NEKTAR THERAPEUTICS
Form 10-K
March 01, 2016

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, 2015

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 o

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 o 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 o

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 o

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 o
Non-accelerated filer o (Do not check if a smaller reporting company)	Smaller reporting company o

Indicate by check mark whether the registrant is a shell company (as defined in Exchange Act Rule 12b-2) Yes o 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 30, 2015, as reported on the NASDAQ Global Select Market, was approximately $1,647,937,071. This calculation excludes approximately 455,416 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 19, 2016, the number of outstanding shares of the registrant's common stock was 135,939,051.

DOCUMENTS INCORPORATED BY REFERENCE

Portions of registrant's definitive Proxy Statement to be filed for its 2016 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.

NEKTAR THERAPEUTICS

2015 ANNUAL REPORT ON FORM 10-K

TABLE OF CONTENTS

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, timing of commercial launches and product sales levels by our collaboration partners and 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 that 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 and registered trademarks of Nektar Therapeutics in the United States (U.S.) 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.

PART I

Item 1. Business

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

In 2014, we achieved the first approval of one of our proprietary drug candidates, MOVANTIK™ (previously referred to as naloxegol and NKTR-118), under a global license agreement with AstraZeneca AB (AstraZeneca). MOVANTIK™ is an oral peripherally-acting mu-opioid antagonist (PAMORA), approved in both the U.S. and Europe for the treatment of opioid-induced constipation, or OIC, a common side effect caused by chronic administration of prescription opioid pain medicines. MOVANTIK™ was developed using our oral small molecule polymer conjugate technology and we advanced this drug through the completion of Phase 2 clinical studies prior to licensing it to AstraZeneca. On March 31, 2015, AstraZeneca announced that it launched MOVANTIK™ in the United States, as a result of which we received a $100 million commercial launch milestone on March 31, 2015. In August 2015, we received an additional $40.0 million payment triggered by the first commercial sale of MOVENTIG® by AstraZeneca in Germany.

We have a collaboration with certain subsidiaries of Baxalta Incorporated (Baxalta), formerly Baxter International Inc. (Baxter) before the separation of Baxalta from Baxter in July 2015, to identify and develop PEGylated drug candidates with the objective of providing new longer-acting therapies for hemophilia patients. Under this collaboration, we worked with Baxter to develop ADYNOVATE™ (previously referred to as BAX 855), an extended half-life recombinant factor VIII (rFVIII) treatment for Hemophilia A based on ADVATE® [Antihemophilic Factor (Recombinant)]. In November 2015, ADYNOVATE™ was approved by the U.S. Food and Drug Administration (FDA) for use in adults and adolescents, aged 12 years and older, who have Hemophilia A. Baxalta announced the launch and first shipments of ADYNOVATE™ in the U.S. on November 30, 2015. In December 2015, Baxalta announced positive Phase 3 study results of ADYNOVATE™ in patients younger than 12 years of age with severe Hemophilia A. With the study results, Baxalta announced that it plans to file for marketing authorization in the European Union and aims to file for a pediatric indication in the U.S. in early 2016. ADYNOVATE™ is currently under regulatory review in Japan, Canada and Switzerland.

NKTR-181 is a novel mu-opioid analgesic drug candidate for chronic pain conditions and is currently in Phase 3 clinical development. We enrolled the first patient in the first Phase 3 efficacy study in February 2015 and the study continues to enroll patients. In this study, we are randomizing patients with chronic low back pain in an enriched enrollment randomized withdrawal design which will include a qualifying screening period, an open-label titration period where NKTR-181 is given to all patients, followed by a 12 week double-blind randomized period where subjects will be randomized on a 1:1 basis to receive either NKTR-181 or placebo. The NKTR-181 Phase 3 study design includes a single interim sample size assessment to be conducted by an independent analysis center (IAC) after approximately fifty percent of the initially planned 416 patients completed the study. The protocol of the NKTR-181 study defined only two possible outcomes for this pre-planned blinded interim sample size assessment: (1) if the

conditional powering at the midpoint of the trial fell between 50-85%, the sample size was to be increased by about 200 patients; or (2) if the conditional powering fell below 50%, or above 85%, the sample size was not to be changed. The IAC's determination is nondiscretionary and was based upon our determination of pre-defined acceptable power to detect a statistically significant difference between NKTR-181 and placebo based on the primary efficacy endpoint. On February 29, 2016, the IAC instructed Nektar to increase the sample size by about 200 patients.

In December 2015, we dosed the first patient in a Phase 1/2 clinical study for NKTR-214, which is our engineered immunostimulatory CD122-biased cytokine designed to preferentially activate the beta and gamma sub-units of the IL-2 receptor in order to proliferate tumor-killing T cells within the body (CD8-positive effector T cells and natural killer T cells) without stimulating regulatory T cells (CD4-positive T cells). The study is being conducted initially at two primary investigator sites: the University of Texas MD Anderson Cancer Center and Yale Cancer Center. The dose-escalation stage of the Phase 1/2 study is designed to evaluate safety, efficacy, and define the recommended Phase 2 dose of NKTR-214 in approximately 20 patients with solid tumors. In addition to a determination of the recommended Phase 2 dose, the study will assess preliminary anti-tumor activity, including objective response rate. The immunologic effect of NKTR-214 on tumor-infiltrating lymphocytes and other immune infiltrating cells in both blood and tumor tissue will also be assessed. Following the dose-escalation stage of the study, dose expansion cohorts are planned to evaluate NKTR-214 in specific tumor types, which may include melanoma, renal cell carcinoma and non-small cell lung cancer.

NKTR-102 (also known as etirinotecan pegol) is our next-generation topoisomerase I inhibitor proprietary drug candidate. On March 17, 2015, we announced topline data from a Phase 3 clinical study for NKTR-102, which we call the BEACON study (BrEAst Cancer Outcomes with NKTR-102), as a single-agent therapy for women with advanced metastatic breast cancer. The BEACON study compared NKTR-102 to an active control arm comprised of a single chemotherapy agent of physician's choice (TPC) in patients who were heavily pre-treated with a median of three prior therapies for metastatic disease. In a topline analysis of 852 patients from the trial, NKTR-102 provided a 2.1 month improvement in median overall survival (OS) over TPC (12.4 months for patients receiving NKTR-102 compared to 10.3 months for patients receiving TPC). Based on a stratified log-rank analysis, the primary endpoint measuring the Hazard Ratio (HR) for survival in the NKTR-102 group compared to the active control arm was 0.87 with a p-value of 0.08, which did not achieve statistical significance. Secondary endpoints in the BEACON study included objective response rate and progression-free survival, which did not achieve statistical significance in the study. We also announced that we observed a significant overall survival benefit in two pre-specified subgroup populations—patients with a history of brain metastases and patients with baseline liver metastases at study entry.

We are currently exploring various future regulatory and development paths forward for NKTR-102 with the EU and U.S. regulatory authorities. In Europe, we have met with the National Authorities in Sweden (MPA) and the United Kingdom (MHRA) to discuss the BEACON data. We also met the European Medicines Agency to discuss filing a marketing authorization application (MAA). Based on the outcome of these meetings, we believe that there is a path forward to file an MAA for conditional approval of NKTR-102 for patients with advanced breast cancer having brain metastases. In connection with any MAA filing, we would be required to start a confirmatory trial in conjunction with the MAA review. In the United States, we met with the FDA and the Oncology Division indicated that we would not be able to use the BEACON data to support an accelerated approval for a new drug application (NDA). However, the FDA staff also indicated that positive results from a completed confirmatory trial for the MAA could support an NDA filing. We are currently evaluating next steps for this program. At this time, we do not plan to advance development of NKTR-102 without a collaboration partner.

We have a 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 NKTR-061 drug candidate and the associated liquid aerosol inhalation platform and entered into a collaboration agreement with Bayer to advance the drug candidate into further clinical development and potential commercialization. Bayer is currently enrolling patients in a Phase 3 clinical program for Amikacin Inhale. Bayer is conducting this study under a Special Protocol Assessment process agreed to with the FDA.

We have a license, manufacturing and supply agreement with Ophthotech Corporation for Fovista®, an anti-platelet-derived growth factor (anti-PDGF) agent, currently in Phase 3 development for the treatment of wet age-related macular degeneration. We have a license, manufacturing and supply agreement with Halozyme Therapeutics, Inc. for PEG-PH20, which is entering Phase 3 development for the treatment of pancreatic cancer. We have a license, manufacturing and supply agreement with UCB Pharma for dapirolizumab pegol, a monovalent

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

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 (Novartis). 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 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. An example of reducing transport across the blood-brain barrier is MOVANTIK™, an orally-available peripherally-acting opioid antagonist that is approved in the United States and European Union. 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 is currently in Phase 3 development.

