the patient s own baseline. Patients that achieved this level of analgesia were then randomized on a 1:1 basis to either continue to receive their analgesic dose of NKTR-181 or to receive placebo for up to 25 days. The primary endpoint of the study was the average change in a patient s pain score from baseline to the end of the double-blind, randomized treatment period. Secondary endpoints of the study included quality-of-life assessment, sleep and motor activity scoring, as well as tolerability endpoints.

On September 26, 2013, we announced results from this Phase 2 efficacy study. Of the 295 patients that entered the study, only 9 (3%) patients were unable to achieve meaningful pain relief with NKTR-181. During the titration phase, 53 patients (18%) discontinued treatment because of adverse events, most of which are those commonly associated with opioids. A total of 213 patients achieved an average 40% reduction in pain and entered the randomized phase of the study. Following the titration period, patients were randomized 1:1 to either continue to receive their analgesic dose of NKTR-181 or to receive placebo for 21 days. NKTR-181 performed as expected as an opioid analgesic throughout the study with patients continuing to show a reduction in pain scores throughout the randomized phase of the study. However, patients who were randomized to placebo did not show the expected increase in pain scores observed in similar enriched enrollment, randomized withdrawal studies. This unusual lack of a placebo rebound caused the Phase 2 study to miss the primary endpoint in the study, which was based upon the average change in a patient s pain score from pre-randomization baseline to the end of the double-blind, randomized treatment period of the study. In December 2013, we met with the FDA to discuss the results of the Phase 2 clinical study and certain preliminary considerations for the Phase 3 study design. We are currently evaluating the appropriate Phase 3 clinical trial design for NKTR-181 and plan to start a Phase 3 clinical study in mid-2014, following the completion of an end-of-Phase 2 meeting with the FDA planned to occur in the first half of 2014.

In the first half of 2013, we conducted a human abuse liability study, or HAL study, for NKTR-181. The HAL study was a randomized, double-blind, placebo- and active-controlled, 5-way crossover trial, that compared the effects of three doses of NKTR-181 oral solution (100 mg, 200 mg, and 400 mg), to the effects of 40 mg of oxycodone oral solution and placebo. Study participants were 42 healthy adults who were not currently physically opioid-dependent but had used opioids to attain non-medical effects on at least 10 occasions during the past year and at least once in the 12 weeks before the study. The study participants sequentially received the five treatments, administered in a randomized, double-blinded fashion, with each treatment separated by a washout period. The study also utilized a Williams Square cross-over design, which uses a series of randomized sequences for each individual subject. The HAL study compared drug liking between each treatment group (oxycodone 40 mg, placebo, and NKTR-181 100 mg, 200 mg, and 400 mg). On the bipolar VAS scale (0-100), a score of 50 indicates that the subject neither likes nor dislikes the drug. In the study, 40 mg of oxycodone oral solution resulted in a maximum mean drug liking score of 85, indicating a strong liking for the effects of oxycodone. The oxycodone liking score was significantly different from placebo as early as 15 minutes after dosing and peaked at 60 minutes. In the placebo arm, the maximum mean drug liking score was 50, indicating that the subjects neither liked nor disliked the effects. In this study, NKTR-181 was rated similar to placebo in drug liking and feeling high scores and had highly statistically significant lower drug liking scores and reduced feeling high scores as compared to oxycodone at all doses tested ($p < 0.0001$). On June 19, 2013, we presented data from the HAL study at the 2013 Annual Meeting of The College on Problems of Drug Dependence in San Diego, California.

According to a 2011 report from the National Academy of Sciences, chronic pain conditions, such as osteoarthritis, back pain and cancer pain, affect at least 100 million adults in the U.S. annually and contribute to over $300 billion a year in lost productivity. Opioids are considered to be the most effective therapeutic option for pain. However, opioids cause significant problems for physicians and patients because of their serious side effects such as respiratory depression and sedation, as well as the risks they pose for addiction, abuse, misuse,

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and diversion. The FDA has cited prescription opioid analgesics as being at the center of a major public health crisis of addiction, misuse, abuse, overdose and death. A 2010 report from the Center for Disease Control and Prevention notes that emergency room visits tied to the abuse of prescription painkillers was at an all-time high at that point, having increased 111 percent over the preceding five-year period.

NKTR-171 (neuropathic pain)

NKTR-171 is a novel, orally-available sodium channel blocker and is being developed as a treatment for neuropathic pain. NKTR-171 is a new molecular entity that is designed to treat neuropathic pain by blocking hyperactive neuronal sodium channels associated with damaged nerves in the peripheral nervous system. Chronic neuropathic pain arises from nerves injured or damaged by systemic disease, infection, toxins, or physical trauma that are in a continuous state of hyper-excitability, often due to aberrant sodium channel firing. This hyper-excitability results in transmission of abnormal pain signals from the periphery to the central nervous system (CNS). Existing therapies that block sodium channels have been shown to provide effective pain relief but are typically associated with significant unwanted CNS side effects, including dizziness, ataxia and somnolence. NKTR-171 is designed to be a peripherally-restricted molecule which selectively blocks hyper-excitable sodium channels without causing the CNS side effects that limit usage of existing therapies. In January 2014, a single-ascending dose Phase 1 clinical study of NKTR-171 was initiated to assess its pharmacokinetics, tolerability, and safety in up to 75 healthy subjects.

NKTR-192 (mu-opioid analgesic molecule for acute pain)

NKTR-192 is a mu-opioid analgesic molecule in preclinical development that is intended to be a short-acting analgesic to treat acute pain. NKTR-192 is also designed to address the abuse liability and serious CNS side effects associated with current opioid therapies. NKTR-192 is also designed to have slow entry into the CNS. Its differentiating properties are inherent to the design of the new molecule and as a new molecular structure, NKTR-192 does not rely on a formulation approach to prevent its conversion into a more abusable form of an opioid. NKTR-192 entered Phase 1 clinical development in 2012. In January 2014, we announced data from the multiple ascending dose study for an oral formulation of NKTR-192. NKTR-192 demonstrated low CNS side effects and achieved the target profile for the treatment of acute pain. However, at the highest doses tested in the study, there were several subjects who had elevated liver enzymes. As a result of these data, NKTR-192 will no longer be developed as an oral formulation. We are currently exploring an injectable formulation of NKTR-192 in preclinical development for the treatment of migraine and cancer pain.

NKTR-214 (cytokine immunostimulatory therapy)

NKTR-214 is an engineered immunostimulatory cytokine and is being developed for the treatment of solid tumors. NKTR-214 is engineered to selectively activate IL-2 receptors on cytotoxic T cells that kill tumor cells, with relatively low affinity for IL-2 receptors on regulatory T cells that dampen the immune response to tumors. This receptor selectivity is intended to increase efficacy and improve safety over existing immunostimulatory cytokine drugs. The product candidate is currently in Investigational New Drug application (IND)-enabling studies in preparation for clinical studies in cancer patients.

Overview of Select Technology Licensing Collaborations and Programs

We have a number of product candidates in clinical development and approved products in collaboration with our partners that use our technology or involve rights over which we have patents or other proprietary intellectual property. In a typical collaboration involving our PEGylation technology, we license our proprietary intellectual property related to our PEGylation technology or proprietary conjugated drug molecules in exchange for upfront payments, development milestone payments and royalties from sales of the resulting commercial product as well as sales milestones. In certain cases, we also manufacture and supply our proprietary PEGylation materials to our partners.

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LEVADEX®, Agreement with MAP Pharmaceuticals, Inc. (a wholly-owned subsidiary of Allergan, Inc.)

In June 2004, we entered into a license agreement with MAP Pharmaceuticals, Inc. (MAP), which includes a worldwide, exclusive license, to certain of our patents and other intellectual property rights to develop and commercialize a formulation of dihydroergotamine (DHE) for administration to patients via the pulmonary or nasal delivery route, which resulted in the development of LEVADEX®. In 2006, we amended and restated this agreement. Under the terms of the agreement, we have the right to receive certain milestone payments based on development criteria that are solely the responsibility of MAP and royalties based on net sales of LEVADEX®. LEVADEX® is a self-administered formulation of DHE using an inhaler device. Our right to receive royalties in any particular country will expire upon the later of (i) 10 years after first commercial sale in that country, (ii) the date upon which the licensed know-how becomes known to the general public, and (iii) expiration of certain patent claims, each on a country-by-country basis. Either party may terminate the agreement upon a material, uncured default of the other party. On May 26, 2011, MAP submitted an NDA to the FDA for LEVADEX®. In March of 2012, the FDA issued a complete response letter identifying issues relating to chemistry, manufacturing and controls deficiencies at a third party manufacturer that needed to be resolved to the FDA s satisfaction as well as citing the need for additional time to complete review of inhaler usability information. In December 2012, MAP announced that its NDA resubmission for LEVADEX® was accepted for filing by the FDA. On March 1, 2013, Allergan, Inc. completed a merger and acquisition transaction with MAP pursuant to which MAP become a wholly-owned subsidiary of Allergan. On April 17, 2013, the FDA issued another complete response letter identifying issues related to a supplier that provided the canister filling unit for LEVADEX®. Allergan has responded to the FDA s latest complete response letter and has stated that it expects a response from the FDA on the NDA for LEVADEX® in the second quarter of 2014.

BAX 855 and Long-Acting Therapies for Hemophilia A, Agreement with Subsidiaries of Baxter International Inc.

In September 2005, we entered into an exclusive research, development, license, manufacturing and supply agreement with Baxter Healthcare SA and Baxter Healthcare Corporation (Baxter) to develop products with an extended half-life for the treatment and prophylaxis of Hemophilia A patients using our proprietary PEGylation technology. The first product in this collaboration, BAX 855, is a longer-acting (PEGylated) form of a full-length recombinant factor VIII (rFVIII) protein. BAX 855 is a full-length PEGylated longer-acting recombinant factor VIII (rFVIII) that was developed to increase the half-life of ADVATE (Antihemophilic Factor (Recombinant) Plasma/Albumin-Free Method). We are entitled to up to $73.0 million in total development and sales milestone payments, as well as royalties on net sales varying by product and country of sale. Our right to receive these royalties in any particular country will expire upon the later of ten years after the first commercial sale of the product in that country or the expiration of patent rights in certain designated countries or in that particular country.

In 2012, Baxter completed a Phase 1 clinical study for BAX 855 that was a prospective, open-label study assessing the safety, tolerability and pharmacokinetics of BAX 855 in 19 previously treated patients age 18 years or older with severe hemophilia A. In January 2013, Baxter announced the top level results from this Phase 1 clinical study. This study demonstrated that the half-life (measuring the duration of activity of the drug in the body) of BAX 855 was approximately 1.5-fold higher compared to ADVATE. A longer half-life was achieved in all patients in the study using BAX 855, no patients developed inhibitors to either base molecule, BAX 855 or PEG, and no patients had allergic reactions. Eleven adverse events were reported in eight patients across both treatment arms, but none was serious, treatment-related or resulted in withdrawal from the study. Baxter commenced patient enrollment in a Phase 3 clinical study of BAX 855 in the U.S. in February 2013 and completed enrollment in November 2013. The Phase 3 clinical study is ongoing and is as a multi-center, open-label study called PROLONG-ATE and enrolled 146 previously treated adult patients with severe hemophilia A in order to assess the efficacy, safety and pharmacokinetics of BAX 855 for prophylaxis and on-demand treatment of bleeding.

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FOVISTA (Anti-PDGF Therapy), Agreement with Ophthotech Corporation

In September 2006, we entered into a license, manufacturing and supply agreement with (OSI) Eyetech, Inc. (Eyetech) under which we granted Eyetech a worldwide, exclusive license to certain of our proprietary PEGylation technology to develop, manufacture and commercialize particular products that use our proprietary PEGylation reagent linked with the active ingredient in Fovista . In July 2007, as a result of a divestiture agreement between Eyetech and Ophthotech Corporation (Ophthotech), Opthotech acquired from Eyetech certain technology rights and other assets owned or controlled by Eyetech relating to particular anti-platelet-derived growth factor aptamers, or anti-PDGFs, including Fovista . As a result of this transaction, Ophthotech assumed the license, manufacturing and supply agreement between Eyetech and us. Fovista is an anti-PDGF agent administered in combination with anti-vascular endothelial growth factor (anti-VEGF) therapy for the treatment of neovascular age-related macular degeneration, (or wet AMD). We are entitled to up to $7.5 million in total development and sales milestone payments, low- to mid- single-digit royalties on net sales that vary by sales levels and are subject to reduction in the absence of patent coverage, and additional consideration if Ophthotech grants certain third-party commercialization rights to Fovista . Our right to receive royalties in any particular country will expire upon the later of ten years after first commercial sale of the product or expiration of patent rights in the particular country. We are the exclusive supplier of all of Ophthotech s clinical and commercial requirements of our proprietary PEGylation reagent used in the manufacture of Fovista .

In June 2012, Ophthotech announced completion of a prospective, randomized, controlled Phase 2b clinical study of 449 patients with wet AMD comparing Fovista , administered in combination with Lucentis® (ranibizumab injection) anti-VEGF therapy with Lucentis® monotherapy. Fovista met the pre-specified primary efficacy endpoint of mean vision gain. Patients receiving the combination of Fovista (1.5 mg) and Lucentis® gained a mean of 10.6 letters of vision at 24 weeks on the Early Treatment Diabetic Retinopathy Study standardized eye chart, compared to 6.5 letters for patients receiving Lucentis monotherapy (p=0.019), representing a statistically significant 62% additional benefit. In September 2013, Ophthotech announced the initiation of patient enrollment in the first of three planned pivotal Phase 3 clinical studies of Fovista in combination with anti-VEGF therapy for the treatment of newly diagnosed patients with wet AMD. These three studies plan to enroll a total of approximately 1,866 patients to evaluate the efficacy and safety of Fovista .

REG1 Anticoagulation System (pegnivacogin), Agreement with Regado Biosciences, Inc.

In December 2006, we entered into a license, manufacturing and supply agreement with Regado Biosciences, Inc. (Regado), in which we granted Regado a worldwide, exclusive license to certain of our proprietary PEGylation technology. Regado is using our PEGylation technology to develop the REG1 Anticoagulation System, or REG1, which is a two-component system comprising a Factor IXa inhibitor anticoagulant (pegnivacogin, a single-stranded, nucleic acid aptamer) and its specific active control agent. REG1 is being developed for use in patients suffering from acute coronary syndrome, including those who undergo coronary revascularization procedures, which include percutaneous coronary intervention (PCI) and coronary artery bypass grafting. These procedures put patients at risk for therapy-related bleeding complications. REG1 is designed to increase therapeutic flexibility while reducing side effects and improving outcomes experienced by patients in this setting. We are entitled to up to $6.5 million in total development and sales milestone payments, mid-single-digit royalties on net sales varying by sales volume and certain additional payments if Regado grants any third parties certain rights to the REG1 product. Our right to receive royalties in any particular country will expire upon the later of ten years after first commercial sale of the product or expiration of patent rights in the particular country. We are the exclusive supplier of all of Regado s clinical and commercial requirements of our proprietary PEGylation reagent used in the manufacture of REG1.

Regado has announced the completion of three Phase 1 and one Phase 2 clinical studies for REG1. In the Phase 2 study, which involved 640 patients, Regado reported that when compared to standard of care heparin, REG1 demonstrated both a rapid and predictable anticoagulant effect, the ability to precisely modulate or eliminate that effect in real time, as well as several important clinical and pharmacoeconomic benefits. In September 2013, Regado announced the enrollment of the first patient in its REGULATE-PCI Phase 3 clinical

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trial that plans to enroll 13,200 patients, described by Regado as a PROBE design (Prospective, Randomized, Open-label, Blinded-Endpoint) superiority study comparing the effects of REG1 to bivalirudin in patients undergoing PCI electively or for the treatment of unstable angina or non-ST elevated myocardial infarction. The primary endpoint of the REGULATE-PCI trial is efficacy compared to bivalrudin based on a composite set of endpoints including death, nonfatal myocardial infarction, nonfatal stroke, and urgent target lesion revascularization through day three. The principal secondary endpoint is safety compared to bivalrudin as measured by major bleeding events through day three.

Cipro DPI (formerly known as Cipro Inhale), Agreement with Bayer Schering Pharma AG Assigned to Novartis as of December 31, 2008

We were a party to a collaborative research, development and commercialization agreement with Bayer Schering Pharma AG, (Bayer), related to the development of an inhaled powder formulation of ciprofloxacin delivered by way of a dry powder inhaler, Cipro DPI (formerly known as Cipro Inhale) for the treatment of chronic lung infections caused by *Pseudomonas aeruginosa* in cystic fibrosis patients. On December 31, 2008, we assigned the agreement to Novartis Pharma AG in connection with the completion of the pulmonary asset sale transaction. However, we retained our economic interest in the future potential net sales royalties if Cipro DPI is approved by health authorities and is successfully commercialized by Bayer. Cipro DPI has completed Phase 2 clinical development for the treatment of chronic lung infections. In August 2012, Bayer initiated a Phase 3 clinical development program which it calls RESPIRE for Cipro DPI in patients with non-cystic fibrosis bronchiectasis. In patients with bronchiectasis, the bronchial tubes are enlarged, allowing mucus to pool and making the area prone to infection. In the two placebo-controlled trials, RESPIRE-1 and RESPIRE-2, Bayer plans to enroll up to 600 patients and to evaluate Cipro DPI as a chronic, intermittent therapy over a period of 48 weeks.

