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