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 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, NKTR-102, 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 Baxalta's ADYNOVATE™ (previously referred to as BAX 855), a longer-acting (PEGylated) form of a full-length recombinant factor VIII (rFVIII) protein, which was approved by the FDA in November 2015 for use in adults and adolescents, aged 12 years and older, who have Hemophilia A.

Large Molecule Pro-Drug Releasable Polymer Conjugates (Cytokines)

Our customized approaches with large molecule polymer conjugates have expanded to include a new approach with biologics, in particular cytokines, which utilizes the polymer as a means to bias action to a certain receptor or receptor sub-type. In addition, a cytokine's pharmacokinetics and pharmacodynamics can be substantially improved and its half-life can be significantly extended. An example of this is NKTR-214, which is a CD122-biased immune-stimulatory cytokine with an every two or every three-week dosing schedule.

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 EU.

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 existing drugs and drug candidates 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.

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. 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 Drugs and Drug Candidates in Clinical Development

The following table summarizes our proprietary drugs and drug candidates that have either received regulatory approval or 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]
MOVANTIK™ (naloxegol tablets)	Opioid-induced constipation in adult patients with chronic non-cancer pain	Approved in U.S. (Partnered with AstraZeneca AB)
MOVENTIG® (brand name for MOVANTIK™ in Europe)	Opioid-induced constipation in adult patients who have an inadequate response to laxatives	Approved in EU (Partnered with AstraZeneca AB)
ADYNOVATE™ (previously referred to as BAX 855, PEGylated rFVIII)	Hemophilia A	Approved in U.S.; Phase 3 ongoing in EU (partnered with Baxalta)
NKTR-102 (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	Phase 3
NKTR-102	Platinum-resistant/refractory ovarian cancer	Completed Phase 2
NKTR-102	Second-line metastatic colorectal cancer in patients with the KRAS gene mutation	Completed Phase 2
NKTR-102 (in combination with 5-Fluorouracil/leucovorin)	Gastrointestinal-related solid tumors	Completed Phase 1
NKTR-214 (CD122-biased immune-stimulatory cytokine)	Oncology	Phase 1/2
MOVANTIK™ fixed-dose combinations (opioid/naloxegol combinations)	Chronic pain without constipation	Research/Preclinical (Partnered with AstraZeneca AB)

(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

* 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.

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 currently license our intellectual property and, in some cases, purchase our proprietary PEGylation materials for their drug products. A total of ten 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 **
MOVANTIK™ (naloxegol tablets)	Opioid-induced constipation in adult patients with chronic non-cancer pain	AstraZeneca AB	Approved in U.S.
MOVENTIG® (brand name for MOVANTIK™ in Europe)	Opioid-induced constipation in adult patients who have an inadequate response to laxatives	AstraZeneca AB	Approved in EU

ADYNOVATE™ (previously referred to as BAX 855, PEGylated rFVIII)	Hemophilia A	Baxalta	Approved in U.S.; Phase 3 ongoing in EU
SEMPRANA®	Migraine	Allergan, Inc.	Filed for approval in U.S.
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***
Dapirolizumab Pegol	Systemic Lupus Erythematosus	UCB Pharma (Biogen)	Phase 2
PEGPH20	Pancreatic and Non-Small Cell Lung Cancer	Halozyme Therapeutics, Inc.	Phase 1 and 2
Longer-acting blood clotting proteins	Hemophilia	Baxalta	Research/Preclinical

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

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

* 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 was 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

MOVANTIK™ and MOVANTIK™ Fixed-Dose Combination Products (previously referred to as naloxegol, NKTR-118 and NKTR-119), License Agreement with AstraZeneca AB

In September 2009, we entered into a global license agreement with AstraZeneca AB 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 MOVANTIK™ and MOVANTIK™ fixed-dose combination products. MOVANTIK™ was developed using our oral small molecule polymer conjugate technology and we advanced this drug through the completion of Phase 2 clinical studies prior to licensing it to AstraZeneca. MOVANTIK™ 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.

On September 16, 2014, the FDA approved MOVANTIK™ as the first once-daily oral peripherally-acting mu-opioid receptor antagonist (PAMORA) medication for the treatment of OIC in adult patients with chronic, non-cancer pain. On December 9, 2014, the European Commission, or EC, granted Marketing Authorisation to MOVENTIG® (the naloxegol brand name in the European Union, or EU) as the first once-daily oral PAMORA to be approved in the EU for the treatment of OIC in adult patients who have had an inadequate response to laxative(s). The EC’s approval applies to all 28 EU member countries plus Iceland and Norway. On January 23, 2015, the Drug Enforcement Administration published the final rule in the Federal Register, effective immediately on the date it was published, removing naloxegol and its salts from the schedules of the Controlled Substances Act. AstraZeneca launched the commercial sales of MOVANTIK™ in the United States in March 2015 and MOVENTIG® in Germany, the first EU member country, in August 2015. Under the terms of our license agreement, AstraZeneca made an initial license payment of $125.0 million to us and has responsibility for all activities and bears all costs associated with research, development and commercialization for MOVANTIK™ and MOVANTIK™ fixed-dose combination products. We received milestone payments of $70.0 million and $25.0 million upon the acceptance of regulatory approval applications of MOVANTIK™ by the FDA and European Medicines Agency (EMA), respectively, in 2013. We

received an additional milestone payment of $35.0 million upon the FDA's approval of MOVANTIK™ in 2014 and a total of $140.0 million upon commercial launches in 2015, including $100.0 million for MOVANTIK™ in the U.S. and $40.0 million for MOVENTIG® in Germany. We are also entitled to up to $375.0 million in sales milestones for MOVANTIK™ if the program achieves certain annual commercial sales levels. For the MOVANTIK™ 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 MOVANTIK™ and the fixed-dose combination products, we are also entitled to significant double-digit royalty payments starting at 20% of net sales in the U.S. and 18% of net sales in the EU and rest of world, 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 MOVANTIK™ fixed-dose combination product and has the right to develop multiple products which combine MOVANTIK™ with opioids.

There are a number of patents relevant to Movantik™, some of which are listed in the FDA's "Orange Book." The "Orange Book" currently lists six patents for Movantik™. Four patents (i.e., U.S. Patent Nos. 7,056,500, 7,662,365, 7,786,133 and 9,012,469) are "composition of matter patents" -- one of which has a patent expiry extending into 2032. In addition, two patents (i.e., U.S. Patent Nos. 8,067,431 and 8,617,530) are directed to methods of treatment.

ADYNOVATE™ (previously referred to as BAX 855, PEGylated rFVIII)

ADYNOVATE™ is an extended half-life recombinant factor VIII (rFVIII) treatment for Hemophilia A based on ADVATE® [Antihemophilic Factor (Recombinant)]. In December 2014, Baxalta announced that it filed a biologic license application with the FDA for ADYNOVATE™. This regulatory submission was based on positive results from a prospective, global, multi-center, open-label, two-arm Phase 3 study of ADYNOVATE™ (previously referred to as BAX 855) in 137 previously treated patients. Baxalta reported that the results demonstrated that ADYNOVATE™ met its primary endpoint in the control and prevention of bleeding episodes and routine prophylaxis for patients who were 12 years or older. In November 2015, ADYNOVATE™ was approved by the FDA for use in adults and adolescents, aged 12 years and older, who have Hemophilia A. On November 30, 2015, Baxalta announced that it had initiated sales of ADYNOVATE™ in the U.S. ADYNOVATE™ is currently under regulatory review in Japan, Canada and Switzerland.

Hemophilia A, also called factor VIII (FVIII) deficiency or classic hemophilia, is a genetic disorder caused by missing or defective factor VIII, a clotting protein. According to the US Centers for Disease Control and Prevention, hemophilia occurs in approximately 1 in 5,000 live births. A 2010 Datamonitor report calculates that there are approximately 78,000 patients reported to have Hemophilia A worldwide. In 2014, according to the Evaluate Group, sales of FVIII replacement products exceeded $6 billion globally.

There are a number of patents relevant to Adynovate™. Among other patents, U.S. Patent Nos. 7,199,223 and 8,247,536 provide "composition of matter" coverage through February 26, 2024, for this important drug (although extensions of patent term may be available under various regulatory mechanisms). Additional patents owned by Nektar Therapeutics provide further layers of patent coverage for Adynovate™.

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

NKTR-181 is an orally-available novel mu-opioid analgesic molecule 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 was created using Nektar's proprietary polymer conjugate technology, which provides it with a long-acting profile and slows its entry into the CNS. NKTR-181's abuse deterrent properties are inherent to its novel molecular structure and do 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 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 enrolled 295 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.