Overview of Select Licensing Partnerships for Approved Products

Neulasta®, Agreement with Amgen, Inc.

In July 1995, we entered into a non-exclusive supply and license agreement (the 1995 Agreement) with Amgen, Inc., pursuant to which we licensed our proprietary PEGylation technology to be used in the development and manufacture of Neulasta®. Neulasta® selectively stimulates the production of neutrophils that are depleted by cytotoxic chemotherapy, a condition called neutropenia that makes it more difficult for the body to fight infections. On October 29, 2010, we amended and restated the 1995 Agreement by entering into a supply, dedicated suite and manufacturing guarantee agreement (the 2010 Agreement) and an amended and restated license agreement with Amgen Inc. and Amgen Manufacturing, Limited (together referred to as Amgen). Under the terms of the 2010 Agreement, we guarantee the manufacture and supply of our proprietary PEGylation materials (Polymer Materials) to Amgen in an existing manufacturing suite to be used exclusively for the manufacture of Polymer Materials for Amgen in our manufacturing facility in Huntsville, Alabama. This supply arrangement is on a non-exclusive basis (other than the use of the manufacturing suite and certain equipment) whereby we are free to manufacture and supply the Polymer Materials to any other third party and Amgen is free to procure the Polymer Materials from any other third party. Under the terms of the 2010 Agreement, we received a $50.0 million upfront payment in return for guaranteeing supply of certain quantities of Polymer Materials to Amgen and the Additional Rights described below, and Amgen will pay manufacturing fees calculated based on fixed and variable components applicable to the Polymer Materials ordered by Amgen and delivered by us. Amgen has no minimum purchase commitments. 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 historically supplied to Amgen), significant additional payments become payable to us in return for guaranteeing supply of additional quantities of the Polymer Materials.

The term of the Agreement runs through October 29, 2020. In the event we become subject to a bankruptcy or insolvency proceeding, we cease to own or control the manufacturing facility in Huntsville, Alabama, we fail to manufacture and supply the Polymer Materials or certain other events occur, Amgen or its designated third party will have the right to elect, among certain other options, to take title to the dedicated equipment and access

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the manufacturing facility to operate the manufacturing suite solely for the purpose of manufacturing the Polymer Materials (Additional Rights). Amgen may terminate the 2010 Agreement for convenience or due to an uncured material default by us. Either party may terminate the 2010 Agreement in the event of insolvency or bankruptcy of the other party.

PEGASYS ®, Agreement with F. Hoffmann-La Roche Ltd

In February 1997, we entered into a license, manufacturing and supply agreement with F. Hoffmann-La Roche Ltd and Hoffmann-La Roche Inc. (Roche), under which we granted Roche a worldwide, exclusive license to use certain intellectual property related to our PEGylation materials to manufacture and commercialize a certain class of products, of which PEGASYS® is the only product currently commercialized. PEGASYS® is approved in the U.S., E.U. and other countries for the treatment of Hepatitis C and is designed to help the patient s immune system fight the Hepatitis C virus. As a result of Roche exercising a license extension option in December 2009, beginning in 2010 Roche has the right to manufacture all of its requirements for our proprietary PEGylation materials for PEGASYS® and we supply raw materials or perform additional manufacturing, if any, only on a back-up basis. In connection with Roche s exercise of the license extension option in December 2009, we received a payment of $31.0 million. The agreement expires on the later of January 10, 2015 or the expiration of our last relevant patent containing a valid claim. In August 2013, we agreed to deliver additional quantities of PEGylation materials used by Roche to produce PEGASYS® and MIRCERA®, all of which were delivered in the last quarter of 2013, for total consideration of approximately $18.6 million.

Somavert ®, Agreement with Pfizer, Inc.

In January 2000, we entered into a license, manufacturing and supply agreement with Sensus Drug Development Corporation (subsequently acquired by Pharmacia Corp. in 2001 and then acquired by Pfizer, Inc. in 2003), for the PEGylation of Somavert® (pegvisomant), a human growth hormone receptor antagonist for the treatment of acromegaly. We currently manufacture our proprietary PEGylation reagent for Pfizer, Inc. on a price per gram basis. The agreement expires on the later of ten years from the grant of first marketing authorization in the designated territory, which occurred in March 2003, or the expiration of our last relevant patent containing a valid claim. In addition, Pfizer, Inc. may terminate the agreement if marketing authorization is withdrawn or marketing is no longer feasible due to certain circumstances, and either party may terminate for cause if certain conditions are met.

PEG-Intron®, Agreement with Merck (through its acquisition of Schering-Plough Corporation)

In February 2000, we entered into a manufacturing and supply agreement with Schering-Plough Corporation (Schering) for the manufacture and supply of our proprietary PEGylation materials to be used by Schering in production of a PEGylated recombinant human interferon-alpha (PEG-Intron). PEG-Intron is a treatment for patients with Hepatitis C. Schering was acquired by, and became a wholly-owned subsidiary of, Merck & Co., Inc. We currently manufacture our proprietary PEGylation materials for Schering on a price per gram basis. In December 2010, the parties amended the manufacturing and supply agreement to provide for a transition plan to an alternative manufacturer and extension of the term through the successful manufacturing transition or December 31, 2018 at the latest. The amended agreement provided for a one-time payment and milestone payments as well as increased pricing for any future manufacturing performed by us.

Macugen®, Agreement with Valeant Pharmaceuticals International, Inc.

In 2002, we entered into a license, manufacturing and supply agreement with Eyetech, Inc. (subsequently acquired by Valeant Pharmaceuticals International, Inc. or Valeant), pursuant to which we license certain intellectual property related to our proprietary PEGylation technology for the development and commercialization of Macugen®, a PEGylated anti-vascular endothelial growth factor aptamer currently approved in the U.S. and E.U. for age-related macular degeneration. We currently manufacture our proprietary

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PEGylation materials for Valeant on a price per gram basis. Under the terms of the agreement, we will receive royalties on net product sales in any particular country for the longer of ten years from the date of the first commercial sale of the product in that country or the duration of patent coverage. We share a portion of the payments received under this agreement with Enzon Pharmaceuticals, Inc. which ends in 2014. The agreement expires upon the expiration of our last relevant patent containing a valid claim. In addition, Valeant may terminate the agreement if marketing authorization is withdrawn or marketing is no longer feasible due to certain circumstances, and either party may terminate for cause if certain conditions are met.

CIMZIA ®, Agreement with UCB Pharma

In December 2000, we entered into a license, manufacturing and supply agreement covering our proprietary PEGylation materials for use in CIMZIA® (certolizumab pegol) with Celltech Chiroscience Ltd., which was acquired by UCB Pharma (UCB) in 2004. Under the terms of the agreement, UCB is responsible for all clinical development, regulatory, and commercialization expenses. We have the right to receive manufacturing revenue on the basis of a fixed price per gram. We were also entitled to receive royalties on net sales of the CIMZIA® product for the longer of ten years from the first commercial sale of the product anywhere in the world or the expiration of patent rights in a particular country. In February 2012, we sold our rights to receive royalties on future worldwide net sales of CIMZIA® effective as of January 1, 2012 until the agreement with UCB is terminated or expires. This sale is further discussed in Note 7 of Item 8, Financial Statements and Supplementary Data. We share a portion of the payments we receive from UCB with Enzon Pharmaceuticals, Inc. which ends in 2014. The agreement expires upon the expiration of all of UCB s royalty obligations, provided that the agreement can be extended for successive two year renewal periods upon mutual agreement of the parties. In addition, UCB may terminate the agreement should it cease the development and marketing of CIMZIA® and either party may terminate for cause under certain conditions.

MIRCERA ® (C.E.R.A.) (Continuous Erythropoietin Receptor Activator), Agreement with F. Hoffmann-La Roche Ltd

In December 2000, we entered into a license, manufacturing and supply agreement with F. Hoffmann-La Roche Ltd and Hoffmann-La Roche Inc. (Roche), which was amended and restated in its entirety in December 2005. Pursuant to the agreement, we license our intellectual property related to our proprietary PEGylation materials for the manufacture and commercialization of Roche s MIRCERA® product. MIRCERA® is a novel continuous erythropoietin receptor activator indicated for the treatment of anemia associated with chronic kidney disease in patients on dialysis and patients not on dialysis. As of the end of 2006, we were no longer required to manufacture and supply our proprietary PEGylation materials for MIRCERA® under our original agreement. In February 2012, we entered into a toll-manufacturing agreement with Roche under which we manufactured our proprietary PEGylation material for MIRCERA®. Roche entered into the toll-manufacturing agreement with the objective of establishing us as a secondary back-up source on a non-exclusive basis. Under the terms of this agreement, Roche paid us an up-front payment of $5.0 million plus a total of $22.0 million in performance-based milestone payments upon our achievement of certain manufacturing readiness, validation and production milestones, including the delivery of specified quantities of PEGylation materials, all of which were successfully completed by the end of January 2013. Roche would also pay us additional consideration for any future orders of the PEGylation materials for MIRCERA® beyond the initial quantities ordered as part of the initial arrangement. In August 2013, we agreed to deliver additional quantities of PEGylation materials used by Roche to produce PEGASYS® and MIRCERA®, all of which were delivered in the last quarter of 2013, for total consideration of approximately $18.6 million. Roche may terminate the toll-manufacturing agreement due to an uncured material default by us or for convenience under certain circumstances and subject to certain financial obligations. We were also entitled to receive royalties on net sales of the MIRCERA® product. In February 2012, we sold all of our future rights to receive royalties on future worldwide net sales of MIRCERA® effective as of January 1, 2012. This sale is further discussed in Note 7 of Item 8, Financial Statements and Supplementary Data.

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OMONTYS® (Peginesatide), Agreement with Affymax, Inc.

In April 2004, we entered into a license, manufacturing and supply agreement with Affymax, Inc. (Affymax), under which we granted Affymax a worldwide, non-exclusive license to certain of our proprietary PEGylation technology to develop, manufacture and commercialize OMONTYS®. OMONTYS® is a synthetic PEGylated peptidic compound that binds to and stimulates the erythropoietin receptor and thus acts as an erythropoietin stimulating agent (ESA). It is the only ESA that is peptide-based and its building blocks (amino acids) are arranged in a different order than erythropoietin (i.e., it has no sequence homology to endogenous erythropoietin). The compound was discovered by Affymax and is being co-developed and marketed by Affymax and Takeda Pharmaceutical Company Limited (Takeda). In March 2012, the FDA approved OMONTYS® for the treatment of dialysis patients with anemia due to chronic kidney disease (CKD). OMONTYS® is the first once-monthly ESA for anemia in CKD for dialysis patients available in the U.S.

On February 23, 2013, Affymax and Takeda announced a voluntary recall of all lots of OMONTYS® drug product to the user level as a result of new post-marketing reports regarding serious hypersensitivity reactions, including anaphylaxis, which can be life-threatening or fatal. The FDA has been notified by Affymax of 19 reports of anaphylaxis with 3 of those cases resulting in death. The reported serious hypersensitivity reactions have occurred within 30 minutes after such administration of OMONTYS®. There have been no reports of such reactions following subsequent dosing, or in patients who have completed their dialysis session. Since launch of the drug, more than 25,000 patients have received OMONTYS® in the post-marketing setting.

Effective as of April 1, 2013, Affymax announced that it had amended its collaboration agreement with Takeda to transfer regulatory, manufacturing, and development responsibilities for OMONTYS® to Takeda. In July 2013, Affymax terminated the license, manufacturing and supply agreement with us.

Government Regulation

The research and development, clinical testing, manufacture and marketing of products using our technologies are subject to regulation by the FDA and by comparable regulatory agencies in other countries. These national agencies and other federal, state and local entities regulate, among other things, research and development activities and the testing (in vitro, in animals, and in human clinical trials), manufacture, labeling, storage, recordkeeping, approval, marketing, advertising and promotion of our products.

The approval process required by the FDA before a product using any of our technologies may be marketed in the U.S. depends on whether the chemical composition of the product has previously been approved for use in other dosage forms. If the product is a new chemical entity that has not been previously approved, the process includes the following:

- extensive preclinical laboratory and animal testing;
- submission of an Investigational New Drug application (IND) prior to commencing clinical trials;
- adequate and well-controlled human clinical trials to establish the safety and efficacy of the drug for the intended indication;
- extensive pharmaceutical development for the characterization of the chemistry, manufacturing process and controls for the active ingredient and drug product; and
- submission to the FDA of an NDA for approval of a drug, a Biological License Application (BLA) for approval of a biological product or a Premarket Approval Application (PMA) or Premarket Notification 510(k) for a medical device product (a 510(k)).

If the active chemical ingredient has been previously approved by the FDA, the approval process is similar, except that certain preclinical tests relating to systemic toxicity normally required for the IND and NDA or BLA may not be necessary if the company has a right of reference to

such data under section 505(j) of the Federal

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Food, Drug, and Cosmetic Act (FDCA) or is eligible for approval under Section 505(b)(2) of the FDCA or the biosimilars provisions of the Public Health Services Act.

Preclinical tests include laboratory evaluation of product chemistry and animal studies to assess the safety and efficacy of the product and its chosen formulation. Preclinical safety tests must be conducted by laboratories that comply with FDA good laboratory practices (GLP) regulations. The results of the preclinical tests for drugs, biological products and combination products subject to the primary jurisdiction of the FDA s Center for Drug Evaluation and Research (CDER) or Center for Biologics Evaluation and Research (CBER) are submitted to the FDA as part of the IND and are reviewed by the FDA before clinical trials can begin. Clinical trials may begin 30 days after receipt of the IND by the FDA, unless the FDA raises objections or requires clarification within that period. Clinical trials involve the administration of the drug to healthy volunteers or patients under the supervision of a qualified, identified medical investigator according to a protocol submitted in the IND for FDA review. Drug products to be used in clinical trials must be manufactured according to current good manufacturing practices (cGMP). Clinical trials are conducted in accordance with protocols that detail the objectives of the study and the parameters to be used to monitor participant safety and product efficacy as well as other criteria to be evaluated in the study. Each protocol is submitted to the FDA in the IND.

Apart from the IND process described above, each clinical study must be reviewed by an independent Institutional Review Board (IRB) and the IRB must be kept current with respect to the status of the clinical study. The IRB considers, among other things, ethical factors, the potential risks to subjects participating in the trial and the possible liability to the institution where the trial is conducted. The IRB also reviews and approves the informed consent form to be signed by the trial participants and any significant changes in the clinical study.

Clinical trials are typically conducted in three sequential phases. Phase 1 involves the initial introduction of the drug into healthy human subjects (in most cases) and the product generally is tested for tolerability, pharmacokinetics, absorption, metabolism and excretion. Phase 2 involves studies in a limited patient population to:

- determine the preliminary efficacy of the product for specific targeted indications;
- determine dosage and regimen of administration; and
- identify possible adverse effects and safety risks.

If Phase 2 trials demonstrate that a product appears to be effective and to have an acceptable safety profile, Phase 3 trials are undertaken to evaluate the further clinical efficacy and safety of the drug and formulation within an expanded patient population at geographically dispersed clinical study sites and in large enough trials to provide statistical proof of efficacy and tolerability. The FDA, the clinical trial sponsor, the investigators or the IRB may suspend clinical trials at any time if any one of them believes that study participants are being subjected to an unacceptable health risk. In some cases, the FDA and the drug sponsor may determine that Phase 2 trials are not needed prior to entering Phase 3 trials.

Following a series of formal meetings and communications between the drug sponsor and the regulatory agencies, the results of product development, preclinical studies and clinical studies are submitted to the FDA as an NDA or BLA for approval of the marketing and commercial shipment of the drug product. The FDA may deny approval if applicable regulatory criteria are not satisfied or may require additional clinical or pharmaceutical testing or requirements. Even if such data are submitted, the FDA may ultimately decide that the NDA or BLA does not satisfy all of the criteria for approval. Additionally, the approved labeling may narrowly limit the conditions of use of the product, including the intended uses, or impose warnings, precautions or contraindications which could significantly limit the potential market for the product. Further, as a condition of approval, the FDA may impose post-market surveillance, or Phase 4, studies or risk evaluation and mitigation strategies. Product approvals, once obtained, may be withdrawn if compliance with regulatory standards is not maintained or if safety concerns arise after the product reaches the market. The FDA may require additional post-marketing clinical testing and pharmacovigilance programs to monitor the effect of drug products that have been

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commercialized and has the power to prevent or limit future marketing of the product based on the results of such programs. After approval, there are ongoing reporting obligations concerning adverse reactions associated with the product, including expedited reports for serious and unexpected adverse events.

Each manufacturing establishment producing drug product for the U.S. market must be registered with the FDA and typically is inspected by the FDA prior to NDA or BLA approval of a drug product manufactured by such establishment. Establishments handling controlled substances must also be licensed by the U.S. Drug Enforcement Administration. Manufacturing establishments of U.S. marketed products are subject to inspections by the FDA for compliance with cGMP and other U.S. regulatory requirements. They are also subject to U.S. federal, state, and local regulations regarding workplace safety, environmental protection and hazardous and controlled substance controls, among others.