In the first half of 2013, we conducted a human abuse liability study, or HAL study, for NKTR-181. In this study, NKTR-181 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.

On September 26, 2013, we announced results from this Phase 2 efficacy study. Of the 295 patients that entered the study, only 9 patients (representing 3% of the patient population) were unable to achieve meaningful pain relief with NKTR-181. A total of 213 patients achieved an average 40% reduction in pain and entered the randomized phase of the study. 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.

In October 2014, we engaged in an end-of-Phase 2 meeting for NKTR-181 with the FDA, which included discussions of the design of the Phase 3 clinical study program. In this Phase 3 program for NKTR-181 we plan to include two separate efficacy studies in patients with chronic lower back pain, a long-term safety study, and a human abuse liability study. We enrolled the first patient in this first Phase 3 study in February 2015. In this first efficacy study, we plan to enroll approximately 416 patients in an enriched enrollment randomized withdrawal design which will include a qualifying screening period, an open-label titration period where NKTR-181 is given to all patients, followed by a 12 week double-blind randomized period where subjects will be randomized on a 1:1 basis to receive either NKTR-181 or placebo. As described above, on February 29, 2016 the independent analysis center (IAC) instructed us to increase the sample size by about 200 patients. The primary endpoint is a change in weekly pain score in the double-blind randomized period relative to the baseline pain score and the key secondary endpoints include percentage of responders (>30% reduction in pain score) and patient impression of change.

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, 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. According to the American Society of Addiction Medicine 2016 report, there are 1.9 million Americans which have a substance use disorder involving prescription pain relievers. This same report attributes 18,893 overdose deaths in 2015 were related to prescription pain relievers.

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

We are developing NKTR-102, a next generation topoisomerase I (topo I) inhibitor which was designed using our PEGylation technology. NKTR-102 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, NKTR-102's pro-drug design results in a lower initial peak concentration of active topo I inhibitor in the blood. The large NKTR-102 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, NKTR-102 achieved a 300-fold increase in tumor concentration as compared to irinotecan. Because NKTR-102 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 NKTR-102 in tumor tissue. Clinical studies have shown that NKTR-102 has an extended pharmacokinetic profile and remains in circulation throughout the entire chemotherapy cycle, providing sustained exposure to topo I inhibition.

NKTR-102 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), 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 NKTR-102 or a single agent chosen from a defined set of physician's choice 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 had triple negative breast cancer. On March 17, 2015, we announced topline data from the BEACON Phase 3 clinical study for NKTR-102. In a topline analysis of 852 patients from the trial, NKTR-102 provided a 2.1 month improvement in median overall survival (OS) over TPC (12.4 months for patients receiving NKTR-102 compared to 10.3 months for patients receiving TPC). Based on a stratified log-rank analysis, the primary endpoint measuring the Hazard Ratio (HR) for survival in the NKTR-102 group compared to the active control arm was 0.87 with a p-value of 0.08, which did not achieve statistical significance. Secondary endpoints in the BEACON

study included objective response rate and progression-free survival, which did not achieve statistical significance in the study. We also announced that we observed a significant overall survival benefit in two pre-specified subgroups—patients with a history of brain metastases and patients with baseline liver metastases at study entry.

We are currently exploring various future regulatory paths forward for NKTR-102 with the EU and U.S. regulatory authorities. In Europe, we have met with the National Authorities in Sweden (MPA) and the United Kingdom (MHRA) to discuss the BEACON data. We also met with the EMA to discuss filing an MAA. Based on the outcome of these meetings, we believe that there is a path forward to file an MAA for conditional approval of NKTR-102 for patients with advanced breast cancer having brain metastases. In connection with any MAA filing, the EMA has informed us that we would be required to start a confirmatory trial in conjunction with the MAA review. In the United States, we met with the FDA and the Oncology Division indicated that we would not be able to use the BEACON data to support an accelerated approval for an NDA. However, the FDA staff also indicated that positive results from a completed confirmatory trial for the MAA could also support an NDA filing. We are currently evaluating next steps for this program. At this time, we do not plan to advance development of NKTR-102 without a collaboration partner.

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 2016, the American Cancer Society estimates there will be 246,660 new cases of invasive breast cancer diagnosed in the U.S. and about 40,450 women will die from breast cancer. 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 indicated to treat breast cancer.

We have also conducted clinical studies for NKTR-102 in other solid tumor settings. In 2013, we completed a Phase 2 clinical study for NKTR-102 in approximately 170 patients with platinum-resistant/refractory ovarian cancer. We also initiated a Phase 2 clinical study of NKTR-102 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 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 EU.

We also conducted a Phase 1 dose-escalation clinical study which enrolled 26 patients to evaluate NKTR-102 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. In addition to the clinical study of NKTR-102 being conducted by us, we have also provided support for four investigator-initiated Phase 2 studies being conducted for NKTR-102. On August 7, 2012, we announced a Phase 2 investigator-initiated clinical study of NKTR-102 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. A separate investigator-initiated clinical study is also being conducted at Stanford to evaluate NKTR-102 in patients with brain metastasis from primary lung cancer. On February 5, 2013, we announced a Phase 2 investigator-initiated clinical study of NKTR-102 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 NKTR-102 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 activities 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. In the U.S., our royalty on annual net sales is a flat 30% and outside of the U.S. our royalty on annual net sales is an escalating royalty equal to an approximate average of 22%. 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 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 nebulizer device containing amikacin 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. In November 2014, the FDA granted qualified infectious disease product (QIDP) designation to Amikacin Inhale. Antimicrobial drugs designed to treat serious and life-threatening infections, designated as QIDP, are eligible for fast-track designation, priority review by FDA and a five-year extension of market exclusivity.

NKTR-214 (cytokine immunostimulatory therapy)

NKTR-214 is a CD122-biased immune-stimulatory cytokine designed for the treatment of solid tumors. NKTR-214 is designed to preferentially activate the IL-2 beta sub-receptors and gamma sub-units of the IL-2 receptor in order to proliferate tumor-killing T cells within the body (CD8-positive effector T cells and natural killer T cells) without stimulating regulatory T cells (CD4-positive T cells). This receptor selectivity is intended to increase efficacy and improve safety over existing immunostimulatory cytokine drugs.

In June 2015, we and The University of Texas MD Anderson Cancer Center announced a research collaboration that includes a Phase 1/2 clinical study to evaluate NKTR-214 in a variety of tumor types as a monotherapy and in combination with other therapies, including PD-1 pathway inhibitors. In December 2015, we announced that dosing had commenced in the Phase 1/2 clinical study evaluating the safety, tolerability and efficacy of NKTR-214 in patients with advanced solid tumors, including melanoma, renal cell carcinoma and non-small cell lung cancer. As part of the Phase 1/2 clinical study program, we will also evaluate NKTR-214 in combination with a checkpoint inhibitor.

On February 1, 2016, we announced positive preclinical data was published in a manuscript in Clinical Cancer Research for NKTR-214. Nektar scientists conducted a series of studies using preclinical models of breast tumors (EMT6) and colon tumors (CT26) to assess the safety and efficacy of both single agent and combination dosing of NKTR-214 with checkpoint inhibitors, either an anti-PD-1 therapy or an anti-CTLA-4 therapy. The studies also compared NKTR-214 single agent and combination dosing regimens with single agent and combination dosing regimens of anti-PD-1 and anti-CTLA-4 therapies. In both the breast and colon tumor models, the combination dosing regimens of NKTR-214 therapy with anti-PD-1 therapy or anti-CTLA-4 therapy resulted in significant tumor growth inhibition as well as complete regression of tumors in some animals. In the aggressive EMT6 breast tumor model where activity with single-agent anti-PD-1 therapy or single-agent anti-CTLA-4 therapy was not observed, combination of NKTR-214 plus either anti-PD-1 or anti-CTLA-4 demonstrated substantial efficacy. The combination of NKTR-214 plus anti-PD-1 or NKTR-214 plus anti-CTLA-4 produced complete tumor regressions in 40% and 70% of the animals, respectively. NKTR-214 was also very well-tolerated when co-administered with either antibody in these preclinical studies.

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. In January 2014, a single-ascending dose Phase 1 clinical study of NKTR-171 was completed. This study assessed the pharmacokinetics, tolerability, and safety of NKTR-171 in healthy subjects. In January 2015, a multiple-ascending dose Phase 1 clinical study was initiated to assess its pharmacokinetics, tolerability, and safety of NKTR-171. Although the results of these studies showed NKTR-171 was well-tolerated, as a result of pipeline prioritization, at this time we do not plan to advance NKTR-171 into any further clinical studies.

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.

ADYNOVATE™ (previously referred to as BAX 855) and Long-Acting Therapies for Hemophilia A, Agreement with Subsidiaries of Baxalta Incorporated

In September 2005, we entered into an exclusive research, development, license, manufacturing and supply agreement with certain subsidiaries of Baxalta, formerly Baxter before the separation of Baxalta from Baxter in July 2015, 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, ADYNOVATE™ (previously referred to as BAX 855), is a longer-acting (PEGylated) form of a full-length recombinant factor VIII (rFVIII) protein. ADYNOVATE™ 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 $55.0 million in total development and sales milestone payments, as well as royalties on net sales varying by product and country of sale. The royalties start in the mid-single digits for net sales of ADYNOVATE™ up to $1.2 billion and then in the low teens for net sales exceeding $1.2 billion. 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, Baxalta completed a Phase 1 clinical study for ADYNOVATE™ that was a prospective, open-label study assessing the safety, tolerability and pharmacokinetics of ADYNOVATE™ in 19 previously treated patients age 18 years or older with severe Hemophilia A. In January 2013, Baxalta 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 ADYNOVATE™ was approximately 1.5-fold higher compared to ADVATE®. A longer half-life was achieved in all patients in the study using ADYNOVATE™, no patients developed inhibitors to either base molecule, ADYNOVATE™ 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. Baxalta commenced patient enrollment in a Phase 3 clinical study of ADYNOVATE™ in the U.S. in February 2013 and completed enrollment in November 2013. The Phase 3 clinical study, a multi-center, open-label study called PROLONG-ATE, enrolled 146 previously treated adult patients with severe Hemophilia A in order to assess the efficacy, safety and pharmacokinetics of ADYNOVATE™ for prophylaxis and on-demand treatment of bleeding. In August 2014, Baxalta announced positive top-line results from the PROLONG-ATE clinical study which met the primary endpoint for the control and prevention of bleeding, routine prophylaxis and perioperative management for patients who were 12 years or older. In December 2014, Baxalta announced that it filed a biologic license application with the FDA for ADYNOVATE™. In November 2015, ADYNOVATE™ was approved by the FDA for use in adults and adolescents, aged 12 years and older, who have Hemophilia A. On November 30, 2015, Baxalta announced that it had initiated sales of ADYNOVATE™ in the U.S.

In December 2015, Baxalta announced positive study results from its prospective, uncontrolled, open-label, multi-center Phase 3 study designed to assess the safety and immunogenicity of ADYNOVATE™. The study enrolled 73 previously-treated patients (PTPs) with severe Hemophilia A younger than 12 years of age and assessed the treatment's hemostatic efficacy in prophylaxis and treatment of bleeding episodes. All participants received prophylactic ADYNOVATE™ treatment (median 1.9 infusions per week) and were followed for six months. ADYNOVATE™ met its primary endpoint in the study, as no patients developed inhibitory antibodies to ADYNOVATE™. In addition, no treatment-related serious adverse events were reported. With the study results, Baxalta announced that it plans to file for marketing authorization in Europe and aims to file for a pediatric indication in the U.S. in early 2016. ADYNOVATE™ is currently under regulatory review in Japan, Canada and Switzerland.

Hemophilia A, also called factor VIII (FVIII) deficiency or classic hemophilia, is a genetic disorder caused by missing or defective factor VIII, a clotting protein. According to the US Centers for Disease Control and Prevention, hemophilia occurs in approximately one in 5,000 live births. There are about 20,000 people with hemophilia in the US. All races and ethnic groups are affected. Hemophilia A is four times as common as Hemophilia B while more than half of patients with Hemophilia A have the severe form of hemophilia. In 2014, according to the Evaluate Group, sales of FVIII replacement products exceeded $6 billion globally.

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. In November 2014, the FDA granted qualified infectious disease product (QIDP) designation to Cipro DPI. Antimicrobial drugs designed to treat serious and life-threatening infections, designated as QIDP, are eligible for fast-track designation, priority review by FDA and a five-year extension of market exclusivity.

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), Ophthotech 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). On May 19, 2014, Ophthotech entered into a Licensing and Commercialization Agreement with Novartis Pharma AG to develop and commercialize Fovista® and related combination products in all countries outside of the U.S. Under our agreement with Ophthotech, we received a $19.75 million payment in June 2014 in connection with this licensing agreement. We are entitled to up to $9.5 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 for all of Ophthotech's clinical and future commercial requirements of our proprietary PEGylation materials 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®.

PEGPH20, Agreement with Halozyme Therapeutics, Inc.

In December 2006, we entered into a license agreement with Halozyme Therapeutics, Inc. (Halozyme), under which we granted Halozyme a worldwide, limited exclusive license to certain of our proprietary PEGylation technology to develop, manufacture and commercialize particular products that use our proprietary PEGylation materials linked only with certain qualifying hyaluronidase protein molecules including PEGPH20. According to Halozyme, certain cancers, including pancreatic, breast, colon and prostate, have been shown to accumulate high levels of hyaluronan (HA). Halozyme's FDA-approved, HYLENEX® recombinant human hyaluronidase, rHuPH20, is administered subcutaneously and temporarily and reversibly degrades HA to facilitate the absorption and dispersion of other injected drugs or fluids and for subcutaneous fluid administration. However, rHuPH20 acts only locally at the injection site, is rapidly inactivated in the body, and does not survive in the blood. PEGPH20 is an investigational PEGylated form of rHuPH20, under development by Halozyme to increase the half-life of the compound in the blood and allow for intravenous administration. Halozyme is currently evaluating PEGPH20 in a Phase 2 multicenter, randomized clinical trial evaluating PEGPH20 as a first-line therapy for patients with stage IV metastatic pancreatic

cancer. Halozyme is also evaluating PEGPH20 in an on-going Phase 1b/2 multi-center, randomized clinical trial evaluating PEGPH20 as a second-line therapy for patients with locally advanced or metastatic non-small cell lung cancer. On October 2, 2014, the FDA granted Orphan Drug designation for PEGPH20 for the treatment of pancreatic cancer. We are entitled to future development milestones and royalties on net sales subject to reduction in the absence of patent coverage. Our right to receive royalties in any particular country will expire upon the later of twelve years after first commercial sale of the product or expiration of patent rights in the particular country. We also manufacture and supply Halozyme with clinical and future commercial supply of our proprietary PEGylation materials used in the manufacture of PEGPH20.

SEMPRANA®, 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 SEMPRANA®, formerly known as 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 SEMPRANA®. Our right to receive royalties for the net sales of SEMPRANA® under the license agreement 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.

SEMPRANA® is a self-administered formulation of DHE using an inhaler device that is currently under review by the FDA. On May 26, 2011, MAP submitted an NDA to the FDA for SEMPRANA®. In March of 2012, the FDA issued a complete response letter to MAP identifying issues relating to chemistry, manufacturing and controls deficiencies of the product at a contracted third party manufacturer. On April 17, 2013, the FDA issued a second complete response letter identifying issues related to a supplier that provided the canister filling unit for SEMPRANA®. In June 2014, Allergan announced that it had received a third complete response letter from the FDA related to specifications around content uniformity on the improved canister filling process and on standards for device actuation. Allergan has responded to the FDA's latest complete response letter and has stated that it continues to work with the FDA to resolve outstanding CMC issues.

On January 28, 2011, MAP entered into a Collaboration Agreement with Allergan, Inc. pursuant to which Allergan received a co-exclusive license to market and promote SEMPRANA® to neurologists and pain specialists in the U.S. Under this arrangement, Allergan paid MAP an upfront payment of $60 million and MAP was also entitled to receive up to an additional $97 million in the form of regulatory milestones, which includes milestones for acceptance of filing of the SEMPRANA® NDA and first commercial sale associated with the initial acute migraine indication. 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 January 23, 2015, we filed a breach of contract action against Allergan and MAP in California Superior Court in San Mateo County seeking monetary damages related to MAP's failure to pay us a certain specified percentage of $80 million in upfront and milestone payments received to date from Allergan under the 2011 Collaboration Agreement which we believe we were entitled to receive under the terms of our license agreement with MAP.

Dapirolizumab Pegol

In 2010, we entered into a license, manufacturing and supply agreement with UCB Pharma S.A., under which we granted UCB a worldwide, exclusive license to certain of our proprietary PEGylation technology to develop, manufacture and commercialize an anti-CD40L PEFylated Fab being developed by UCB and their partner Biogen Idec, for the treatment of autoimmune disorders, including systemic lupus erythemastosus (SLE). In 2014, UCB and Biogen completed a Phase 1b randomized, double-blind, placebo-controlled clinical study in approximately 24 patients with SLE. Data from the study was published in September 2015 at the Annual American College of Rheumatology Meeting and showed that multiple administrations of dapirolizumab pegol given over 12 weeks were well-tolerated and the safety profile supported further development of the compound. Exploratory analyses from the same study showed greater improvement in clinical measures of disease activity in the dapriolizumab pegol group versus placebo. Based on the results of this clinical study, Biogen and UCB announced that they planned to initiate a Phase 2 clinical study in 2016 in patients with SLE.