A number of the drugs we are developing are already approved for marketing by the FDA in another form or using another delivery system. We believe that, when working with drugs approved in other forms, the approval process for products using our alternative drug delivery or formulation technologies may involve less risk and require fewer tests than new chemical entities do. However, we expect that our formulations will often use excipients not currently approved for use. Use of these excipients will require additional toxicological testing that may increase the costs of, or length of time needed to, gain regulatory approval. In addition, as they relate to our products, regulatory procedures may change as regulators gain relevant experience, and any such changes may delay or increase the cost of regulatory approvals.

For product candidates currently under development utilizing pulmonary technology, the pulmonary inhaler devices are considered to be part of a drug and device combination for deep lung delivery of each specific molecule. The FDA will make a determination as to the most appropriate center and division within the agency that will assume primary responsibility for the review of the applicable applications, which would consist of an IND and an NDA or BLA where CDER or CBER are determined to have primary jurisdiction or an investigational device exemption application and PMA or 510(k) where the Center for Devices and Radiological Health (CDRH) is determined to have primary jurisdiction. In the case of our product candidates, CDER in consultation with CDRH could be involved in the review. The assessment of jurisdiction within the FDA is based upon the primary mode of action of the drug or the location of the specific expertise in one of the centers.

Where CDRH is determined to have primary jurisdiction over a product, 510(k) clearance or PMA approval is required. Medical devices are classified into one of three classes Class I, Class II, or Class III depending on the degree of risk associated with each medical device and the extent of control needed to ensure safety and effectiveness. Devices deemed to pose lower risks are placed in either Class I or II, which requires the manufacturer to submit to the FDA a Premarket Notification requesting permission to commercially distribute the device. This process is known as 510(k) clearance. Some low risk devices are exempted from this requirement. Devices deemed by the FDA to pose the greatest risk, such as life-sustaining, life-supporting or implantable devices, or devices deemed not substantially equivalent to a previously cleared 510(k) device are placed in Class III, requiring PMA approval.

To date, our partners have generally been responsible for clinical and regulatory approval procedures, but we may participate in this process by submitting to the FDA a drug master file developed and maintained by us which contains data concerning the manufacturing processes for the inhaler device, PEGylation materials or drug. For our proprietary products, we prepare and submit an IND and are responsible for additional clinical and regulatory procedures for product candidates being developed under an IND. The clinical and manufacturing, development and regulatory review and approval process generally takes a number of years and requires the expenditure of substantial resources. Our ability to manufacture and market products, whether developed by us or under collaboration agreements, ultimately depends upon the completion of satisfactory clinical trials and success in obtaining marketing approvals from the FDA and equivalent foreign health authorities.

Sales of our products outside the U.S. are subject to local regulatory requirements governing clinical trials and marketing approval for drugs. Such requirements vary widely from country to country.

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In the U.S., under the Orphan Drug Act, the FDA may grant orphan drug designation to drugs intended to treat a rare disease or condition, which is generally a disease or condition that affects fewer than 200,000 individuals in the U.S. The company that obtains the first FDA approval for a designated orphan drug for a rare disease receives marketing exclusivity for use of that drug for the designated condition for a period of seven years. In addition, the Orphan Drug Act provides for protocol assistance, tax credits, research grants, and exclusions from user fees for sponsors of orphan products. Once a product receives orphan drug exclusivity, a second product that is considered to be the same drug for the same indication may be approved during the exclusivity period only if the second product is shown to be clinically superior to the original orphan drug in that it is more effective, safer or otherwise makes a major contribution to patient care or the holder of exclusive approval cannot assure the availability of sufficient quantities of the orphan drug to meet the needs of patients with the disease or condition for which the drug was designated. Similar incentives also are available for orphan drugs in the E.U.

In the U.S., the FDA may grant Fast Track or Breakthrough designation to a product candidate, which allows the FDA to expedite the review of new drugs that are intended for serious or life-threatening conditions and that demonstrate the potential to address unmet medical needs. Important features of Fast Track or Breakthrough designation include a potentially reduced clinical program and close, early communication between the FDA and the sponsor company to improve the efficiency of product development.

Patents and Proprietary Rights

We own more than 175 U.S. and 500 foreign patents and a number of pending patent applications that cover various aspects of our technologies. We have filed patent applications, and plan to file additional patent applications, covering various aspects of our PEGylation and advanced polymer conjugate technologies and our proprietary product candidates. More specifically, our patents and patent applications cover polymer architecture, drug conjugates, formulations, methods of making polymers and polymer conjugates, methods of administering polymer conjugates, and methods of manufacturing polymers and polymer conjugates. Our patent portfolio contains patents and patent applications that encompass our PEGylation and advanced polymer conjugate technology platforms, some of which we acquired in our acquisition of Shearwater Corporation in June 2001. Our patent strategy is to file patent applications on innovations and improvements to cover a significant majority of the major pharmaceutical markets in the world. Generally, patents have a term of twenty years from the earliest priority date (assuming all maintenance fees are paid). In some instances, patent terms can be increased or decreased, depending on the laws and regulations of the country or jurisdiction that issued the patent.

In January 2002, we entered into a Cross-License and Option Agreement with Enzon Pharmaceuticals, Inc. (Enzon), pursuant to which we and Enzon provided certain licenses to selected portions of each party s PEGylation patent portfolio. In certain cases, we have the option to license certain of Enzon s PEGylation patents for use in our proprietary products or for sublicenses to third parties in each case in exchange for payments to Enzon based on manufacturing profits, revenue share or royalties on net sales if a designated product candidate is approved in one or more markets.

On December 31, 2008, we completed the sale of certain assets related to our pulmonary business, associated technology and intellectual property to Novartis Pharma AG and Novartis Pharmaceuticals Corporation (together referred to as Novartis) for a purchase price of $115.0 million in cash (Novartis Pulmonary Asset Sale). In connection with the Novartis Pulmonary Asset Sale, as of December 31, 2008, we entered into an exclusive license agreement with Novartis Pharma AG. Pursuant to the exclusive license agreement, Novartis Pharma AG grants back to us an exclusive, irrevocable, perpetual, royalty-free and worldwide license under certain specific patent rights and other related intellectual property rights acquired by Novartis from us in the Novartis Pulmonary Asset Sale, as well as certain improvements or modifications thereto that are made by Novartis. Certain of such patent rights and other related intellectual property rights relate to our development program for inhaled vancomycin or are necessary for us to satisfy certain continuing contractual obligations to third parties, including in connection with development, manufacture, sale, and commercialization activities related to BAY41-6551 partnered with Bayer Healthcare LLC.

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We also rely on trade secret protection for our confidential and proprietary information. No assurance can be given that we can meaningfully protect our trade secrets. Others may independently develop substantially equivalent confidential and proprietary information or otherwise gain access to, or disclose, our trade secrets. Please refer to Item 1A, Risk Factors, including but not limited to 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. In certain situations in which we work with drugs covered by one or more patents, our ability to develop and commercialize our technologies may be affected by limitations in our access to these proprietary drugs. Even if we believe we are free to work with a proprietary drug, we cannot guarantee that we will not be accused of, or determined to be, infringing a third party s rights and be prohibited from working with the drug or found liable for damages. Any such restriction on access or liability for damages would have a material adverse effect on our business, results of operations and financial condition.

The patent positions of pharmaceutical and biotechnology companies, such as ours, are uncertain and involve complex legal and factual issues. There can be no assurance that patents that have issued will be held valid and enforceable in a court of law. Even for patents that are held valid and enforceable, the legal process associated with obtaining such a judgment is time consuming and costly. Additionally, issued patents can be subject to opposition or other proceedings that can result in the revocation of the patent or maintenance of the patent in amended form (and potentially in a form that renders the patent without commercially relevant or broad coverage). Further, our competitors may be able to circumvent and otherwise design around our patents. Even if a patent is issued and enforceable, because development and commercialization of pharmaceutical products can be subject to substantial delays, patents may expire early and provide only a short period of protection, if any, following the commercialization of products encompassed by our patent. We may have to participate in interference proceedings declared by the U.S. Patent and Trademark Office, which could result in a loss of the patent and/or substantial cost to us. Please refer to Item 1A, Risk Factors, including without limitation, If any of our pending patent applications do not issue, or are deemed invalid following issuance, we may lose valuable intellectual property protection.

U.S. and foreign patent rights and other proprietary rights exist that are owned by third parties and relate to pharmaceutical compositions and reagents, medical devices and equipment and methods for preparation, packaging and delivery of pharmaceutical compositions. We cannot predict with any certainty which, if any, of these rights will be considered relevant to our technology 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. We could incur substantial costs in defending ourselves and our partners against any such claims. Furthermore, parties making such claims may be able to obtain injunctive or other equitable relief, which could effectively block our ability to develop or commercialize some or all of our products in the U.S. and abroad and could result in the award of substantial damages. In the event of a claim of infringement, we or our partners may be required to obtain one or more licenses from third parties. 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 alternative technology. The failure to obtain licenses if needed may have a material adverse effect on our business, results of operations and financial condition. Please refer to Item 1A, Risk Factors, including without limitation, We may not be able to obtain intellectual property licenses related to the development of our drug candidates on a commercially reasonable basis, if at all.

It is our policy to require our employees and consultants, outside scientific collaborators, sponsored researchers and other advisors who receive confidential information from us to execute confidentiality agreements upon the commencement of employment or consulting relationships with us. These agreements provide that all confidential information developed or made known to the individual during the course of the individual s relationship with us is to be kept confidential and not disclosed to third parties except in specific circumstances. The agreements provide that all inventions conceived by an employee shall be our property. There can be no assurance, however, that these agreements will provide meaningful protection or adequate remedies for our trade secrets in the event of unauthorized use or disclosure of such information.

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Customer Concentrations

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. Roche, UCB Pharma, AstraZeneca, and Bayer represented 28%, 21%, 17%, and 10% of our revenue, respectively, for the year ended December 31, 2013. No other collaboration partner accounted for more than 10% of our total revenue during the year ended December 31, 2013.

Backlog

Pursuant to our collaboration agreements, we manufacture and supply our proprietary PEGylation materials. Inventory is produced and sales are made pursuant to customer purchase orders for delivery. The volume of our proprietary PEGylation materials actually ordered by our customers, as well as shipment schedules, are subject to frequent revisions that reflect changes in both the customers needs and our manufacturing capacity. In our partnered programs where we provide contract research services, those services are typically provided under a work plan that is subject to frequent revisions that change based on the development needs and status of the program. The backlog at a particular time is affected by a number of factors, including scheduled date of manufacture and delivery and development program status. In light of industry practice and our own experience, we do not believe that backlog as of any particular date is indicative of future results.

Competition

Competition in the pharmaceutical and biotechnology industry is intense and characterized by aggressive research and development and rapidly-evolving science, technology, and standards of medical care throughout the world. We frequently compete with pharmaceutical companies and other institutions with 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.

Science and Technology Competition

We believe that our proprietary and partnered products will compete with others in the market on the basis of one or more of the following parameters: efficacy, safety, ease of use and cost. We face intense science and technology competition from a multitude of technologies seeking to enhance the efficacy, safety and ease of use of approved drugs and new drug molecule candidates. A number of the drug candidates in our pipeline have direct and indirect competition from large pharmaceutical companies and biopharmaceutical companies. With our PEGylation and advanced polymer conjugate technologies, we believe we have competitive advantages relating to factors such as efficacy, safety, ease of use and cost for certain applications and molecules. We constantly monitor scientific and medical developments in order to improve our current technologies, seek licensing opportunities where appropriate, and determine the best applications for our technology platforms.

In the fields of PEGylation and advanced polymer conjugate technologies, our competitors include Biogen Idec Inc., Savient Pharmaceuticals, Inc., Dr. Reddy s Laboratories, Ltd., Enzon Pharmaceuticals, Inc., Mountain View Pharmaceuticals, Inc., SunBio Corporation, NOF Corporation, and Novo Nordisk A/S (assets formerly held by Neose Technologies, Inc.). Several other chemical, biotechnology and pharmaceutical companies may also be developing PEGylation technology, advanced polymer conjugate technology or technologies intended to deliver similar scientific and medical benefits. Some of these companies license intellectual property or PEGylation materials to other companies, while others apply the technology to create their own drug candidates.

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Product and Program Specific Competition

Naloxegol (formerly NKTR-118) (orally-available peripheral opioid antagonist)

There are no once-daily oral drugs that act specifically to block or reverse the action of opioids on receptors in the gastrointestinal tract which are approved specifically for the treatment of opioid-induced constipation (OIC) or opioid bowel dysfunction (OBD) in patients with chronic, non-cancer pain. The only approved treatment for opioid-induced constipation in adults with chronic, non-cancer pain is a twice daily oral therapy called AMITIZA (lubiprostone), which acts by specifically activating CIC-2 chloride channels in the gastrointestinal tract to increase secretions. AMITIZA is marketed by Sucampo Pharmaceuticals and Takeda. There is also a subcutaneous treatment known as methylnaltrexone bromide marketed by Salix Pharmaceuticals, Ltd under a license from Progenics Pharmaceuticals, Inc. Methylnaltrexone bromide is indicated for the treatment of opioid-induced constipation only in patients with advanced illness who are receiving palliative care, when response to laxative therapy has not been sufficient. Other therapies used to treat OIC and OBD include over-the-counter laxatives and stool softeners, such as docusate sodium, senna, and milk of magnesia. These therapies do not address the underlying cause of constipation as a result of opioid use and are generally viewed as ineffective or only partially effective to treat the symptoms of OIC and OBD.

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. Potential competitors include Progenics Pharmaceuticals, Inc. in collaboration with Salix Pharmaceuticals, Ltd., Cubist Pharmaceuticals, Inc., GlaxoSmithKline plc, Mundipharma Int. Limited, Theravance, Inc., Develco Pharma, Sucampo Pharmaceuticals, Inc., and Takeda Pharmaceutical Company Limited.

Etirinotecan pegol (NKTR-102, next-generation, long acting topoisomerase I inhibitor)

There are a number of chemotherapies and cancer therapies approved today and in various stages of clinical development for breast and ovarian cancers including but not limited to: Abraxane (paclitaxel protein-bound particles for injectable suspension (albumin bound)), Afinitor® (everolimus), Doxil® (doxorubicin HCl), Ellence® (epirubicin), Gemzar® (gemcitabine), Halaven® (eribulin), Herceptin® (trastuzumab), Hycamtin® (topotecan), Ixempra® (ixabepilone), Navelbine® (vinolrebine), Paraplatin® (carboplatin), Taxol® (paclitaxel) and Taxotere® (docetaxel). These therapies are only partially effective in treating breast and ovarian cancer. Major pharmaceutical or biotechnology companies with approved drugs or drugs in development for these cancers include Bristol-Meyers Squibb Company, Eisai, Inc., Roche Holding Group (including its Genentech subsidiary), GlaxoSmithKline plc, Pfizer, Inc., Eli Lilly & Co., Johnson & Johnson, Sanofi Aventis S.A., and many others. There are currently no drugs in Phase 3 development to specifically treat metastatic breast cancer in all receptor types following anthracycline, taxane and capecitabine therapy in either the adjuvant or metastatic setting.

There are also a number of chemotherapies and cancer therapies approved today and in clinical development for the treatment of colorectal cancer. Approved therapies for the treatment of colorectal cancer include Eloxatin® (oxaliplatin), Camptosar® (irinotecan), Avastin® (bevacizumab), Zaltrap® (Ziv-afilbercept), Stivarga® (regorafenib), Erbitux® (cetuximab), Vectibix® (panitumumab), Xeloda® (capecitabine), Adrucil® (fluorouracil), and Wellcovorin® (leucovorin). These therapies are only partially effective in treating the disease. 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. If these drugs are approved, they could be competitive with etirinotecan pegol if it is approved by government health authorities. These include products in development from Bristol-Myers Squibb Company, Pfizer, Inc., GlaxoSmithKline plc, Antigenics, Inc., F. Hoffman-La Roche Ltd, Novartis AG, Cell Therapeutics, Inc., Neopharm Inc., Meditech Research Ltd, Alchemia Limited, Enzon Pharmaceuticals Inc. and many others.

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BAY41-6551 (Amikacin Inhale, formerly NKTR-061)

There are currently no approved drugs on the market for adjunctive treatment or prevention of gram-negative pneumonias in mechanically ventilated patients which are also administered via the pulmonary route. The current standard of care includes approved intravenous antibiotics which are partially effective for the treatment of either hospital-acquired pneumonia or ventilator-associated pneumonia in patients on mechanical ventilators. These drugs include drugs that fall into the categories of antipseudomonal cephalosporins, antipseudomonal carbepenems, beta-lactam/beta-lactamase inhibitors, antipseudomonal fluoroquinolones, such as ciprofloxacin or levofloxacin, and aminoglycosides, such as amikacin, gentamycin or tobramycin.