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 2010 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 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., EU 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. 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. The agreement expires on the expiration of our last relevant patent containing a valid claim. As of December 31, 2015, we no longer have any continuing manufacturing or supply obligations under this PEGASYS® agreement.

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 EU for age-related macular degeneration. We currently manufacture our proprietary 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. 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 also manufacture and supply UCB with our proprietary PEGylation reagent used in the manufacture of CIMZIA® on 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. 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 through December 31, 2016. 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 by the fourth 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.

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, including those relating to systemic toxicity normally required for the IND and NDA or BLA, and clinical trials, may not be necessary if the company has a right of reference to existing preclinical or clinical data under section 505(j) of the Federal 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 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 the active pharmaceutical ingredient and finished 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. Such inspections are also held periodically after the commercialization. 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.

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.

In situations where our partners are 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.

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 generally 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 EU.

In the U.S., the FDA may grant Fast Track or Breakthrough Therapy 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 Therapy 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 215 U.S. and 750 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.

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.

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 product sales revenue. AstraZeneca and UCB represented 57% and 13% of our revenue, respectively, for the year ended December 31, 2015. No other collaboration partner accounted for more than 10% of our total revenue during the year ended December 31, 2015.

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., 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.

Product and Program Specific Competition

MOVANTIK™ (previously referred to as naloxegol and NKTR-118) (orally-available peripheral opioid antagonist)

There are no other 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 oral 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 RELISTOR® Subjectaneous Injection (methylnaltrexone bromide) marketed by Valeant Pharmaceuticals, Ltd (formerly Salix) under a license from Progenics Pharmaceuticals, Inc. In 2014, RELISTOR® Subjectaneous Injection was approved by the FDA for adult patients with chronic non-cancer pain. On June 23, 2015, Valeant submitted an NDA to the FDA for Relistor (methylnaltrexone bromide) oral tablets for the treatment of OCI in adult patients with chronic non-cancer pain. 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 Merck & Co., Inc., GlaxoSmithKline plc, Ironwood Pharmaceuticals, Inc. in collaboration with Actavis plc, Mundipharma Int. Limited, Theravance, Inc., Develco Pharma, Sucampo Pharmaceuticals, Inc., and Takeda Pharmaceutical Company Limited.

ADYNOVATE™ (previously referred to as BAX 855, PEGylated rFVIII)

On June 6, 2014, the FDA approved Biogen Idec ’s ELOCTATE™ [Antihemophilic Factor (Recombinant), Fc Fusion Protein] for the control and prevention of bleeding episodes, perioperative (surgical) management and routine prophylaxis in adults and children with Hemophilia A. ELOCTATE™ is intended to be an extended half-life Factor VIII therapy with prolonged circulation in the body with the potential to extend the interval between prophylactic infusions. Prior to its 2014 approval, the fusion protein in ELOCTATE™ was not used outside of the clinical trial setting for Hemophilia A patients. There are other long-acting Factor VIII programs in late-stage development for Hemophilia A patients. Bayer Healthcare and Novo Nordisk have ongoing Phase 3 clinical development programs for longer acting Factor VIII proteins based on pegylation technology approaches. These programs, if developed successfully and approved by health authorities, would be competitors in the longer acting Factor VIII market.

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., Cara Therapeutics, Inc., Collegium Pharmaceutical, Inc., Egalet Ltd, Elite Pharmaceuticals, Inc., Endo Health Solutions Inc., KemPharm, Inc., Pfizer, Inc., Purdue Pharma L.P., and Teva Pharmaceutical Industries Ltd.

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),

Ibrance® (palbociclib), Ixempra® (ixabepilone), Navelbine® (vinolrebine), Paraplatin® (carboplatin), Taxol® (paclitaxel), Xeloda® (capecitabine) 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.

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.

NKTR-214 (immunostimulatory CD122-biased cytokine)

There are numerous companies engaged in developing immunotherapies to be used alone, or in combination, to treat a wide range of oncology indications targeting both solid and liquid tumors. In particular, we expect to compete with therapies with tumor infiltrating lymphocytes, or TILS, chimeric antigen receptor-expressing T cells, or CAR-T, cytokine-based therapies, and checkpoint inhibitors. Potential competitors in the TIL and CAR-T space include Kite Pharma/NCI, Adaptimmune LLC, Celgene Corporation, Juno Therapeutics, and Novartis, Alkermes, Altor, and Armo in the cytokine-based therapies space, and Tesaro, Macrogenics, Merck, BMS, and Roche in the checkpoint inhibitor space.

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,		
	2015	2014	2013
Third party and direct materials costs	$89.3	$57.9	$105.6
Personnel, overhead and other costs	77.8	75.6	69.0
Stock-based compensation and depreciation	15.7	14.2	15.4
Research and development expense	$182.8	$147.7	$190.0

Manufacturing and Supply

We have a manufacturing facility located in Huntsville, Alabama that is capable of manufacturing our proprietary PEGylation materials for active pharmaceutical ingredients (APIs). The facility is also used to produce APIs and finished drug products 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 APIs (including biologics) nor finished drug products for all of our development programs, we primarily utilize contract manufacturers to manufacture active pharmaceutical ingredients and 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 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 also 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, 2015 we had 425 employees, of which 322 employees were engaged in research and development, commercial operations and quality activities and 103 employees were engaged in general administration and business development. Of the 425 employees, 347 were located in the U.S. and 78 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.

EXECUTIVE OFFICERS OF THE REGISTRANT

The following table sets forth the names, ages and positions of our executive officers as of February 15, 2016:

Name	Age	Position
Howard W. Robin	63	Director, President and Chief Executive Officer
John Nicholson	64	Senior Vice President and Chief Financial Officer
Ivan P. Gergel, M.D.	55	Senior Vice President, Drug Development and Chief Medical Officer
Stephen K. Doberstein, Ph.D.	57	Senior Vice President and Chief Scientific Officer
Gil M. Labrucherie, J.D.	44	Senior Vice President, General Counsel and Secretary
Maninder Hora, Ph.D	62	Senior Vice President, Pharmaceutical Development and Manufacturing Operations
Jillian B. Thomsen	50	Senior Vice President, Finance and Chief Accounting Officer

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

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

Ivan P. Gergel, M.D. has served as our Senior Vice President, Drug Development and Chief Medical Officer since May 2014. From April 2008 through March 2014, Dr. Gergel served as Executive Vice President, Research & Development and Chief Scientific Officer of Endo Pharmaceuticals, a pharmaceutical company. Prior to joining Endo Pharmaceuticals, he was Senior Vice President of Scientific Affairs and President of the Forest Research Institute of Forest Laboratories Inc. Prior to that, Dr. Gergel served as Vice President and Chief Medical Officer at Forest and Executive Vice President of the Forest Research Institute. He joined Forest in 1998 as Executive Director of Clinical Research following nine years at SmithKline Beecham, and was named Vice President of Clinical Development and Clinical Affairs in 1999. Dr. Gergel is a member of the Board of Directors of Corium International, Inc., a commercial-stage biopharmaceutical company. Dr. Gergel received his M.D. from the Royal Free Medical School of the University of London and an MBA from the Wharton School.

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

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

Maninder Hora, Ph.D. has served as our Senior Vice President, Pharmaceutical Development and Manufacturing Operations since August 2010. From July 2006 to July 2010, he held various executive positions most recently as Vice President, Product and Quality Operations at Facet Biotech Corporation (now Abbvie Biotherapeutics), a clinical stage biotechnology company, which was acquired in 2010 by Abbvie Biotherapeutics (formerly Abbot). From 1986 to 2006, Dr. Hora held positions of increasing responsibility with Chiron Corporation (acquired in 2005 by Novartis), a pharmaceutical company, serving most recently at Chiron as Vice President of Process and Product Development. Dr. Hora has also held positions at Wyeth Pharmaceuticals and GlaxoSmithKline plc prior to joining Chiron. Dr. Hora served as a key member of various teams that successfully registered ten drugs or vaccines in the U.S. and Europe during his professional career. Dr. Hora completed his Ph.D. in Bioengineering from the Indian Institute of Technology, Delhi, India, and was a Fulbright Scholar at the University of Washington, and received his B.S. in chemistry from the University of Jabalpur.

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

Item 1A. Risk Factors

We are providing the following cautionary discussion of risk factors, uncertainties and assumptions that we believe are relevant to our business. These are factors that, individually or in the aggregate, we think could cause our actual

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

Risks Related to Our Business

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

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

Drug development is a highly uncertain scientific and medical endeavor, and failure can unexpectedly occur at any stage of preclinical and clinical development. Typically, there is a high rate of attrition for drug candidates in preclinical and clinical trials due to scientific feasibility, safety, efficacy, changing standards of medical care and other variables. The risk of failure increases for our drug candidates that are based on new technologies, such as the application of our advanced polymer conjugate technology to NKTR-102, NKTR-181, NKTR-214 and other drug candidates currently in discovery research or preclinical development. For example, while we believe our NKTR-181 Phase 3 clinical program employs the most appropriate clinical trial design, we were unable to identify a single cause for the Phase 2 study for NKTR-181 not meeting its primary efficacy endpoint, and therefore there is increased risk in effectively designing a Phase 3 clinical program for NKTR-181. The failure of one or more of our drug candidates could have a material adverse effect on our business, financial condition and results of operations.

The risk of clinical failure for any drug candidate remains high prior to regulatory approval.

A number of companies have suffered significant unforeseen failures in clinical studies due to factors such as inconclusive efficacy or safety, even after achieving preclinical proof-of-concept or positive results from earlier clinical studies that were satisfactory both to them and to reviewing regulatory authorities. Clinical study outcomes remain very unpredictable and it is possible that one or more of our clinical studies could fail at any time due to efficacy, safety or other important clinical findings or regulatory requirements. The results from preclinical testing or early clinical trials of a product candidate may not predict the results that will be obtained in later phase clinical trials of the product candidate. We, the FDA, IRB, an independent ethics committee, or other applicable regulatory authorities may suspend clinical trials of a product candidate at any time for various reasons, including a belief that subjects participating in such trials are being exposed to unacceptable health risks or adverse side effects. Similarly, an IRB or ethics committee may suspend a clinical trial at a particular trial site. If one or more of our drug candidates fail in clinical studies, it could have a material adverse effect on our business, financial condition and results of operations.

Our results of operations and financial condition depend significantly on the ability of our collaboration partners to successfully develop and market drugs and they may fail to do so.

Under our collaboration agreements with various pharmaceutical or biotechnology companies, our collaboration partner is generally solely responsible for:

- designing and conducting large scale clinical studies;
- preparing and filing documents necessary to obtain government approvals to sell a given drug candidate; and/or
- marketing and selling the drugs when and if they are approved.

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

- we have very little control over the timing and level of resources that our collaboration partners dedicate to commercial marketing efforts such as the amount of investment in sales and marketing personnel, general marketing

campaigns, direct-to-consumer advertising, product sampling, pricing agreements and rebate strategies with government and private payers, manufacturing and supply of drug product, and other marketing and selling activities that need to be undertaken and well executed for a drug to have the potential to achieve commercial success;

- collaboration partners with commercial rights may choose to devote fewer resources to the marketing of our partnered drugs than they devote to their own drugs or other drugs that they have in-licensed;
- we have very little control over the timing and amount of resources our partners devote to development programs in one or more major markets;
- disagreements with partners could lead to delays in, or termination of, the research, development or commercialization of product candidates or to litigation or arbitration proceedings;

- disputes may arise or escalate in the future with respect to the ownership of rights to technology or intellectual property developed with partners;
- we do not have the ability to unilaterally terminate agreements (or partners may have extension or renewal rights) that we believe are not on commercially reasonable terms or consistent with our current business strategy;
- partners may be unable to pay us as expected; and
- partners may terminate their agreements with us unilaterally for any or no reason, in some cases with the payment of a termination fee penalty and in other cases with no termination fee penalty.

Given these risks, the success of our current and future collaboration partnerships is highly unpredictable and can have a substantial negative or positive impact on our business—in particular, we expect the commercial outcomes of MOVANTIK™ and ADYNOVATE™ (previously referred to as BAX 855) to have a particularly significant impact on our near to mid- term financial results and financial condition. Additionally, there are also several important drugs in later stage development with collaboration partners including Amikacin Inhale, Cipro DPI, and Fovista®. If the approved drugs fail to achieve commercial success or the drugs in development fail to have positive late stage clinical outcomes sufficient to support regulatory approval in major markets, it could significantly impair our access to capital necessary to fund our research and development efforts for our proprietary drug candidates. If we are unable to obtain sufficient capital resources to advance our drug candidate pipeline, it would negatively impact the value of our business, results of operations and financial condition.

We are a party to numerous collaboration agreements and other significant agreements which contain complex commercial terms that could result in disputes, litigation or indemnification liability that could adversely affect our business, results of operations and financial condition.

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

- clinical development and commercialization obligations that are based on certain commercial reasonableness performance standards that can often be difficult to enforce if disputes arise as to adequacy of our partner's performance;
- research and development performance and reimbursement obligations for our personnel and other resources allocated to partnered drug candidate development programs;
- clinical and commercial manufacturing agreements, some of which are priced on an actual cost basis for products supplied by us to our partners with complicated cost allocation formulas and methodologies;
- intellectual property ownership allocation between us and our partners for improvements and new inventions developed during the course of the collaboration;
- royalties on drug sales based on a number of complex variables, including net sales calculations, geography, scope of patent claim coverage, patent life, generic competitors, bundled pricing and other factors; and
- indemnity obligations for intellectual property infringement, product liability and certain other claims.

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

From time to time, we have informal dispute resolution discussions with third parties regarding the appropriate interpretation of the complex commercial terms contained in our agreements. For example, in 2015 we filed a lawsuit against Allergan and MAP seeking economic damages related to a dispute over the economic sharing provisions of our license agreement with MAP. One or more disputes may arise or escalate in the future regarding our collaboration

agreements, transaction documents, or third-party license agreements that may ultimately result in costly litigation and unfavorable interpretation of contract terms, which would have a material adverse effect on our business, financial condition and results of operations.

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

We or our partners may not obtain regulatory approval for drug candidates on a timely basis, or at all, or the terms of any approval (which in some countries includes pricing approval) may impose significant restrictions or limitations on use. Drug candidates must undergo rigorous animal and human testing and an extensive review process for safety and efficacy by the FDA and equivalent foreign regulatory authorities. The time required for obtaining regulatory decisions is uncertain and difficult to predict. The FDA and other U.S. and foreign regulatory authorities have substantial discretion, at any phase of development, to terminate clinical studies, require additional clinical development or other testing, delay or withhold registration and marketing approval and mandate product withdrawals, including recalls. For example, while data from certain pre-specified subgroups in the BEACON study was positive, the study did not achieve statistical significance for its primary endpoint and the FDA and European Medicines Agency rarely approve drugs on the basis of studies that do not achieve statistical significance on the primary endpoint. Further, regulatory authorities have the discretion to analyze data using their own methodologies that may differ from those used by us or our partners which could lead such authorities to arrive at different conclusions regarding the safety or efficacy of a drug candidate. In addition, undesirable side effects caused by our drug candidates could cause us or regulatory authorities to interrupt, delay or halt clinical trials and could result in a more restricted label or the delay or denial of regulatory approval by regulatory authorities. For example, AstraZeneca will be conducting a post-marketing, observational epidemiological study comparing MOVANTIK™ to other treatments of OIC in patients with chronic, non-cancer pain and the results of this study could at some point in the future negatively impact the labeling, regulatory status, and commercial potential of MOVANTIK™.

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

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

As of December 31, 2015, we had cash and investments in marketable securities valued at approximately $308.9 million. Also, as of December 31, 2015, we had $255.8 million in debt, including $250.0 million in principal of senior secured notes and $5.8 million of capital lease obligations. While we believe that our cash position will be sufficient to meet our liquidity requirements through at least the next 12 months, our future capital requirements will depend upon numerous unpredictable factors, including:

- the cost, timing and outcomes of clinical studies and regulatory reviews of our proprietary drug candidates that we have licensed to our collaboration partners —important examples include Amikacin Inhale and CIPRO Inhale licensed to Bayer;
- the commercial launch and sales levels of products marketed by our collaboration partners for which we are entitled to royalties and sales milestones—importantly, the level of success in marketing and selling MOVANTIK™ (or MOVENTIG®, the naloxegol brand name in the EU) by AstraZeneca and ADYNOVATE™ by Baxalta, respectively;

- if and when we receive potential milestone payments and royalties from our existing collaborations if the drug candidates subject to those collaborations achieve clinical, regulatory or commercial success;
- the progress, timing, cost and results of our clinical development programs;
- the success, progress, timing and costs of our efforts to implement new collaborations, licenses and other transactions that increase our current net cash, such as the sale of additional royalty interests held by us, term loan or other debt arrangements, and the issuance of securities;
- the number of patients, enrollment criteria, primary and secondary endpoints, and the number of clinical studies required by the regulatory authorities in order to consider for approval our drug candidates and those of our collaboration partners;
- our general and administrative expenses, capital expenditures and other uses of cash; and
- disputes concerning patents, proprietary rights, or license and collaboration agreements that negatively impact our receipt of milestone payments or royalties or require us to make significant payments arising from licenses, settlements, adverse judgments or ongoing royalties.