BAX 855 (PEGylated rFVIII)

There are other long-acting Factor VII programs in late-stage development for hemophilia A patients. Biogen Idec Inc. has completed a Phase 3 development program for ELOCTATE, a recombinant factor VIII Fc fusion protein, which is designed to be longer acting than current treatments available for hemophilia A patients. Biogen Idec Inc. submitted a Biologics License Application to the FDA for marketing approval of ELOCTATE during the first quarter of 2013. In addition, Bayer Healthcare has an ongoing Phase 3 clinical development program for BAY94-9027, a PEGylated Factor VIII molecule, which is also designed to be longer acting than current treatments available for hemophilia A patients. ELOCTATE and BAY94-9027, if approved by health authorities, will be competitive to BAX 855 in the longer-acting Factor VIII market, if BAX 855 successfully completes Phase 3 clinical development and is approved by health authorities.

NKTR-181(mu-opioid analgesic molecule for chronic pain)

There are numerous companies developing pain therapies designed to have less abuse potential primarily through formulation technologies and techniques applied to existing pain therapies. Potential competitors include Acura Pharmaceuticals, Inc., Collegium Pharmaceutical, Inc., Egalet Ltd, Elite Pharmaceuticals, Inc., Endo Health Solutions Inc., KemPharm, Inc., Pfizer, Inc., Purdue Pharma L.P., and Signature Therapeutics, Inc.

Research and Development

Our total research and development expenditures can be disaggregated into the following significant types of expenses (in millions):

	Year Ended December 31,		
	2013	2012	2011
Third party and direct materials costs	105.6	65.6	50.4
Personnel, overhead and other costs	69.0	68.8	59.5
Stock-based compensation and depreciation	15.4	14.3	16.9
Research and development expense	$ 190.0	$ 148.7	$ 126.8

Manufacturing and Supply

We have a manufacturing facility located in Huntsville, Alabama that is capable of manufacturing PEGylated derivatives and starting materials for active pharmaceutical ingredients (APIs). The facility is also used to produce APIs to support the early phases of clinical development of our proprietary drug candidates. The facility and associated equipment are designed and operated to be consistent with all applicable laws and regulations.

As we do not maintain the capability to manufacture finished drug products, we utilize contract manufacturers to manufacture the finished drug product for us. We source drug starting materials for our manufacturing activities from one or more suppliers. For the drug starting materials necessary for our proprietary

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drug candidate development, we have agreements for the supply of such drug components with drug manufacturers or suppliers that we believe have sufficient capacity to meet our demands. However, from time to time, we source critical raw materials and services from one or a limited number of suppliers and there is a risk that if such supply or services were interrupted, it would materially harm our business. In addition, we typically order raw materials and services on a purchase order basis and do not enter into long-term dedicated capacity or minimum supply arrangements. We utilize the services of contract manufacturers to manufacture APIs required for later phases of clinical development and eventual commercialization for us under all applicable laws and regulations.

Environment

As a manufacturer of PEG reagents for the U.S. market, we are subject to inspections by the FDA for compliance with cGMP and other U.S. regulatory requirements, including U.S. federal, state and local regulations regarding environmental protection and hazardous and controlled substance controls, among others. Environmental laws and regulations are complex, change frequently and have tended to become more stringent over time. We have incurred, and may continue to incur, significant expenditures to ensure we are in compliance with these laws and regulations. We would be subject to significant penalties for failure to comply with these laws and regulations.

Employees and Consultants

As of December 31, 2013, we had 445 employees, of which 337 employees were engaged in research and development, commercial operations and quality activities and 108 employees were engaged in general administration and business development. Of the 445 employees, 363 were located in the United States and 82 were located in India. We have a number of employees who hold advanced degrees, such as Ph.D.s. None of our employees are covered by a collective bargaining agreement, and we have experienced no work stoppages. We believe that we maintain good relations with our employees.

To complement our own expert professional staff, we utilize specialists in regulatory affairs, pharmacovigilance, process engineering, manufacturing, quality assurance, clinical development and business development. These individuals include scientific advisors as well as independent consultants.

Available Information

Our website address is *http://www.nektar.com*. The information in, or that can be accessed through, our website is not part of this annual report on Form 10-K. Our annual reports on Form 10-K, quarterly reports on Form 10-Q and current reports on Form 8-K and amendments to those reports are available, free of charge, on or through our website as soon as reasonably practicable after we electronically file such material with, or furnish it to, the Securities Exchange Commission (SEC). The public may read and copy any materials we file with the SEC at the SEC s Public Reference Room at 100 F Street, NE, Washington, D.C. 20549. Information on the operation of the Public Reference Room can be obtained by calling 1-800-SEC-0330. The SEC maintains an Internet site that contains reports, proxy and information statements and other information regarding our filings at *www.sec.gov*.

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EXECUTIVE OFFICERS OF THE REGISTRANT

The following table sets forth the names, ages and positions of our executive officers as of February 27, 2014:

Name	Age	Position
Howard W. Robin	61	Director, President and Chief Executive Officer
John Nicholson	62	Senior Vice President and Chief Financial Officer
Robert A. Medve, M.D.	48	Senior Vice President and Chief Medical Officer
Stephen K. Doberstein, Ph.D.	55	Senior Vice President and Chief Scientific Officer
Gil M. Labrucherie, J.D.	42	Senior Vice President, General Counsel and Secretary
Maninder Hora, Ph.D	60	Senior Vice President, Pharmaceutical Development and Manufacturing Operations
Jillian B. Thomsen	48	Senior Vice President, Finance and Chief Accounting Officer

Howard W. Robin has served as our President and Chief Executive Officer since January 2007 and has served as a member of our board of directors since February 2007. Mr. Robin served as Chief Executive Officer, President and a director of Sirna Therapeutics, Inc., a biotechnology company, from July 2001 to November 2006 and from January 2001 to June 2001, served as their Chief Operating Officer, President and as a director. From 1991 to 2001, Mr. Robin was Corporate Vice President and General Manager at Berlex Laboratories, Inc. (Berlex), a pharmaceutical products company that is a subsidiary of Schering, AG, and from 1987 to 1991 he served as Vice President of Finance and Business Development and Chief Financial Officer of Berlex. From 1984 to 1987, Mr. Robin was Director of Business Planning and Development at Berlex. He was a Senior Associate with Arthur Andersen & Co. prior to joining Berlex. Mr. Robin serves as a director of the Biotechnology Industry Organization, the world s largest biotechnology industry trade organization, and also serves as a director of BayBio, a non-profit trade association serving the Northern California life sciences community. He received his B.S. in Accounting and Finance from Fairleigh Dickinson University in 1974.

John Nicholson has served as our Senior Vice President and Chief Financial Officer since December 2007. Mr. Nicholson joined the Company as Senior Vice President of Corporate Development and Business Operations in October 2007 and was appointed Senior Vice President and Chief Financial Officer in December 2007. Before joining Nektar, Mr. Nicholson spent 18 years in various executive roles at Schering Berlin, Inc., the U.S. management holding company of Bayer Schering Pharma AG, a pharmaceutical company. From 1997 to September 2007, Mr. Nicholson served as Schering Berlin Inc. s Vice President of Corporate Development and Treasurer. From 2001 to September 2007, he concurrently served as President of Schering Berlin Insurance Co., and from February 2007 through September 2007, he also concurrently served as President of Bayer Pharma Chemicals and Schering Berlin Capital Corp. Mr. Nicholson holds a B.B.A. from the University of Toledo.

Robert A. Medve, M.D. has served as our Senior Vice President and Chief Medical Officer since June 2011 and previously served as our Vice President Drug Development and Medical Affairs when he joined Nektar in March 2011 until June 2011. From November 2006 to March 2011, he was Chief Medical and Regulatory Officer at NeurAxon, Inc., a privately held biotechnology company developing drug candidates for the treatment of pain and CNS disorders. From April 2006 to November 2006, Dr. Medve served as Corporate Vice President, Science, Research and Development for Lifetree Clinical Research, and thereafter served in a consulting capacity from time to time. From May 2003 to November 2005, Dr. Medve served as Senior Vice President, Drug Development and Chief Medical and Regulatory Officer for Metaphore Pharmaceuticals, Inc., a biotechnology company developing drug candidates for pain and inflammation. From January 1998 to May 2003, he served in various leadership positions at Johnson & Johnson, a pharmaceutical company, most recently as Executive Director of Pediatric Drug Development. From May 1996 to January 1998, he served in the medical affairs group at Knoll Pharmaceutical Company, a wholly-owned pharmaceutical subsidiary of BASF acquired by Abbott Laboratories in 2001, most recently as Director of Medical Affairs. Prior to joining industry, Dr. Medve served

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as the Director of Pediatric Pain Management and Instructor of Anesthesiology at the State University of New York at Buffalo (SUNY) and also completed a Pain Management Fellowship at SUNY. He completed his residency in anesthesia at Thomas Jefferson University Hospital and served as a surgical intern at Mercy Health Systems Medical Center. Dr. Medve received his M.D. from Jefferson Medical College and received his B.S. in Biology from the Pennsylvania State University.

Stephen K. Doberstein, Ph.D. has served as our Senior Vice President and Chief Scientific Officer since January 2010. From October 2008 through December 2009, Dr. Doberstein served as Vice President, Research at Xoma (US) LLC, a publicly traded clinical stage biotechnology company. From July 2004 until August 2008, he served as Vice President, Research at privately held Five Prime Therapeutics, Inc., a clinical stage biotechnology company. From September 2001 until July 2004, Dr. Doberstein was Vice President, Research at privately held Xencor, Inc., a clinical stage biotechnology company. From 1997 to 2000, he held various pharmaceutical research positions at Exelixis, Inc. (Exelixis), a publicly traded clinical stage biotechnology company. Prior to working at Exelixis, Dr. Doberstein was a Howard Hughes Postdoctoral Fellow and a Muscular Dystrophy Association Senior Postdoctoral Fellow at the University of California, Berkeley. Dr. Doberstein received his Ph.D. Biochemistry, Cell and Molecular Biology from the Johns Hopkins University School of Medicine and received a B.S. in Chemical Engineering from the University of Delaware.

Gil M. Labrucherie has served as our Senior Vice President, General Counsel and Secretary since April 2007, responsible for all aspects of our legal affairs. Mr. Labrucherie served as our Vice President, Corporate Legal from October 2005 through April 2007. From October 2000 to September 2005, Mr. Labrucherie was Vice President of Corporate Development at E2open. While at E2open, Mr. Labrucherie was responsible for global corporate alliances and merger and acquisitions. Prior to E2open, he was the Senior Director of Corporate Development at AltaVista Company, an Internet search company, where he was responsible for strategic partnerships and mergers and acquisitions. Mr. Labrucherie serves on the General Counsel Committee of the Biotechnology Industry Organization, the world s largest biotechnology industry trade organization. Mr. Labrucherie began his career as an associate in the corporate practice of the law firm of Wilson Sonsini Goodrich & Rosati, P.C. Mr. Labrucherie received his J.D. from the Berkeley Law School and a B.A. from the University of California Davis.

Maninder Hora, Ph.D. has served as our Senior Vice President, Pharmaceutical Development and Manufacturing Operations since August 2010. From December 2008 to July 2010, he was Vice President, Product and Quality Operations at Facet Biotech Corporation, a clinical stage biotechnology company, which was acquired by Abbott Laboratories in April 2010. From July 2006 to December 2008, Dr. Hora served in various management capacities at PDL Biopharma, Inc., a biopharmaceutical company, most recently as Vice President, Product Operations. From 1986 to 2006, Dr. Hora held positions of increasing responsibility with Chiron Corporation (Chiron and now Novartis), a pharmaceutical company, serving most recently at Chiron as Vice President of Process and Product Development. Dr. Hora served as a key member of various teams that successfully registered eight drugs or vaccines in the U.S. and Europe during his 20-year tenure at Chiron. Dr. Hora has also held positions at Wyeth Pharmaceuticals and GlaxoSmithKline plc prior to joining Chiron. Dr. Hora completed his Ph.D. in Bioengineering from the Indian Institute of Technology, Delhi, India, and was a Fulbright Scholar at the University of Washington, and received his B.S. in chemistry from the University of Jabalpur.

Jillian B. Thomsen has served as our Senior Vice President, Finance and Chief Accounting Officer since February 2010. From March 2006 through March 2008, Ms. Thomsen served as our Vice President Finance and Corporate Controller and from April 2008 through January 2010 she served as our Vice President Finance and Chief Accounting Officer. Before joining Nektar, Ms. Thomsen was Vice President Finance and Deputy Corporate Controller of Calpine Corporation from September 2002 to February 2006. Ms. Thomsen is a certified public accountant and previously was a senior manager at Arthur Andersen LLP, where she worked from 1990 to 2002, and specialized in audits of multinational consumer products, life sciences, manufacturing and energy companies. Ms. Thomsen holds a Masters of Accountancy from the University of Denver and a B.A. in Business Economics from Colorado College.

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Item 1A. ***Risk Factors***

We are providing the following cautionary discussion of risk factors, uncertainties and assumptions that we believe are relevant to our business. These are factors that, individually or in the aggregate, we think could cause our actual results to differ materially from expected and historical results and our forward-looking statements. We note these factors for investors as permitted by Section 21E of the Exchange Act and Section 27A of the Securities Act. You should understand that it is not possible to predict or identify all such factors. Consequently, you should not consider this section to be a complete discussion of all potential risks or uncertainties that may substantially impact our business. Moreover, we operate in a competitive and rapidly changing environment. New factors emerge from time to time and it is not possible to predict the impact of all of these factors on our business, financial condition or results of operations.

Risks Related to Our Business

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

We have a number of proprietary drug candidates and partnered drug candidates in research and development ranging from the early discovery research phase through preclinical testing and clinical trials. Preclinical testing and clinical studies are long, expensive and highly uncertain processes. It will take us, or our collaborative partners, several years to complete clinical studies. The start or end of a clinical study is often delayed or halted due to changing regulatory requirements, manufacturing challenges, required clinical trial administrative actions, slower than anticipated patient enrollment, changing standards of care, availability or prevalence of use of a comparator drug or required prior therapy, clinical outcomes, or our and our partners financial constraints.

Drug development is a highly uncertain scientific and medical endeavor, and failure can unexpectedly occur at any stage of preclinical and clinical development. Typically, there is a high rate of attrition for drug candidates in preclinical and clinical trials due to scientific feasibility, safety, efficacy, changing standards of medical care and other variables. The risk of failure increases for our drug candidates that are based on new technologies, such as the application of our advanced polymer conjugate technology to small molecules, including naloxegol, etirinotecan pegol (also known as NKTR-102), NKTR-181, NKTR-192, NKTR-171 and other drug candidates currently in discovery research or preclinical development. The failure of one or more of our drug candidates could have a material adverse effect on our business, financial condition and results of operations.

If we or our partners do not obtain regulatory approval for our drug 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 drug 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. Drug candidates must undergo rigorous animal and human testing and an extensive review process for safety and efficacy by the U.S. Food and Drug Administration (FDA) and equivalent foreign government health authorities. The time required for obtaining regulatory decisions is uncertain and difficult to predict. The FDA and other U.S. and foreign health authorities have substantial discretion, at any phase of development, to terminate clinical studies, require additional clinical development or other testing, delay or withhold registration and marketing approval and mandate product withdrawals, including recalls. Further, health authorities have the discretion to analyze data using their own methodologies that may differ from those used by us or our partners which could lead such authorities to arrive at different conclusions regarding the safety or efficacy of a drug candidate. In addition, undesirable side effects caused by our drug 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.

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Even if we or our partners receive regulatory approval of a product, the approval may limit the indicated uses for which the drug may be marketed. Our partnered drugs 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.

If the FDA requires a cardiovascular safety study for naloxegol, it could have a material adverse impact on the naloxegol program and our business prospects and financial condition.

The FDA is exploring whether there is any evidence of potential elevated cardiovascular risk possibly related to the class of mu-opioid antagonist drugs and naloxegol is a mu-opioid antagonist. AstraZeneca completed a 52-week, long-term controlled safety trial of naloxegol as part of the Phase 3 naloxegol development program. The FDA s general safety concern is based on data from other mu-opioid antagonist programs that may indicate increased cardiovascular risk associated with opioid withdrawal or the antagonism of the delta subtype of the opioid receptor, for which the FDA has not yet made a causal connection between these mechanisms and elevated cardiovascular risk. The FDA is currently planning to hold an advisory committee meeting for the purposes of reviewing the cardiovascular safety study requirements for peripheral mu-opioid receptor antagonists including naloxegol. The advisory committee meeting, which had been originally scheduled for March 10-11, 2014, is being rescheduled due to scheduling conflicts.

We amended our license agreement with AstraZeneca to enter into a risk sharing arrangement in the event that pre-approval or post-approval cardiovascular safety studies are required by the FDA for naloxegol. The amendment provides that if the FDA requires a cardiovascular safety study as a condition to approval of naloxegol and, as a result, AstraZeneca terminates its agreement with us in its entirety, we would be required to repay AstraZeneca the $70.0 million we received upon the FDA s acceptance for review of the naloxegol NDA plus accrued interest at 4.5% compounded annually. If AstraZeneca elects to terminate the agreement only with respect to its license agreement rights in the U.S. due to a pre-approval cardiovascular safety study, then such amount would be paid through a 50% reduction of non-U.S. royalty amounts otherwise payable to us until the aggregate amount of such royalty reduction equals the total principal amount of $70.0 million plus accumulated interest at 4.5% compounded annually. On the other hand, if the FDA determines a pre-approval cardiovascular safety study of naloxegol is not required, AstraZeneca is obligated to pay us an additional $35.0 million milestone payment. However, if the FDA requires a post-approval cardiovascular safety study as a condition to regulatory approval, then the royalty rate payable to us from net sales of naloxegol in the U.S. by AstraZeneca would be reduced by two percentage points until the aggregate amount of such royalty payment reduction is equal to a maximum of $35.0 million.