A significant multi-year capital commitment is required to advance our drug candidates through the various stages of research and development in order to generate sufficient data to enable high value collaboration partnerships with significant upfront payments or to successfully achieve regulatory approval. In the event we do not enter into any new collaboration partnerships with significant upfront payments and we choose to continue our later stage research and development programs, we may need to pursue financing alternatives, including dilutive equity-based financings, such as an offering of convertible debt or common stock, which would dilute the percentage ownership of our current common stockholders and could significantly lower the market value of our common stock. If sufficient capital is not available to us or is not available on commercially reasonable terms, it could require us to delay or reduce one or more of our research and development programs. If we are unable to sufficiently advance our research and development programs, it could substantially impair the value of such programs and result in a material adverse effect on our business, financial condition and results of operations.

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

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

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

It is very difficult to estimate the commercial potential of product candidates due to important factors such as safety and efficacy compared to other available treatments, including potential generic drug alternatives with similar efficacy profiles, changing standards of care, third party payer reimbursement standards, patient and physician preferences, drug scheduling status, the availability of competitive alternatives that may emerge either during the long drug development process or after commercial introduction, and the availability of generic versions of our product candidates following approval by regulatory authorities based on the expiration of regulatory exclusivity or our inability to prevent generic versions from coming to market by asserting our patents. If due to one or more of these risks the market potential for a drug candidate is lower than we anticipated, it could significantly and negatively impact the commercial terms of any collaboration partnership potential for such drug candidate or, if we have already entered into a collaboration for such drug candidate, the revenue potential from royalty and milestone payments could be significantly diminished and this would negatively impact our business, financial condition and results of operations. We also depend on our relationships with other companies for sales and marketing performance and the commercialization of product candidates. Poor performance by these companies, or disputes with these companies, could negatively impact our revenue and financial condition.

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

We intend to continue to seek partnerships with pharmaceutical and biotechnology partners to fund a portion of our research and development capital requirements. The timing of new collaboration partnerships is difficult to predict due to availability of clinical data, the outcomes from our clinical studies, the number of potential partners that need to complete due diligence and approval processes, the definitive agreement negotiation process and numerous other

unpredictable factors that can delay, impede or prevent significant transactions. If we are unable to find suitable partners or negotiate collaboration arrangements with favorable commercial terms with respect to our existing and future drug candidates or the licensing of our intellectual property, or if any arrangements we negotiate, or have negotiated, are terminated, it could have a material adverse effect on our business, financial condition and results of operations.

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

From time to time, we publish preliminary or interim data from our clinical studies. Preliminary data remain subject to audit confirmation and verification procedures that may result in the final data being materially different from the preliminary data we previously published. Interim data are also subject to the risk that one or more of the clinical outcomes may materially change as

patient enrollment continues and more patient data become available. As a result, preliminary and interim data should be viewed with caution until the final data are available. Material adverse changes in the final data could significantly harm our business prospects.

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

We or our partners may experience delays in clinical trials of drug candidates. We currently have ongoing clinical studies for NKTR-181 in patients with chronic lower back pain and initiated a Phase 1/2 clinical study for NKTR-214 in December 2015. In addition, our collaboration partners have several ongoing Phase 3 clinical programs including Baxalta for ADYNOVATE™ (previously referred to as BAX 855), Bayer for Amikacin Inhale and CIPRO Inhale, and Ophthotech for Fovista®. These and other clinical studies may not begin on time, enroll a sufficient number of patients or be completed on schedule, if at all. Clinical trials for any of our product candidates could be delayed for a variety of reasons, including:

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

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

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

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

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

The patent positions of pharmaceutical and biotechnology companies, such as ours, are uncertain and involve complex legal and factual issues. We own more than 215 U.S. and 750 foreign patents and a number of pending patent applications that cover various aspects of our technologies. There can be no assurance that patents that have issued will be held valid and enforceable in a court of law. Even for patents that are held valid and enforceable, the legal process associated with obtaining such a judgment is time consuming and costly. Additionally, issued patents can be subject to opposition or other proceedings that can result in the revocation of the patent or maintenance of the patent in amended form (and potentially in a form that renders the patent without commercially relevant and/or broad coverage). Further, our competitors may be able to circumvent and otherwise design around our patents. Even if a patent is issued and enforceable, because development and commercialization of pharmaceutical products can be subject to

substantial delays, patents may expire early and provide only a short period of protection, if any, following the commercialization of products encompassed by our patents. We may have to participate in interference proceedings declared by the U.S. Patent and Trademark Office, which could result in a loss of the patent and/or substantial cost to us.

We have filed patent applications, and plan to file additional patent applications, covering various aspects of our PEGylation and advanced polymer conjugate technologies and our proprietary product candidates. There can be no assurance that the patent applications for which we apply would actually issue as patents, or do so with commercially relevant and/or broad coverage. The coverage claimed in a patent application can be significantly reduced before the patent is issued. The scope of our claim coverage can be critical to our ability to enter into licensing transactions with third parties and our right to receive royalties from our collaboration partnerships. Since publication of discoveries in scientific or patent literature often lags behind the date of such discoveries, we cannot be certain that we were the first inventor of inventions covered by our patents or patent applications. In addition, there is no guarantee that we will be the first to file a patent application directed to an invention.

An adverse outcome in any judicial proceeding involving intellectual property, including patents, could subject us to significant liabilities to third parties, require disputed rights to be licensed from or to third parties or require us to cease using the technology in dispute. In those instances where we seek an intellectual property license from another, we may not be able to obtain the license on a commercially reasonable basis, if at all, thereby raising concerns on our ability to freely commercialize our technologies or products.

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

From time to time, third parties have asserted, and may in the future assert, that we or our partners infringe their proprietary rights, such as patents and trade secrets, or have otherwise breached our obligations to them. A third party often bases its assertions on a claim that its patents cover our technology platform or drug candidates or that we have misappropriated its confidential or proprietary information. Similar assertions of infringement could be based on future patents that may issue to third parties. In certain of our agreements with our partners, we are obligated to indemnify and hold harmless our collaboration partners from intellectual property infringement, product liability and certain other claims, which could cause us to incur substantial costs and liability if we are called upon to defend ourselves and our partners against any claims. If a third party obtains injunctive or other equitable relief against us or our partners, they could effectively prevent us, or our partners, from developing or commercializing, or deriving revenue from, certain drugs or drug candidates in the U.S. and abroad. Costs associated with litigation, substantial damage claims, indemnification claims or royalties paid for licenses from third parties could have a material adverse effect on our business, financial condition and results of operations.

Third-party claims involving proprietary rights or other matters could also result in substantial settlement payments or substantial damages to be paid by us. For instance, a settlement might require us to enter a license agreement under which we would pay substantial royalties or other compensation to a third party, diminishing our future economic returns from the related drug. In December 2013, we entered into a litigation settlement with the Research Foundation of the State University of New York (SUNY) pursuant to which we agreed to pay $12.0 million and certain other terms and conditions in exchange for the full release of certain breach of contract claims by SUNY.

In addition, from time to time, we are involved in legal proceedings where we or other third parties are enforcing or seeking intellectual property rights, invalidating or limiting patent rights that have already been allowed or issued, or otherwise asserting proprietary rights through one or more potential legal remedies. For example, we are currently involved in a German litigation proceeding whereby Bayer is seeking co-ownership rights in certain of our patent filings pending at the European Patent Office covering (among other things) PEGylated Factor VIII which we have exclusively licensed to Baxalta. The subject matter of our patent filings in this proceeding relates to Bayer's investigational PEGylated recombinant Factor VIII compound. We believe that Bayer's claim to an ownership interest

in these patent filings is without merit and are vigorously defending sole and exclusive ownership rights to this intellectual property. We are also regularly involved in opposition proceedings at the European Patent Office where third parties seek to invalidate or limit the scope of our allowed European patent applications covering (among other things) our drugs and platform technologies. We are also aware of an inter partes review petition that was filed with the U.S. Patent and Trademark Office by Neptune Generics, which is an affiliate of Gerchen Keller Capital. The filing is directed to one of six Orange Book listed patents covering MOVANTIK™. We believe this petition is without merit and AstraZeneca and Nektar will vigorously defend the validity of this patent. The cost to us in initiating or defending any litigation or other proceeding, even if resolved in our favor, could be substantial, and litigation would divert our management's attention. Uncertainties resulting from the initiation and continuation of patent litigation or other proceedings could delay our research and development efforts or result in financial implications either in terms of seeking license arrangements or payment of damages or royalties.