Even with success in previously completed clinical trials, the risk of clinical failure for any drug candidate remains high prior to regulatory approval.

A number of companies have suffered significant unforeseen failures in late stage clinical studies due to factors such as inconclusive efficacy or safety, even after achieving positive results in earlier clinical studies that were satisfactory both to them and to reviewing government health authorities. While etirinotecan pegol, Amikacin Inhale, and BAX 855 have each demonstrated positive results from earlier clinical studies, there is a substantial risk that Phase 3 clinical study outcomes for these drug candidates from larger patient populations will not demonstrate positive efficacy, safety or other clinical outcomes sufficient to support regulatory filings and achieve regulatory approval. Phase 3 clinical study outcomes remain very unpredictable and it is possible that one or more of these Phase 3 clinical studies could fail at any time due to efficacy, safety or other important clinical findings or regulatory requirements. If one or more of these drug candidates fail in Phase 3 clinical studies, it would have a material adverse effect on our business, financial condition and results of operations.

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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 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 our partner s performance;
- research and development performance and reimbursement obligations for our personnel and other resources allocated to partnered drug candidate development programs;
- 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 collaboration;
- royalties on drug sales based on a number of complex variables, including net sales calculations, geography, scope of patent claim coverage, patent life, generic competitors, bundled pricing and other factors; and
- indemnity obligations for intellectual property infringement, product liability and certain other claims.

We are a party to certain significant agreements, including an asset purchase agreement with Novartis pursuant to which we sold a significant portion of our pulmonary business at the end of 2008, the worldwide exclusive license agreement with AstraZeneca related to the further development and commercialization of naloxegol, and the purchase and sale agreement with RPI Finance Trust (RPI) related to the sale of our royalty interests in UCB s CIMZIA® and Roche s MIRCERA® that we completed in February 2012. Each of these agreements contains complex representations and warranties, covenants and indemnification obligations. If we breach any of our agreements with Novartis, AstraZeneca, RPI or any third party agreements impacted by these complex transactions, such a breach could result in substantial future liability and harm our financial condition.

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 effect on our business, financial condition and results of operations.

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We have substantial future capital requirements and there is a risk we may not have access to sufficient capital to meet our current business plan. If we do not receive substantial milestone payments from our existing collaboration agreements, execute new high value collaborations or other arrangements, or are unable to raise additional capital in one or more financing transactions, we would be unable to continue our current level of investment in research and development.

As of December 31, 2013, we had cash and investments in marketable securities valued at approximately $262.0 million, of which $25.0 million was restricted in relation to our 12.0% senior secured notes, and indebtedness of approximately $160.8 million. The indebtedness includes approximately $125.0 million in senior secured notes due July 2017, but excludes our long-term liability relating to the sale of future royalties. While this royalty obligation liability will not generally be settled in cash, we expect to be required to make a cash payment of $7.0 million in 2014, as a certain performance target is not expected to be met. While we believe that our cash position will be sufficient to meet our liquidity requirements through at least the next 12 months, our future capital requirements will depend upon numerous unpredictable factors, including:

- the cost, timing and outcomes of clinical studies and regulatory reviews of our proprietary drug candidates that we have licensed to our collaboration partners important examples include naloxegol that has been licensed to AstraZeneca, Amikacin Inhale that has been licensed to Bayer, and BAX 855 that is being developed by Baxter under an intellectual property license from us;

- if and when we receive potential milestone payments and royalties from our existing collaborations if the drug candidates subject to those collaborations achieve clinical, regulatory or commercial success;

- the progress, timing, cost and results of our clinical development programs in particular our Phase 3 BEACON study for etirinotecan pegol and our clinical studies for NKTR-181;

- the success, progress, timing and costs of our efforts to implement new collaborations, licenses and other transactions that increase our current net cash, such as the sale of additional royalty interests held by us, term loan or other debt arrangements, and the issuance of securities;

- the outcome of the regulatory review process and commercial success of drug products for which we are entitled to receive royalties (e.g., naloxegol being developed by AstraZeneca);

- the number of patients, enrollment criteria, primary and secondary endpoints, and the number of clinical studies required by the government health authorities in order to consider for approval our drug candidates and those of our collaboration partners;

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

- disputes concerning patents, proprietary rights, or license and collaboration agreements that negatively impact our receipt of milestone payments or royalties or require us to make significant payments arising from licenses, settlements, adverse judgments or ongoing royalties.

A significant multi-year capital commitment is required to advance our drug candidates through the various stages of research and development in order to generate sufficient data to enable high value collaboration partnerships with significant upfront payments or to successfully achieve regulatory approval. In the event we do not enter into any new collaboration partnerships with significant upfront payments and we choose to continue our later stage research and development programs, we may need to pursue financing alternatives, including dilutive equity-based financings, such as an offering of convertible debt or common stock, which would dilute the percentage ownership of our current common stockholders and could significantly lower the market value of our common stock. If sufficient capital is not available to us or is not available on

commercially reasonable terms, it could require us to delay or reduce one or more of our research and development programs. If we are unable to sufficiently advance our research and development programs, it could substantially impair the value of such programs and result in a material adverse effect on our business, financial condition and results of operations.

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While we have conducted numerous experiments using laboratory and home-based chemistry techniques that have not been able to convert NKTR-181 into a rapid-acting and more abusable opioid, there is a risk that in the future a technique could be discovered to convert NKTR-181 into a rapid-acting and more abusable opioid, which would significantly diminish the value of this drug candidate.

An important objective of our NKTR-181 drug development program is to create a unique opioid molecule that does not rapidly enter a patient s central nervous system and therefore has the potential to be less susceptible to abuse than alternative opioid therapies. To date, we have conducted numerous experiments using laboratory and home-based chemistry techniques that have been unable to convert NKTR-181 into a rapidly-acting, more abusable form of opioid. In the future, an alternative chemistry technique, process or method of administration, or combination thereof, may be discovered to enable the conversion of NKTR-181 into a more abusable opioid, which could significantly and negatively impact the potential of NKTR-181.

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 capital requirements. The timing of new collaboration partnerships is difficult to predict due to availability of clinical data, the outcomes from our clinical studies, 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 collaboration arrangements with favorable commercial terms with respect to our existing and future drug candidates or the licensing of our intellectual property, or if any arrangements we negotiate, or have negotiated, are terminated, it could have a material adverse effect on our business, financial condition and results of operations.

Preliminary and interim data from our clinical studies that we announce or publish from time to time is subject to audit and verification procedures that could result in material changes in the final data and may change as more patient data becomes available.

From time to time, we publish preliminary or interim data from our clinical studies. For example, we have announced preliminary topline data from our Phase 2 clinical study for NKTR-181. Preliminary data remains subject to audit confirmation and verification procedures that may result in the final data being materially different from the preliminary data we previously published. Interim data is also subject to the risk that one or more of the clinical outcomes may materially change as patient enrollment continues and more patient data becomes available. As a result, preliminary and interim data should be viewed with caution until the final data are available. Material adverse changes in the final data could significantly harm our business prospects.

Delays in clinical studies are common and have many causes, and any significant delay in clinical studies being conducted by us or our partners could result in delay in regulatory approvals and jeopardize the ability to proceed to commercialization.

We or our partners may experience delays in clinical trials of drug candidates. Etirinotecan pegol in patients with metastatic breast cancer and BAX 855 are currently in Phase 3 clinical studies, and Bayer has initiated Phase 3 clinical development of BAY41-6551 with the first patient enrolled in April 2013. A Phase 2 clinical study for etirinotecan pegol in patients with metastatic colorectal cancer is still open for enrollment. We are currently evaluating the recently announced results from our Phase 2 efficacy clinical study for NKTR-181 and are in the planning stage for a Phase 3 clinical study for NKTR-181 including continuing consultations with leaders in the pain clinical trial field and interactions with the FDA. Because it is unlikely that we will be able to identify a single cause for the NKTR-181 Phase 2 study not meeting its primary efficacy endpoint, there is increased risk in effectively designing a Phase 3 clinical study to demonstrate the efficacy of NKTR-181. These

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and other of our planned clinical studies may not begin on time, have an effective design, enroll a sufficient number of patients or be completed on schedule, if at all. Our clinical trials for any of our product candidates could be delayed for a variety of reasons, including:

- delays in obtaining regulatory approval to commence a clinical study;
- delays in reaching agreement with applicable health authorities on a clinical study design;
- imposition of a clinical hold following an inspection of our clinical trial operations or trial sites by the FDA or other health authorities;
- suspension or termination of a clinical study by us, our partners, the FDA or foreign health authorities due to adverse side effects of a drug on subjects in the trial;
- delays in recruiting suitable patients to participate in a trial;
- delays in having patients complete participation in a trial or return for post-treatment follow-up;
- clinical sites dropping out of a trial to the detriment of enrollment rates;
- delays in manufacturing and delivery of sufficient supply of clinical trial materials; and
- changes in health authorities policies or guidance applicable to our drug candidates.

If initiation or completion of any of the planned clinical studies are delayed for our drug candidates for any of the above reasons or otherwise, the approval process could be delayed and the ability to commercialize and commence sales of these drug candidates could be materially harmed, which could have a material adverse effect on our business, financial condition and results of operations.

The commercial potential of a drug candidate in development is difficult to predict. If the market size for a new drug is significantly smaller than we anticipate, 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 important factors such as safety and efficacy compared to other available treatments, including potential generic drug alternatives with similar efficacy profiles, changing standards of care, third party payer reimbursement standards, patient and physician preferences, drug scheduling status, 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 government health authorities based on the expiration of regulatory exclusivity or our inability to prevent generic versions from coming to market by asserting our patents. If due to one or more of these risks the market potential for a drug candidate is lower than we anticipated, it could significantly and negatively impact the commercial terms of any collaboration partnership potential for such drug 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 business, financial condition and results of operations.

We may not be able to obtain intellectual property licenses related to the development of our drug candidates 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, methods of preparation and manufacturing, and methods of use and administration. We cannot predict with any certainty which, if any, patent references will be considered relevant to our or our collaboration 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

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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, we may be prevented from developing and selling the drug, which could significantly harm our business, results of operations, and financial condition.

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 and biotechnology companies, such as ours, are uncertain and involve complex legal and factual issues. We own more than 175 U.S. and 500 foreign patents and a number of pending patent applications that cover various aspects of our technologies. There can be no assurance that patents that have issued will be held valid and enforceable in a court of law. Even for patents that are held valid and enforceable, the legal process associated with obtaining such a judgment is time consuming and costly. Additionally, issued patents can be subject to opposition or other proceedings that can result in the revocation of the patent or maintenance of the patent in amended form (and potentially in a form that renders the patent without commercially relevant and/or broad coverage). Further, our competitors may be able to circumvent and otherwise design around our patents. Even if a patent is issued and enforceable, because development and commercialization of pharmaceutical products can be subject to substantial delays, patents may expire early and provide only a short period of protection, if any, following the commercialization of products encompassed by our patents. We may have to participate in interference proceedings declared by the U.S. Patent and Trademark Office, which could result in a loss of the patent and/or substantial cost to us.

We have filed patent applications, and plan 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 the patent applications for which we apply would actually issue as patents, or do so with commercially relevant and/or broad coverage. The coverage claimed in a patent application can be significantly reduced before the patent is issued. The scope of our claim coverage can be critical to our ability to enter into licensing transactions with third parties and our right to receive royalties from our collaboration partnerships. 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. In addition, there is no guarantee that we will be the first to file a patent application directed to an invention.

An adverse outcome in any judicial proceeding involving intellectual property, including patents, 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. In those instances where we seek an intellectual property license from another, we may not be able to obtain the license on a commercially reasonable basis, if at all, thereby raising concerns on our ability to freely commercialize our technologies or products.

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

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 platform or drug candidates 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 collaboration partners from intellectual property infringement, product liability and certain other claims, which could cause us to incur substantial costs and liability 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,

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from developing or commercializing, or deriving revenue from, certain drugs or drug candidates in the U.S. and abroad. Costs associated with litigation, substantial damage claims, indemnification claims or royalties paid for licenses from third parties could have a material adverse effect on our business, financial condition and results of operations.

Third-party claims involving proprietary rights or other matters could also result in substantial settlement payments or substantial damages to be paid by us. For instance, a settlement might require us to enter a license agreement under which we would pay substantial royalties or other compensation to a third party, diminishing our future economic returns from the related drug. In December 2013, we entered into a litigation settlement with the Research Foundation of the State University of New York (SUNY) pursuant to which we agree to the payment of a total of $12 million in future installments and certain other terms and conditions in exchange for the full release of certain breach of contract claims by SUNY. In October 2011, we entered into a settlement related to trade secret and breach of contract litigation where we agreed to make an upfront payment of $2.7 million and a future contingent payment of $3.0 million if a certain drug candidate receives FDA approval. 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.

In addition, from time to time, we may in the future assert claims against third parties, based on infringement of our proprietary rights or otherwise. Any such claims may not ultimately be successful, and we may incur substantial costs and liabilities in pursuing them.

Our manufacturing operations and those of our contract manufacturers are subject to laws and other governmental regulatory 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 with laws and regulations governing manufacture and distribution of controlled substances, and are subject to inspections by the FDA, DEA 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 and other laws and governmental 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 laws and 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 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.

If we or our contract manufacturers are not able to manufacture drugs or drug substances in sufficient quantities that meet applicable quality standards, it could delay clinical studies, result in reduced sales or constitute a breach of our contractual obligations, any of which could significantly harm our business, financial condition and results of operations.

If we or our contract manufacturers are not able to manufacture and supply sufficient drug quantities meeting applicable quality standards required to support large clinical studies or commercial manufacturing in a

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timely manner, we risk delaying our clinical studies or those of our collaboration partners, reducing drug sales by our collaboration partners or breaching contractual obligations. As a result, we could incur substantial costs and damages, and reduce or even eliminate product or royalty revenue. In some cases, we rely on contract manufacturing organizations to manufacture and supply drug product for our clinical studies and those of our collaboration partners. Pharmaceutical manufacturing of drugs and devices 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 and analytical methods validations, device performance and challenges in controlling for all of these variables. We have faced and may in the future face significant difficulties, delays and unexpected expenses as we validate third party contract manufacturers required for drug and device supply to support our clinical studies and the clinical studies and products of our collaboration partners. Failure by us or our contract manufacturers to supply drug product or devices in sufficient quantities that meet all applicable quality requirements could result in supply shortages for our clinical studies or the clinical studies and commercial activities of our collaboration partners. Such failures could significantly and materially delay clinical trials and regulatory submissions or result in reduced sales, any of which could significantly harm our business prospects, results of operations and financial condition.

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. We experienced repeated significant delays in starting the Phase 3 clinical development program for Amikacin Inhale as we sought to finalize and validate the device design with a demonstrated capability to be manufactured at commercial scale. 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 and 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.

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, from which we receive contract research payments, milestone payments based on clinical progress, regulatory progress or net sales achievements, royalties and manufacturing revenue. Significant variations in the timing of receipt of cash payments and our recognition of revenue can result from significant milestone payments based on the execution of new collaboration agreements, the timing of clinical outcomes, regulatory approval, commercial launch and the achievement of certain annual sales thresholds. 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 collaboration partners achieve clinical, regulatory and sales milestones, the timing of regulatory approvals in one or more major markets, reimbursement levels by private and government payers, and the market introduction of new drugs or generic versions of the approved drug, as well as other factors. Our past revenue generated from collaboration agreements is not necessarily indicative of our future revenue. If any of our existing or future collaboration partners fails to develop, obtain regulatory approval for, manufacture or ultimately commercialize any product candidate under our collaboration agreement, our business, financial condition, results of operations and prospectus could be materially and adversely affected.

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

When we sign a collaborative development agreement or license agreement to develop a drug 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 drug candidate; and/or
- market and sell the drugs 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;
- 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;
- 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 collaboration agreements in the past that have been subsequently terminated, such as our collaboration agreement with Pfizer, Inc. for the development and commercialization of inhaled insulin that was terminated by Pfizer, Inc. in November 2007. If other collaboration agreements 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.

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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 currently have no sales, marketing or distribution capabilities. To commercialize any of our drugs that receive regulatory approval for commercialization, we must either develop internal sales, marketing and distribution capabilities, which would 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 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 collaborations, 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 the event that we market our products without a partner, we would be required to build a sales and marketing organization and infrastructure, which would require a significant investment and we may not be successful in building this organization and infrastructure in a timely or efficient manner.

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. 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 our costs.

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 difficult to

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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 year ended December 31, 2013, we reported a net loss of $162.0 million. 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 drugs 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 the BEACON study and the clinical studies for NKTR-181;
- 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 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. We rely heavily on these parties for successful execution of our clinical trials. Though we are ultimately responsible for the results of their

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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 trials, 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.

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 Biogen Idec Inc., Savient Pharmaceuticals, Inc., Dr. Reddy s Laboratories Ltd., 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 naloxegol, there are currently several alternative therapies used to address opioid-induced constipation (OIC) and opioid-induced bowel dysfunction (OBD), including subcutaneous Relistor® (methylnaltrexone bromide), oral Amitizia (lubiprostone), 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 Cubist Pharmaceuticals, Inc., Progenics Pharmaceuticals, Inc. in collaboration with Salix Pharmaceuticals, Ltd., Mundipharma Int. Limited, Sucampo Pharmaceuticals, Inc., Develco Pharma, Alkermes, Inc., GlaxoSmithKline plc, Theravance, Inc., and Takeda Pharmaceutical Company Limited. For etirinotecan pegol, there are a number of chemotherapies and cancer therapies approved today and in various stages of clinical development for breast and ovarian cancers, including, but not limited to: Abraxane® (paclitaxel protein-bound particles for injectable suspension (albumin bound)), Afinitor® (everolimus), Doxil® (doxorubicin HCl), Ellence® (epirubicin), Gemzar® (gemcitabine), Halaven® (eribulin), Herceptin® (trastuzumab), Hycamtin® (topotecan), Ixempra® (ixabepilone), Navelbine® (vinolrebine), Iniparib, Paraplatin® (carboplatin), Taxol® (paclitaxel) and Taxotere® (docetaxel). Major pharmaceutical or biotechnology companies with approved drugs or drugs in development for these cancers include, but are not limited to, Bristol-Meyers Squibb Company, Eli Lilly & Co., Roche, GlaxoSmithKline plc, Johnson and Johnson, Pfizer, Inc. Eisai, Inc., and Sanofi Aventis S.A. There are approved therapies for the treatment of colorectal cancer, including Eloxatin® (oxaliplatin), Camptosar® (irinotecan), Avastin® (bevacizumab), Zaltrap® (Ziv-afilbercept), Stivarga® (regorafenib), Erbitux® (cetuximab), Vectibix® (panitumumab), Xeloda® (capecitabine), Adrucil® (fluorouracil) and Wellcovorin ® (leucovorin). 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, and Enzon Pharmaceuticals, Inc.

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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.

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 drug 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 capital necessary to support this strategy. Our decision to bear a majority or all of the clinical development costs of etirinotecan pegol substantially increases our future capital requirements. 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 reductions in our workforce, which could 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.

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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, research, regulatory and finance, and may need to attract and retain marketing and distribution experts and develop additional expertise in our existing personnel. 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 or 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 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 earthquakes, floods, 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.

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.

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

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

Our stock price is volatile. During the year ended December 31, 2013, based on closing prices on The NASDAQ Global Select Market, our stock price ranged from $13.96 to $7.54 per share. We expect our stock price to remain volatile. A variety of factors may have a significant effect on the market price of our common stock, including:

- announcements of data from, or material developments in, our clinical studies and those of our collaboration partners, including data regarding efficacy and safety, delays in clinical development, regulatory approval or commercial launch;
- announcements by collaboration partners as to their plans or expectations related to drug candidates and approved drugs in which we have a substantial economic interest;
- announcements regarding terminations or disputes under our collaboration agreements;
- fluctuations in our results of operations;
- developments in patent or other proprietary rights, including intellectual property litigation or entering into intellectual property license agreements and the costs associated with those arrangements;
- announcements of technological innovations or new therapeutic products that may compete with our approved products or products under development;
- announcements of changes in governmental regulation affecting us or our competitors;
- litigation brought against us or third parties to whom we have indemnification obligations;
- public concern as to the safety of drug formulations developed by us or others;
- our financing needs and activities; and
- general market conditions.

The indenture governing the senior secured notes imposes significant operating and financial restrictions on us and our subsidiaries that may prevent us from pursuing certain business opportunities and restrict our ability to operate our business.

The indenture governing the senior secured notes contains covenants that restrict our and our subsidiaries ability to take various actions, such as:

incur or guarantee additional indebtedness or issue disqualified capital stock or cause certain of our subsidiaries to issue preferred stock;

pay dividends or distributions, redeem equity interests or subordinated indebtedness or make certain types of investments;

create or incur liens;

transfer, sell, lease or otherwise dispose of assets and issue or sell equity interests in certain of our subsidiaries;

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incur restrictions on certain of our subsidiaries ability to pay dividends or other distributions to the Company or to make intercompany loans or asset transfers;

enter into transactions with affiliates;

engage in any business other than businesses which are the same, similar, ancillary or reasonably related to our business as of July 11, 2012; and

consummate a merger, consolidation, reorganization or business combination, or sell, assign, transfer, lease or otherwise dispose of all or substantially all of our assets.

In addition, the indenture governing the senior secured notes contains a financial maintenance covenant requiring us to maintain a $25.0 million segregated cash reserve account until July 1, 2015 to be applied to interest payments on the notes in the event of a default, subject to certain conditions. This indenture also requires us not to permit, thereafter and through the quarter ending June 30, 2017, the aggregate balance of our unrestricted cash and cash equivalents at the end of any two consecutive fiscal quarters to be less than $25.0 million, subject to certain conditions. Our ability to comply with these covenants will likely be affected by many factors, including events beyond our control, and we may not satisfy those requirements. Our failure to comply with our debt-related obligations could result in an event of default under our other indebtedness and the acceleration of our other indebtedness, in whole or in part, could result in an event of default under the indenture governing the senior secured notes.

The restrictions contained in the indenture governing the senior secured notes could also limit our ability to plan for or react to market conditions, meet capital needs or otherwise restrict our activities or business plans and adversely affect our ability to finance our operations, enter into acquisitions or to engage in other business activities that would be in our interest.

Item 1B. ***Unresolved Staff Comments***

None.

Item 2. ***Properties***

California

We lease a 102,283 square foot facility in the Mission Bay Area of San Francisco, California (Mission Bay Facility), under an operating lease which expires in 2020. In November 2010, we moved into the Mission Bay Facility relocating all of our functions from the San Carlos, California facility (San Carlos Facility), including our corporate headquarters and research and development for our PEGylation and advanced polymer conjugate technology operations. In December 2011, we expanded our lease of the Mission Bay Facility to include an additional 24,002 square feet of space, which will expire in 2020, on the same date as the original lease agreement for the Mission Bay Facility.

Our lease for approximately 100,000 square feet of the San Carlos Facility is under a capital lease which expires in 2016. We have subleased all of the San Carlos Facility.

Alabama

We currently own four facilities consisting of approximately 165,000 square feet in Huntsville, Alabama, which house laboratories as well as administrative, clinical and commercial manufacturing facilities for our PEGylation and advanced polymer conjugate technology operations as well as manufacturing of APIs for early clinical studies.

In July 2012, we consolidated our U.S.-based research activities into our Mission Bay Facility and ceased use of one of our buildings located in Huntsville that was dedicated to research activities. We are currently seeking a buyer for the land and building.

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India

We own a research and development facility consisting of approximately 88,000 square feet, near Hyderabad, India. In addition, we lease approximately 504 square feet of office space in Hyderabad, India, under a one-year operating lease that will expire in 2014.

Item 3. ***Legal Proceedings***

From time to time, we are subject to legal proceedings, including the proceedings described specifically below. We are not currently a party to or aware of any proceedings that we believe will have, individually or in the aggregate, a material adverse effect on our business, financial condition or results of operations.

On November 18, 2009, the Research Foundation of the State University of New York, or SUNY filed an action against us in the United States District Court for the Northern District of New York. SUNY sought to recover amounts it alleged it was owed pursuant to a technology licensing contract between us and SUNY. On December 20, 2013, we entered into a Settlement Agreement and Release (the Settlement) with SUNY. Under the terms of the Settlement, SUNY agreed to dismiss the action with prejudice and relinquish all rights it may have had to a portion of future development and regulatory milestone payments payable to us under the Co-Development, License and Co-Promotion Agreement, dated August 1, 2007, between us (and our subsidiaries) and Bayer Healthcare LLC, as amended, related to the inhaled amikacin program in exchange for (i) a $5 million payment due on April 1, 2014; (ii) a $5 million payment due on January 1, 2015, (iii) a series of four $500,000 payments each due on April 1, 2014, January 1, 2015, January 1, 2016, and January 1, 2017, respectively; and (iv) certain other terms and conditions.

Item 4. ***Mine Safety Disclosures***

Not applicable.

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PART II

Item 5. ***Market for Registrant s Common Equity, Related Stockholder Matters and Issuer Purchases of Equity Securities***

Our common stock trades on The NASDAQ Global Select Market under the symbol NKTR. The table below sets forth the high and low closing sales prices for our common stock as reported on The NASDAQ Global Select Market during the periods indicated.

	High	Low
Year Ended December 31, 2012:		
1st Quarter	$ 8.22	$ 5.68
2nd Quarter	8.14	6.41
3rd Quarter	10.78	7.99
4th Quarter	10.83	5.99
Year Ended December 31, 2013:		
1st Quarter	$ 11.06	$ 7.54
2nd Quarter	11.70	8.83
3rd Quarter	13.96	10.45
4th Quarter	12.56	8.96

Holders of Record

As of February 20, 2014, there were approximately 215 holders of record of our common stock.

Dividend Policy

We have never declared or paid any cash dividends on our common stock. We currently expect to retain any future earnings for use in the operation and expansion of our business and do not anticipate paying any cash dividends on our common stock in the foreseeable future.

There were no sales of unregistered securities and there were no common stock repurchases made during the year ended December 31, 2013.

Securities Authorized for Issuance Under Equity Compensation Plans

Information regarding our equity compensation plans as of December 31, 2013 is disclosed in Item 12 Security Ownership of Certain Beneficial Owners and Management and Related Stockholder Matters of this Annual Report on Form 10-K and is incorporated herein by reference from our proxy statement for our 2014 annual meeting of stockholders to be filed with the SEC pursuant to Regulation 14A not later than 120 days after the end of the fiscal year covered by this Annual Report on Form 10-K.

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Performance Measurement Comparison

The material in this section is being furnished and shall not be deemed filed with the SEC for purposes of Section 18 of the Exchange Act or otherwise subject to the liability of that section, nor shall the material in this section be deemed to be incorporated by reference in any registration statement or other document filed with the SEC under the Securities Act or the Exchange Act, except as otherwise expressly stated in such filing.

The following graph compares, for the five year period ended December 31, 2013, the cumulative total stockholder return (change in stock price plus reinvested dividends) of our common stock with (i) the NASDAQ Composite Index, (ii) the NASDAQ Pharmaceutical Index, (iii) the RGD SmallCap Pharmaceutical Index, (iv) the NASDAQ Biotechnology Index and (v) the RDG SmallCap Biotechnology Index. Measurement points are the last trading day of each of our fiscal years ended December 31, 2009, December 31, 2010, December 31, 2011, December 31, 2012 and December 31, 2013. The graph assumes that $100 was invested on December 31, 2008 in the common stock of the Company, the NASDAQ Composite Index, the Nasdaq Pharmaceutical Index, the RGD SmallCap Pharmaceutical Index, the NASDAQ Biotechnology Index and the RDG SmallCap Biotechnology Index and assumes reinvestment of any dividends. The stock price performance in the graph is not intended to forecast or indicate future stock price performance.

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Item 6. ***Selected Financial Data***

SELECTED CONSOLIDATED FINANCIAL INFORMATION

(In thousands, except per share information)

The selected consolidated financial data set forth below should be read together with the consolidated financial statements and related notes, Management s Discussion and Analysis of Financial Condition and Results of Operations, and the other information contained herein.

	Year Ended December 31,				
	2013	2012	2011	2010	2009
Statements of Operations Data:					
Revenue:					
Product sales	$ 44,846	$ 35,399	$ 24,864	$ 27,412	$ 30,116
Royalty revenue	1,148	4,874	10,327	7,255	5,172
Non cash royalty revenue related to sale of future royalties[1]	22,055	10,791			
License, collaboration and other revenue	80,872	30,127	36,289	124,372	36,643
Total revenue	148,921	81,191	71,480	159,039	71,931
Total operating costs and expenses	269,051	222,392	195,417	187,294	167,063
Loss from operations	(120,130)	(141,201)	(123,937)	(28,255)	(95,132)
Non-cash interest expense on liability related to sale of future royalties[1]	(22,309)	(18,057)			
Interest and other income (expense), net	(17,329)	(12,191)	(9,023)	(8,802)	(7,640)
Provision (benefit) for income taxes	2,245	406	1,018	881	(253)
Net loss	$ (162,013)	$ (171,855)	$ (133,978)	$ (37,938)	$ (102,519)
Basic and diluted net loss per share[2]	$ (1.40)	$ (1.50)	$ (1.19)	$ (0.40)	$ (1.11)
Weighted average shares outstanding used in computing basic and diluted net loss per share[2]	115,732	114,820	112,942	94,079	92,772

	As of December 31,				
	2013	2012	2011	2010	2009
Balance Sheet Data:					
Cash, cash equivalents and investments	$ 262,026	$ 302,194	$ 414,936	$ 315,932	$ 396,211
Working capital	$ 159,661	$ 236,094	$ 1,174	$ 289,871	$ 260,650
Total assets	$ 434,527	$ 497,790	$ 606,550	$ 521,225	$ 575,518
Deferred revenue	$ 106,048	$ 118,447	$ 127,831	$ 145,347	$ 192,372
Convertible subordinated notes	$	$	$ 214,955	$ 214,955	$ 214,955
Senior secured notes	$ 125,000	$ 125,000	$	$	$
Liability related to the sale of future royalties[1]	$ 128,520	$ 131,266	$	$	$
Other long-term liabilities	$ 25,775	$ 20,014	$ 21,741	$ 22,585	$ 23,344
Accumulated deficit	$ (1,732,393)	$ (1,570,380)	$ (1,398,525)	$ (1,264,547)	$ (1,226,609)
Total stockholders equity (deficit)	$ (89,903)	$ 47,018	$ 197,811	$ 90,662	$ 102,367

(1)

In February 2012, we sold all of our rights to receive future royalty payments on net sales of UCB s CIMZIA® and Roche s MIRCERA®. As described in Note 7 to our Consolidated Financial Statements, this royalty sale transaction has been recorded as a liability that amortizes over the estimated royalty payment

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period. As a result of this liability accounting, even though the royalties from UCB and Roche are remitted directly to the purchaser of these royalty interests starting in the second quarter of 2012, we will continue to record revenue for these royalties.

(2) Basic and diluted net loss per share is based upon the weighted average number of common shares outstanding.

The following discussion contains forward-looking statements that involve risks and uncertainties. Our actual results could differ materially from those discussed here. Factors that could cause or contribute to such differences include, but are not limited to, those discussed in this section as well as factors described in Part I, Item 1A Risk Factors.

Item 7. *Management s Discussion and Analysis of Financial Condition and Results of Operations*

Overview

Strategic Direction of Our Business

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

Our most advanced proprietary product candidate, naloxegol (formerly known as NKTR-118), is an oral peripheral opioid antagonist which has completed Phase 3 clinical studies and has been filed for regulatory approvals in the US, E.U. and Canada for the treatment of opioid-induced constipation (OIC) in patients with non-cancer pain. We are a party to an exclusive worldwide license agreement with AstraZeneca AB (AstraZeneca) for the global development and commercialization of naloxegol and naloxegol fixed-dose combination products (formerly known as NKTR-119). The core Phase 3 clinical development program for naloxegol, which AstraZeneca calls the KODIAC program, is comprised of four clinical trials which are designed to investigate the safety and efficacy of naloxegol for the treatment of OIC in patients with non-cancer related pain. The outcome and timing of the naloxegol regulatory review events will have a substantial impact on our financial condition as we are entitled to up to $35.0 million in regulatory milestones and $140.0 million in commercial launch milestones, as well as up to $75 million of payments related to the naloxegol fixed-dose combination program. The naloxegol fixed-dose combination program is an early stage research and development program that is designed to combine various opioids with naloxegol AstraZeneca is responsible for all clinical, regulatory and commercialization costs for both the naloxegol drug candidate and all drug candidates within the naloxegol fixed-dose combination program.

On November 12, 2012, AstraZeneca announced positive top-line results for naloxegol from two Phase 3 efficacy and safety clinical trials and from a safety extension trial (KODIAC-04, -05, and -07). On February 26, 2013, AstraZeneca announced positive top-line results from the long-term safety study (KODIAC-08) of naloxegol in patients with OIC. On September 25, 2013, the EMA notified AstraZeneca that it had accepted for review the naloxegol regulatory approval application filed by AstraZeneca in August 2013. As a result, we were

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entitled to a $25.0 million payment from AstraZeneca, which was received on September 30, 2013. On September 16, 2013, AstraZeneca filed an NDA with the FDA for naloxegol, which was accepted for review by the FDA on November 16, 2013, resulting in a $70.0 million milestone payment to Nektar from AstraZeneca in November 2013. If the FDA does not require a future clinical trial or other significant studies to assess the cardiovascular safety (CV Safety Study) of naloxegol prior to an approval decision, AstraZeneca is obligated to pay us an additional $35.0 million. If the FDA does require a CV Safety Study, AstraZeneca may terminate the license agreement with us in its entirety or only with respect to its rights in the United States. If AstraZeneca elects to terminate the license agreement in its entirety due to a CV Safety Study, we will be required to repay them the $70.0 million we received plus accrued interest at 4.5% compounded annually in four installments in accordance with the following payment schedule: $10.0 million plus accrued interest on January 15, 2015, $10.0 million plus accrued interest on January 15, 2016, $20.0 million plus accrued interest on January 15, 2017 and $30.0 million plus accrued interest on January 15, 2018. If AstraZeneca elects to terminate the license agreement only with respect to its rights in the U.S., then such repayment amount would be funded through a 50% reduction of non-U.S. royalty amounts otherwise payable to us until the aggregate amount of such royalty reduction equals the total principal amount of $70.0 million plus accumulated interest at 4.5% compounded annually. If the FDA requires a post-approval cardiovascular safety study as a condition to approval of the naloxegol NDA, then the royalty rate payable to us from net sales of naloxegol in the U.S. by AstraZeneca would be reduced by two percentage points until the aggregate accumulated amount of such royalty payment reduction is equal to a maximum of $35.0 million. We will be entitled to $140.0 million in commercial launch milestone payments if naloxegol is approved by the FDA and EMA and commercial launch is achieved in the U.S. and one major country in the E.U. As a result, the FDA s determination as to whether to require a CV Safety Study prior to an approval determination and the decisions of both the FDA and E.U. with regard to the marketing applications currently filed for naloxegol is critical to our financial position as well as our future business prospects.

Our second most advanced proprietary drug candidate, etirinotecan pegol (also known as NKTR-102), is a next-generation topoisomerase I inhibitor. Etirinotecan pegol is currently being evaluated as a single-agent therapy in a Phase 3 open-label, randomized, multicenter clinical study in patients with metastatic breast cancer. This Phase 3 clinical study, which we call the BEACON study (BrEAst Cancer Outcomes with NKTR-102), enrolled approximately 850 patients with metastatic breast cancer that have previously received treatment with an anthracycline, a taxane, and capecitabine. We completed enrollment in the BEACON study in late July 2013. On January 14, 2014, we announced that the Independent Data Monitoring Committee, or the DMC, created to provide safety oversight for the BEACON study recommended continuation of the Phase 3 BEACON study following an interim data analysis which was performed after reaching 50% of the events needed to achieve the primary endpoint of overall survival. The BEACON study will require a substantial investment over the next two years.

Our third most advanced proprietary drug candidate, NKTR-181, is a novel mu-opioid analgesic drug candidate for chronic pain conditions. The molecule has been designed to have a slow rate of entry into the brain, which is expected to reduce the attractiveness of the molecule as a target of abuse and reduce other serious central nervous system-related side effects, such as sedation and respiratory depression, which are commonly associated with standard opioid therapies. In May 2012, the development program for NKTR-181 for the treatment of moderate to severe chronic pain was granted Fast Track designation by the FDA. On June 19, 2013, we announced positive data from a human abuse liability study of NKTR-181. On September 26, 2013, we announced preliminary topline results from a Phase 2 clinical study of NKTR-181 in patients with moderate to severe chronic pain from osteoarthritis of the knee. The Phase 2 study utilized a double-blind, placebo-controlled, randomized withdrawal study design to assess the efficacy, safety and tolerability of NKTR-181. Of the 295 patients that entered the study, only 9 (3%) patients did not achieve meaningful pain relief with NKTR-181. During the titration period, 53 (18%) patients discontinued treatment because of adverse events, most of which are those commonly associated with opioids. A total of 213 patients achieved an average 40% reduction in pain and entered the randomized phase of the study. In this study, NKTR-181 performed as expected as an opioid analgesic throughout the study. However, patients who were randomized to the placebo arm did not show the expected increase in pain scores observed in similar enriched enrollment, randomized withdrawal studies. This

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lack of a placebo rebound caused the Phase 2 study to miss the primary endpoint, which was the average change in a patient s pain score from baseline to the end of the double-blind, randomized treatment period. In December 2013, we met with the FDA to discuss the results of the Phase 2 clinical study and certain preliminary considerations for the Phase 3 clinical study design. We are currently evaluating the appropriate Phase 3 clinical study design for NKTR-181 and expect to start a Phase 3 clinical study in mid-2014.

We have a significant collaboration with Bayer Healthcare LLC (Bayer) to develop BAY41-6551 (Amikacin Inhale, formerly known as NKTR-061), which is an inhaled solution of amikacin, an aminoglycoside antibiotic. Bayer has initiated a Phase 3 clinical development of BAY41-6551 with the first patient enrolled in April 2013. We originally developed the liquid aerosol inhalation platform and Amikacin Inhale and entered into a collaboration agreement with Bayer in August 2007 to further advance the drug candidate s development and potential commercialization. In 2011, Bayer achieved agreement with the FDA on the design of the planned Phase 3 clinical studies of BAY41-6551 under the Special Protocol Assessment process that is intended to support the submission of an NDA if the ongoing Phase 3 clinical study is successful.

We also have a significant collaboration with Baxter Healthcare to identify and develop PEGylated drug candidates with the objective of providing new long-acting therapies for hemophilia patients. Under the terms of this collaboration, we are providing a license to our PEGylation intellectual property, technology and expertise. Baxter is responsible for all clinical development. The first drug candidate in this collaboration, BAX 855, is a longer-acting (PEGylated) form of a full-length recombinant factor VIII (rFVIII) protein which has completed Phase 1 clinical development in patients with Hemophilia A. In February 2013, Baxter initiated a Phase 3 multi-center, open-label clinical study called PROLONG-ATE in previously treated adult patients with severe hemophilia A to assess the efficacy, safety and pharmacokinetics of BAX 855 for prophylaxis and on-demand treatment of bleeding. On November 13, 2013, Baxter announced that it had completed enrollment of 146 patients in the PROLONG-ATE clinical study. If BAX 855 is approved by health authorities and is successfully commercialized by Baxter, this will represent a substantial royalty revenue opportunity for us, subject to significant risks and uncertainties relating to the outcome of the ongoing Phase 3 clinical study, the health authority regulatory review process, and if approved, subsequent commercial success.

While the late stage clinical development programs described above are key elements of the future success of our company, we believe it is critically important that we continue to make substantial investments in our earlier-stage drug candidate pipeline. In January 2014, we initiated a single-ascending dose Phase 1 clinical study of NKTR-171. Further, we have several drug candidates in research that we are preparing to advance into the clinic in future years. While we believe that our substantial investment in research and development has the potential to create significant value if one or more of our drug candidates demonstrate positive clinical results and receive regulatory approval in one or more major markets, drug research and development is an inherently uncertain process and there is a high risk of failure at every stage prior to approval and the timing and outcome of clinical trial results are extremely difficult to predict. Clinical development successes and failures can have a disproportionate positive or negative impact on our scientific and medical prospects, financial prospects, financial condition, and market value.

Historically, we have entered into a number of license and supply contracts under which we manufactured and supplied our proprietary PEGylation reagents on a cost-plus or fixed price basis. Our current strategy is to manufacture and supply PEGylation reagents to support our proprietary drug candidates or our third-party collaborators where we have a strategic development and commercialization relationship or where we derive substantial economic benefit.

Key Developments and Trends in Liquidity and Capital Resources

As of December 31, 2013, we estimated that we had at least twelve months of working capital to fund our current business plans. At December 31, 2013, we had approximately $262.0 million in cash and investments in marketable securities, of which $25.0 million was restricted in relation to our 12.0% senior secured notes, and

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$160.8 million in indebtedness. The indebtedness includes $125.0 million in aggregate principal amount of 12.0% senior secured notes due July 15, 2017, but excludes our long-term liability relating to the sale of future royalties under the Purchase and Sale Agreement with RPI Finance Trust. As is further described in Note 7 to our Consolidated Financial Statements, this royalty obligation liability will generally not be settled in cash, but we expect to make a cash payment of $7.0 million in 2014 as a specified worldwide 2013 net sales threshold of MIRCERA® is not expected to be met.

On January 28, 2014, we completed the issuance and sale of 9,775,000 shares of our common stock with gross proceeds of approximately $117.2 million. Additionally, we incurred approximately $0.6 million in legal and accounting fees, filing fees, and other offering expenses.

Results of Operations

Years Ended December 31, 2013, 2012, and 2011

Revenue (in thousands, except percentages)

	Year Ended December 31,			Increase/ (Decrease) 2013 vs. 2012	Increase/ (Decrease) 2012 vs. 2011	Percentage Increase/ (Decrease) 2013 vs. 2012	Percentage Increase/ (Decrease) 2012 vs. 2011
	2013	2012	2011				
Product sales	$ 44,846	$ 35,399	$ 24,864	$ 9,447	$ 10,535	27%	42%
Royalty revenue	1,148	4,874	10,327	(3,726)	(5,453)	(76)%	(53)%
Non cash royalty revenue related to sale of future royalties	22,055	10,791		11,264	10,791	>100%	100%
License, collaboration and other revenue	80,872	30,127	36,289	50,745	(6,162)	>100%	(17)%
Total revenue	$ 148,921	$ 81,191	$ 71,480	$ 67,730	$ 9,711	83%	14%

Our revenue is derived from our collaboration agreements, under which we may receive product sales revenue, royalties, license fees, milestone payments or contract research payments. Revenue is recognized when there is persuasive evidence that an arrangement exists, delivery has occurred, the price is fixed or determinable, and collection is reasonably assured. The amount of upfront fees received under our license and collaboration agreements allocated to continuing obligations, such as manufacturing and supply commitments, are recognized ratably over our expected performance period under the arrangement. As a result, there may be significant variations in the timing of receipt of cash payments and our recognition of revenue. We make our best estimate of the period over which we expect to fulfill our performance obligations. Given the uncertainties in research and development collaborations, significant judgment is required by us to determine the performance periods.

Product sales

Product sales include fixed price and cost-plus manufacturing and supply agreements with our collaboration partners. The timing of shipments is based solely on the demand and requirements of our collaboration partners and is not ratable throughout the year.

Product sales increased for the year ended December 31, 2013 compared to the year ended December 31, 2012 primarily as a result of an $9.0 million increase in product sales to one of our collaboration partners. Product sales increased during the year ended December 31, 2012 compared to the year ended December 31, 2011 as a result of increased product demand from a number of our collaboration partners.

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We currently expect product sales to decrease substantially in 2014 as compared to 2013 due to decreased product demand from our collaboration partners.

Royalty revenue and non-cash royalty revenue related to sale of future royalties

We receive royalty revenue from certain of our collaboration partners based on their net sales of commercial products. Royalty revenue received in cash decreased during the year ended December 31, 2013 compared to the year ended December 31, 2012 and decreased during the year ended December 31, 2012 compared to the year ended December 31, 2011 primarily as a result of the sale of our rights to receive the royalties from product sales of UCB s CIMZIA® and Roche s MIRCERA® as is further described below. Royalties from CIMZIA® and MIRCERA® recognized after the royalty sale transaction took effect are presented on a separate revenue line item entitled Non-cash royalty revenue related to sale of future royalties. We expect royalty revenue received in cash to decrease in 2014 as compared to 2013.

In February 2012, we sold all of our rights to receive future royalty payments on CIMZIA® and MIRCERA®. As described in Note 7 to our Consolidated Financial Statements, this royalty sale transaction has been recorded as a liability that amortizes over the estimated royalty payment period. As a result of this liability accounting, even though the royalties from UCB and Roche are remitted directly to the purchaser of these royalty interests, we will continue to record revenue for these royalties. During the year ended December 31, 2013 and 2012, we recognized $22.1 million and $13.5 million, respectively, in aggregate royalties from net sales of CIMZIA® and MIRCERA®, of which the $2.7 million recognized in the three months ended March 31, 2012 was retained by us as these amounts resulted from product sales in the fourth quarter of 2011. We expect non-cash royalties from net sales of CIMZIA® and MIRCERA® to decrease slightly in 2014 as compared to 2013.

License, collaboration and other revenue

License, collaboration and other revenue includes the recognition of upfront payments and milestone payments received in connection with our license and collaboration agreements and reimbursed research and development expenses. The level of license, collaboration and other revenue depends in part upon the estimated amortization period of the upfront payments, the achievement of milestones, the continuation of existing collaborations, the amount of reimbursed research and development work, and entering into new collaboration agreements, if any.

License, collaboration and other revenue increased for the year ended December 31, 2013 compared to the year ended December 31, 2012 primarily as a result of the recognition of a $25.0 million payment from AstraZeneca achieved in September 2013 on the acceptance for review by the EMA of the naloxegol regulatory approval application filed by AstraZeneca, the recognition of a $10.0 million milestone achieved upon the start of the Amikacin Inhale Phase 3 clinical trial by Bayer in April 2013, the recognition of $7.9 million related to the delivery of additional quantities of our proprietary PEGylation reagent to Roche in the fourth quarter of 2013, and the recognition of the remaining $6.7 million deferred revenue balance related to our agreement with Affymax as a result of the termination of that agreement.

License, collaboration and other revenue for the year ended December 31, 2012 decreased compared to the year ended December 31, 2011 primarily due to the recognition in 2011 of a $5.0 million license fee from an agreement signed in September 2011.

We expect license, collaboration and other revenue in 2014 will be significantly impacted by the outcome and timing of the naloxegol regulatory review events. In particular, in the event naloxegol is approved by the FDA, we would expect to recognize as revenue the $70.0 million payment received from AstraZeneca in November 2013 and we would be entitled to a $35.0 million milestone payment. If these activities occur in 2014, our license, collaboration and other revenue in 2014 will increase significantly from 2013.

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The timing and future success of our drug development programs and those of our collaboration partners are subject to a number of risks and uncertainties. See Part I, Item 1A Risk Factors for discussion of the risks associated with the complex nature of our collaboration agreements.

Revenue by geography

Revenue by geographic area is based on locations of our partners. The following table sets forth revenue by geographic area (in thousands):

	Year Ended December 31,		
	2013	**2012**	**2011**
United States	$ 42,535	$ 34,591	$ 37,896
Europe	106,386	46,600	33,584
Total revenue	$ 148,921	$ 81,191	$ 71,480

The increase in revenue attributable to European countries for the year ended December 31, 2013 compared to the year ended December 31, 2012 is primarily attributable to increased milestone and royalty revenues from our existing European collaboration partners, including the $25.0 million milestone payment from AstraZeneca described above. The increase in revenue attributable to European countries for the year ended December 31, 2012 compared to the year ended December 31, 2011 is primarily attributable to increased product sales and royalty revenues from our existing European collaboration partners.

Cost of goods sold (in thousands, except percentages)

	Year Ended December 31,						
	2013	**2012**	**2011**	**Increase/ (Decrease) 2013 vs. 2012**	**Increase/ (Decrease) 2012 vs. 2011**	**Percentage Increase/ (Decrease) 2013 vs. 2012**	**Percentage Increase/ (Decrease) 2012 vs. 2011**
Cost of goods sold	$ 38,509	$ 30,428	$ 21,891	$ 8,081	$ 8,537	27%	39%
Product gross profit	6,337	4,971	2,973	1,366	1,998	27%	67%
Product gross margin	14%	14%	12%				

Cost of goods sold and product gross profit increased during the year ended December 31, 2013 compared to the year ended December 31, 2012 primarily due to the $9.4 million increase in product sales in the year ended December 31, 2013 compared to the year ended December 31, 2012. Product gross margin in the year ended December 31, 2013 was consistent with the year ended December 31, 2012.

Cost of goods sold increased during the year ended December 31, 2012 compared to the year ended December 31, 2011 primarily due to the $10.5 million increase in product sales in 2012. The increase in product gross margin during the year ended December 31, 2012 compared to the year ended December 31, 2011 is primarily due to the decreased cost per unit in 2012 resulting from increased manufacturing activity and improved overhead absorption.

We expect product gross margin to fluctuate in future periods depending on the level and mix of manufacturing orders from our customers due to the predominantly fixed cost base associated with our manufacturing activities. We currently expect product gross margin to decrease in 2014 as compared to 2013 as a result of the anticipated reduction in product sales.

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Research and development expense (in thousands, except percentages)

	Year Ended December 31,			Increase/ (Decrease) 2013 vs. 2012	Increase/ (Decrease) 2012 vs. 2011	Percentage Increase/ (Decrease) 2013 vs. 2012	Percentage Increase/ (Decrease) 2012 vs. 2011
	2013	2012	2011				
Research and development expense	$ 190,010	$ 148,675	$ 126,766	$ 41,335	$ 21,909	28%	17%

Research and development expense consists primarily of clinical study costs, direct costs of outside research, materials, supplies, licenses and fees as well as personnel costs (including salaries, benefits, and stock-based compensation). Research and development expense also includes certain overhead allocations consisting of support and facilities-related costs.

Research and development expense increased during the year ended December 31, 2013 compared to the year ended December 31, 2012 primarily due to the etirinotecan pegol (NKTR-102) Phase 3 BEACON clinical study initiated in December 2011 as well as the NKTR-181 Phase 2 clinical study initiated in July 2012. In addition, during the year ended December 31, 2013, we recorded a charge of $11.3 million resulting from the settlement of a dispute with the Research Foundation of the State University of New York related to our collaboration with Bayer to develop inhaled amikacin (see Note 8 to our Consolidated Financial Statements).

The increase in research and development expense for the year ended December 31, 2012 compared to the year ended December 31, 2011 is primarily attributable to the $15.2 million increase in direct research and development program costs, a substantial portion of which is attributable to our etirinotecan pegol Phase 3 BEACON study as well as the NKTR-181 Phase 2 clinical study. In addition, research and development expense increased due to a $6.2 million increase in salaries and employee benefits resulting from increased headcount to support our expanded clinical development activities.

We utilize our employee and infrastructure resources across multiple development and research programs. The following table shows expenses incurred for clinical and regulatory services, clinical supplies, and preclinical study support provided by third parties as well as direct materials costs for each of our drug candidates. The table also presents other costs and overhead consisting of personnel, facilities and other indirect costs (in thousands):

	Clinical Study Status[1]	Year Ended December 31,		
		2013	2012	2011
Etirinotecan pegol (NKTR-102) (topoisomerase I inhibitor-polymer conjugate)[2]	Phase 3	$ 44,669	$ 31,650	$ 13,106
BAY41-6551 (Amikacin Inhale)[3]	Phase 3	26,716	13,512	11,389
NKTR-181 (mu-opioid analgesic molecule for chronic pain)	Phase 2	22,955	13,537	9,747
NKTR-171 (neuropathic pain)	Phase 1	3,635	432	
NKTR-192 (mu-opioid analgesic molecule for acute pain)	Preclinical	2,691	2,676	3,100
Other product candidates	Various	4,901	3,831	13,059
Total third party and direct materials costs		105,567	65,638	50,401
Personnel, overhead and other costs		68,993	68,781	59,433
Stock-based compensation and depreciation		15,450	14,256	16,932
Research and development expense		$ 190,010	$ 148,675	$ 126,766

(1) Clinical Study Status definitions are provided in the chart found in Part I, Item 1. Business.
(2) In addition, during the year ended December 31, 2011, we made $11.2 million of prepayments to certain vendors in our BEACON study.

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(3) We partnered this program with Bayer Healthcare LLC in August 2007. As part of the Novartis Pulmonary Asset Sale in 2008, we retained an exclusive license to this technology for the development and commercialization of this drug candidate.

We expect research and development expense to decrease in 2014 as compared to 2013 and to continue at or above the 2012 level. We plan to continue to advance etirinotecan pegol in the Phase 3 BEACON study for metastatic breast cancer for which we expect the clinical study to continue through early 2015. The clinical development costs for the BEACON clinical study will continue to be significant. We estimate that the total third party and direct material costs over the life of the BEACON study will be approximately $100.0 million, of which $64.7 million was incurred through the end of 2013. We have also studied or have ongoing studies being conducted for etirinotecan pegol, including investigator-initiated clinical studies, in bevacizumab (Avastin)-resistant high-grade glioma, colorectal cancer, metastatic and recurrent non-small cell lung cancer, and ovarian cancer. We are unable to estimate the timing or costs to complete the clinical development for etirinotecan pegol across all the potential oncology indications.

In addition to our etirinotecan pegol development activities, in 2014, we plan to commence Phase 3 clinical studies for NKTR-181 and we also plan to continue to advance the development of NKTR-171.

In addition, we plan to continue to make substantial investments to support the clinical and commercial manufacturing preparation and scale-up for the nebulizer devices to supply Bayer for the Amikacin Inhale program. Under our collaboration agreement with Bayer, we are responsible for all clinical and commercial supply of the nebulizer devices for this drug candidate. We do not expect to have any significant future research and development costs associated with naloxegol or the naloxegol fixed-dose combination products as AstraZeneca is responsible for all further development and commercialization costs for these drug candidates.

In addition to our drug candidates that we plan to have in clinical development during 2014 and beyond, we believe it is vitally important to continue our substantial investment in a diverse pipeline of new drug candidates to continue to build the value of our drug candidate pipeline and our business. Our discovery research organization is identifying new drug candidates by applying our PEGylation technology platform to a wide range of molecule classes, including small molecules and large proteins, peptides and antibodies, across multiple therapeutic areas. We plan to continue to advance our most promising early research drug candidates into preclinical development with the objective to advance these early stage research programs to human clinical studies over the next several years.

Our expenditures on current and future preclinical and clinical development programs are subject to numerous uncertainties in timing and cost to completion. In order to advance our drug candidates through clinical development, each drug candidate must be tested in numerous preclinical safety, toxicology and efficacy studies. We then conduct clinical studies for our drug candidates that take several years to complete. The cost and time required to complete clinical trials may vary significantly over the life of a clinical development program as a result of a variety of factors, including but not limited to:

- the number of patients required for a given clinical study design;
- the length of time required to enroll clinical study participants;
- the number and location of sites included in the clinical studies;
- the clinical study designs required by the health authorities (i.e. primary and secondary end points as well as the size of the study needed to demonstrate efficacy and safety outcomes);
- the potential for changing standards of care for the target patient population;
- the competition for patient recruitment from competitive drug candidates being studied in the same clinical setting;

the costs of producing supplies of the product candidates needed for clinical trials and regulatory submissions;

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the safety and efficacy profile of the drug candidate;

the use of clinical research organizations to assist with the management of the trials; and

the costs and timing of, and the ability to secure, approvals from government health authorities.

Furthermore, our strategy includes the potential of entering into collaborations with third parties to participate in the development and commercialization of some of our drug candidates such as those collaborations that we have already completed for naloxegol and Amikacin Inhale. In these situations, the clinical development program and process for a drug candidate and the estimated completion date will largely be under the control of that third party and not under our control. We cannot forecast with any degree of certainty which of our drug candidates will be subject to future collaborations or how such arrangements would affect our development plans or capital requirements.

The risks and uncertainties associated with our research and development projects are discussed more fully in Item 1A Risk Factors. As a result of the uncertainties discussed above, we are unable to determine with any degree of certainty the duration and completion costs of our research and development projects, anticipated completion dates or when and to what extent we will receive cash inflows from a collaboration arrangement or the commercialization of a drug candidate.

General and administrative expense (in thousands, except percentages)

	Year Ended December 31,			Increase/ (Decrease) 2013 vs. 2012	Increase/ (Decrease) 2012 vs. 2011	Percentage Increase/ (Decrease) 2013 vs. 2012	Percentage Increase/ (Decrease) 2012 vs. 2011
	2013	2012	2011				
General and administrative expense	$ 40,532	$ 41,614	$ 46,760	$ (1,082)	$ (5,146)	(3)%	(11)%

General and administrative expense includes the cost of administrative staffing, business development, marketing, finance, and legal activities. General and administrative expense during the year ended December 31, 2013 was consistent with the year ended December 31, 2012. General and administrative expense decreased during the year ended December 31, 2012 compared to the year ended December 31, 2011 primarily as a result of a $2.7 million payment obligation incurred in 2011 related to the settlement of a commercial litigation matter as well as a $2.1 million decrease in non-cash stock-based compensation expense in 2012 as compared to 2011. In 2014, we expect general and administrative expenses to be consistent with 2013.

Interest income (in thousands except percentages)

	Year Ended December 31,			Increase/ (Decrease) 2013 vs. 2012	Increase/ (Decrease) 2012 vs. 2011	Percentage Increase/ (Decrease) 2013 vs. 2012	Percentage Increase/ (Decrease) 2012 vs. 2011
	2013	2012	2011				
Interest income	$ 732	$ 2,315	$ 2,244	$ (1,583)	$ 71	(68)%	3%

Interest income for the year ended December 31, 2013 decreased as compared to the year ended December 31, 2012 as a result of lower average cash and investment balances as well as the impact of lower interest rates earned on our investment balances. Interest income for the year ended December 31, 2012 was consistent with the year ended December 31, 2011.

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Interest expense (in thousands except percentages)

	Year Ended December 31,			Increase/ (Decrease) 2013 vs. 2012	Increase/ (Decrease) 2012 vs. 2011	Percentage Increase/ (Decrease) 2013 vs. 2012	Percentage Increase/ (Decrease) 2012 vs. 2011
	2013	2012	2011				
Interest expense	$ 18,453	$ 15,489	$ 10,223	$ 2,964	$ 5,266	19%	52%
Non-cash interest expense on liability related to sale of future royalties	$ 22,309	$ 18,057	$	$ 4,252	$ 18,057	24%	100%

The increase in interest expense for the year ended December 31, 2013 compared to the year ended December 31, 2012 and the year ended December 31, 2011 is attributable to the interest expense recorded on the senior secured notes we issued in 2012. On July 11, 2012, we issued $125.0 million of 12% senior secured notes maturing on July 15, 2017. In connection with this transaction, we retired a principal amount of $42.5 million of our $215.0 million in aggregate principal amount of 3.25% convertible subordinated notes in exchange for $42.5 million in principal amount of 12% senior secured notes. We repaid the remaining $172.4 million in principal amount of convertible subordinated notes in full at maturity on September 28, 2012.

The increase in non-cash interest expense on liability related to sale of future royalties for the year ended December 31, 2013 compared to the year ended December 31, 2012 and the year ended December 31, 2011 is attributable to the royalty sale transaction that we completed in 2012. On February 24, 2012, we sold all of our rights to receive future royalty payments on CIMZIA® and MIRCERA® in exchange for $124.0 million. As described in Note 7 to our Consolidated Financial Statements, this royalty sale transaction has been recorded as a liability that amortizes over the estimated royalty payment period as CIMZIA® and MIRCERA® royalties are remitted directly to the purchaser. We impute interest on the transaction and record interest expense at the effective interest rate, which we currently estimate to be approximately 17%. There are a number of factors that could materially affect the estimated interest rate and we will assess this estimate on a periodic basis. As a result, future interest rates could differ significantly and any such change in interest rate will be adjusted prospectively.

We expect interest expense and non-cash interest expense in 2014 to be consistent with 2013.

Liquidity and Capital Resources

We have financed our operations primarily through revenue from product sales, royalties and collaboration agreements, as well as public and private placements of debt and equity. At December 31, 2013, we had approximately $262.0 million in cash and investments in marketable securities, of which $25.0 million was restricted in relation to our 12.0% senior secured notes, and $160.8 million in indebtedness. The indebtedness includes $125.0 million in aggregate principal amount of 12.0% senior secured notes due July 15, 2017, but excludes our long-term liability relating to the sale of future royalties. As is further described in Note 7 to our Consolidated Financial Statements, this royalty obligation liability will not generally be settled in cash, but we expect to make a payment of $7.0 million in 2014 as a specified worldwide 2013 net sales threshold of MIRCERA® is not expected to be met.

On January 28, 2014, we completed the issuance and sale of 9,775,000 shares of our common stock for gross proceeds to the Company of approximately $117.2 million. Additionally, we incurred approximately $0.6 million in legal and accounting fees, filing fees, and other offering expenses.

As of December 31, 2013, we estimated that we had at least twelve months of working capital to fund our current business plans. We expect the clinical development of our proprietary drug candidates, including etirinotecan pegol (also known as NKTR-102), Amikacin Inhale, NKTR-181, and NKTR-171, will require significant investment in order to continue to advance in clinical development with the objective of entering into

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a collaboration partnership or obtaining regulatory approval. However, we have no credit facility or any other sources of committed capital. In addition, while in the past we have received a number of significant payments from license and collaboration agreements and other significant transactions, we do not currently anticipate completing new transactions with substantial upfront payments in the near-term. Our current business plan is also subject to significant uncertainties and risks as a result of, among other factors, expenses being higher than anticipated, unplanned expenses, cash receipts being lower than anticipated, and the need to satisfy contingent liabilities, including litigation matters and indemnification obligations.

The availability and terms of various financing alternatives substantially depend on the success or failure of our drug development programs, including naloxegol, etirinotecan pegol, BAX 855, Amikacin Inhale, NKTR-181, and NKTR-171. The availability and terms of financing alternatives and any future significant payments from existing or new collaborations all depend on the positive outcome of ongoing or planned clinical studies, whether we or our partners are successful in obtaining health authority approvals in major markets, and if approved, the commercial success of these drugs. In the event we do not enter into any new collaboration partnerships with significant upfront payments or do not receive the naloxegol milestone payments as discussed above, we would likely be required to pursue financing alternatives. In the event we determine to pursue financing alternatives, our objective would be to first explore financing alternatives that are not dilutive to the ownership of our common stock security holders. However, if non-dilutive financing alternatives are not available to us on commercially reasonable terms or at all, we could be required to pursue dilutive equity-based financing alternatives such as an offering of convertible debt or common stock. If we do not receive substantial milestone payments from our existing collaboration agreements, execute new high-value collaborations or other arrangements, or are unable to raise additional capital in one or more financing transactions, we would be unable to continue our current level of investment in research and development.

Due to the potential for continued uncertainty in the credit markets in 2014 and thereafter, we may experience reduced liquidity with respect to some of our investments in marketable securities. These investments are generally held to maturity, which, in accordance with our investment policy, is less than two years. However, if the need arises to liquidate such securities before maturity, we may experience losses on liquidation. At December 31, 2013, the average time to maturity of the investments held in our portfolio was approximately five months and the maturity of any single investment did not exceed one year. To date we have not experienced any liquidity issues with respect to these securities, but if such issues arise, we may be required to hold some, or all, of these securities until maturity. We believe that, even allowing for potential liquidity issues with respect to these securities, our remaining cash and investments in marketable securities will be sufficient to meet our anticipated cash needs for at least the next twelve months.

Cash flows from operating activities

Cash flows used in operating activities for the year ended December 31, 2013 totaled $38.5 million, which includes $158.3 million of net operating cash uses as well as $15.2 million for interest payments on our senior secured notes, partially offset by the receipt of $135.0 million for milestones from collaboration agreements. We expect that cash flows used in operating activities, excluding upfront and milestone payments received, if any, will increase in 2014 as a result of increased spending on our proprietary research and development programs.

Cash flows used in operating activities for the year ended December 31, 2012 totaled $129.8 million, which includes $148.3 million of net operating cash uses, partially offset by the receipt of $18.5 million from collaboration agreements. Net operating cash uses also include $6.7 million in interest payments on our convertible subordinated notes retired in full on September 28, 2012.

Cash flows used in operating activities for the year ended December 31, 2011 totaled $113.7 million, which includes $7.0 million for semi-annual interest payments on our convertible subordinated notes, $11.2 million of prepayments to certain vendors in our BEACON study, and $125.0 million of other net operating cash uses,

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partially offset by the receipt of $29.5 million from collaboration agreements, of which $16.5 million was included in accounts receivable at December 31, 2010 resulting from an upfront payment obligation arising from an amendment to one of our manufacturing and supply agreements.

Cash flows from investing activities

We paid $4.1 million, $10.6 million, and $9.7 million to purchase property and equipment in the years ended December 31, 2013, 2012, and 2011, respectively. We expect our capital expenditures in 2014 to increase significantly as compared to 2013 primarily as a result of our plan to build commercial manufacturing capability for the devices for the Amikacin Inhale program.

Cash flows used in financing activities

On February 24, 2012, we sold all of our rights to receive future royalty payments on CIMZIA® and MIRCERA® in exchange for $124.0 million. As part of this sale, we incurred approximately $4.4 million in transaction costs. During the year ended December 31, 2013, we made a $3.0 million payment to the purchaser of these royalties because the minimum 2012 MIRCERA® net sales threshold was not met.

On July 11, 2012, we issued $125.0 million of senior secured notes maturing on July 15, 2017. As part of this transaction, we incurred approximately $4.5 million in issuance costs. In connection with this transaction, we retired the principal amount of $42.5 million of our $215.0 million in aggregate principal amount of convertible subordinated notes in exchange for $42.5 million in principal amount of the senior secured notes. In addition, $25.0 million of the proceeds from the senior secured notes issuance is required to be maintained in a restricted account until July 1, 2015. On September 28, 2012, we repaid the remaining $172.4 million in principal amount of the convertible subordinated notes.

On January 24, 2011, we completed a public offering of our common stock with gross proceeds of approximately $220.4 million. As part of the public offering, we incurred approximately $0.6 million in legal and accounting fees, filing fees, and other offering expenses.

We received proceeds from issuance of common stock related to our employee option and stock purchase plans of $8.2 million, $4.1 million, and $4.5 million in the years ended December 31, 2013, 2012, and 2011, respectively.

On January 28, 2014, we completed the issuance and sale of 9,775,000 shares of our common stock for gross proceeds to the Company of approximately $117.2 million. Additionally, we incurred approximately $0.6 million in legal and accounting fees, filing fees, and other offering expenses.

Contractual Obligations (in thousands)

		Payments Due by Period			
	Total	<=1 Yr 2014	2-3 Yrs 2015-2016	4-5 Yrs 2017-2018	2019+
Obligations[1]					
12% Senior secured notes due July 2017, including interest	$ 185,000	$ 15,000	$ 30,000	$ 140,000	$
Operating leases[2]	28,221	2,559	9,642	10,224	5,796
Capital leases, including interest[3]	14,483	5,169			