Our manufacturing operations and those of our contract manufacturers are subject to laws and other governmental regulatory requirements, which, if not met, would have a material adverse effect on our business, results of operations and financial condition.

We and our contract manufacturers are required in certain cases to maintain compliance with current good manufacturing practices (cGMP), including cGMP guidelines applicable to active pharmaceutical ingredients, and with laws and regulations governing manufacture and distribution of controlled substances, and are subject to inspections by the FDA, the Drug Enforcement Administration or comparable agencies in other jurisdictions administering such requirements. We anticipate periodic regulatory inspections of our drug manufacturing facilities and the manufacturing facilities of our contract manufacturers for compliance with applicable regulatory requirements. Any failure to follow and document our or our contract manufacturers' adherence to such cGMP and other laws and governmental regulations or satisfy other manufacturing and product release regulatory requirements may disrupt our ability to meet our manufacturing obligations to our customers, lead to significant delays in the availability of products for commercial use or clinical study, result in the termination or hold on a clinical study or delay or prevent filing or approval of marketing applications for our products. Failure to comply with applicable laws and regulations may also result in sanctions being imposed on us, including fines, injunctions, civil penalties, failure of regulatory authorities to grant marketing approval of our products, delays, suspension or withdrawal of approvals, license revocation, seizures, administrative detention, or recalls of products, operating restrictions and criminal prosecutions, any of which could harm our business. Regulatory inspections could result in costly manufacturing changes or facility or capital equipment upgrades to satisfy the FDA that our manufacturing and quality control procedures are in substantial compliance with cGMP. Manufacturing delays, for us or our contract manufacturers, pending resolution of regulatory deficiencies or suspensions could have a material adverse effect on our business, results of operations and financial condition.

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

If we or our contract manufacturers are not able to manufacture and supply sufficient drug quantities meeting applicable quality standards required to support large clinical studies or commercial manufacturing in a timely manner, it could delay our or our collaboration partners' clinical studies or result in a breach of our contractual obligations, which could in turn reduce the potential commercial sales of our or our collaboration partners' products. As a result, we could incur substantial costs and damages and any product sales or royalty revenue that we would otherwise be entitled to receive could be reduced, delayed or eliminated. In some cases, we rely on contract manufacturing organizations to manufacture and supply drug product for our clinical studies and those of our collaboration partners. Pharmaceutical manufacturing of drugs and devices involves significant risks and uncertainties related to the demonstration of adequate stability, sufficient purification of the drug substance and drug product, the identification and elimination of impurities, optimal formulations, process and analytical methods validations, device performance and challenges in controlling for all of these variables. We have faced and may in the future face significant difficulties, delays and unexpected expenses as we validate third party contract manufacturers required for drug and device supply to support our clinical studies and the clinical studies and products of our collaboration partners. Failure by us or our contract manufacturers to supply drug product or devices in sufficient quantities that meet all applicable quality requirements could result in supply shortages for our clinical studies or the clinical studies and commercial activities of our collaboration partners. Such failures could significantly and materially delay clinical trials and regulatory submissions or result in reduced sales, any of which could significantly harm our business prospects, results of operations and financial condition.

Building and validating large scale clinical or commercial-scale manufacturing facilities and processes, recruiting and training qualified personnel and obtaining necessary regulatory approvals is complex, expensive and time consuming. In the past we have encountered challenges in scaling up manufacturing to meet the requirements of large scale

clinical trials without making modifications to the drug formulation, which may cause significant delays in clinical development. We experienced repeated significant delays in starting the Phase 3 clinical development program for Amikacin Inhale as we sought to finalize and validate the device design with a demonstrated capability to be manufactured at commercial scale. Drug/device combination products are particularly complex, expensive and time-consuming to develop due to the number of variables involved in the final product design, including ease of patient and doctor use, maintenance of clinical efficacy, reliability and cost of manufacturing, regulatory approval requirements and standards and other important factors. There continues to be substantial and unpredictable risk and uncertainty related to manufacturing and supply until such time as the commercial supply chain is validated and proven.

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

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

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

We currently have no sales, marketing or distribution capabilities. To commercialize any of our drugs that receive regulatory approval for commercialization, we must either develop internal sales, marketing and distribution capabilities, which would be expensive and time consuming, or enter into collaboration arrangements with third parties to perform these services. If we decide to market our products directly, we must commit significant financial and managerial resources to develop a marketing and sales force with technical expertise and with supporting distribution, administration and compliance capabilities. Factors that may inhibit our efforts to commercialize our products directly or indirectly with our partners include:

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

If we, or our partners through our collaborations, are not successful in recruiting sales and marketing personnel or in building a sales and marketing infrastructure, we will have difficulty commercializing our products, which would adversely affect our business, results of operations and financial condition.

To the extent we rely on other pharmaceutical or biotechnology companies with established sales, marketing and distribution systems to market our products, we will need to establish and maintain partnership arrangements, and we may not be able to enter into these arrangements on acceptable terms or at all. To the extent that we enter into co-promotion or other arrangements, any revenue we receive will depend upon the efforts of third parties, which may not be successful and over which we have little or no control—important examples of this risk include MOVANTIK™ partnered with AstraZeneca and ADYNOVATE™ (previously referred to as BAX 855) partnered with Baxalta. In the event that we market our products without a partner, we would be required to build a sales and marketing organization and infrastructure, which would require a significant investment, and we may not be successful in building this organization and infrastructure in a timely or efficient manner.

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

We often face very limited supply of a critical raw material that can only be obtained from a single, or a limited number of, suppliers, which could cause production delays, clinical trial delays, substantial lost revenue opportunities or contract liabilities to third parties. For example, there are only a limited number of qualified suppliers, and in some cases single source suppliers, for the raw materials included in our PEGylation and advanced polymer conjugate drug formulations. Any interruption in supply or failure to procure such raw materials on commercially feasible terms could harm our business by delaying our clinical trials, impeding commercialization of approved drugs or increasing our costs.

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

We rely on trade secret protection for our confidential and proprietary information. No assurance can be given that others will not independently develop substantially equivalent confidential and proprietary information or otherwise gain access to our trade secrets or disclose such technology, or that we can meaningfully protect our trade secrets. In addition, unpatented proprietary rights, including trade secrets and know-how, can be difficult to protect and may lose their value if they are independently developed by a third party or if their secrecy is lost. Any loss of trade secret protection or other unpatented proprietary rights could harm our business, results of operations and financial condition.

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

For the year ended December 31, 2015, we reported a net loss of $81.2 million. If and when we achieve profitability depends upon a number of factors, including the timing and recognition of milestone and other contingent payments and royalties received, the timing of revenue under our collaboration agreements, the amount of investments we make in our proprietary product candidates and the regulatory approval and market success of our product candidates. We may not be able to achieve and sustain profitability.

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

- develop drugs utilizing our technologies, either independently or in collaboration with other pharmaceutical or biotech companies;
- effectively estimate and manage clinical development costs, particularly the cost of the clinical studies for NKTR-181 and NKTR-214;
- receive necessary regulatory and marketing approvals;
- maintain or expand manufacturing at necessary levels;
- achieve market acceptance of our partnered products;
- receive royalties on products that have been approved, marketed or submitted for marketing approval with regulatory authorities; and
- maintain sufficient funds to finance our activities.

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

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

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

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

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

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

There are many competitors for our proprietary product candidates currently in development. For Amikacin Inhale, the current standard of care includes several approved intravenous antibiotics for the treatment of either hospital-acquired pneumonia or ventilator-associated pneumonia in patients on mechanical ventilators. For MOVANTIK™, there are currently several alternative therapies used to address opioid-induced constipation (OIC) and opioid-induced bowel dysfunction (OBD), including Relistor® (methylnaltrexone bromide) Subcutaneous Injection, oral Amitizia (lubiprostone), and oral and rectal over-the-counter laxatives and stool softeners such as docusate sodium, senna and milk of magnesia. In addition, there are a number of companies developing potential products which are in various stages of clinical development and are being evaluated for the treatment of OIC and OBD in different patient populations, including Merck & Co., Inc., Progenics Pharmaceuticals, Inc. in collaboration with Salix Pharmaceuticals, Ltd., Mundipharma Int. Limited, Sucampo Pharmaceuticals, Inc., Develco Pharma GmbH, Alkermes plc, GlaxoSmithKline plc, Theravance, Inc., and Takeda Pharmaceutical Company Limited. For ADYNOVATE™, on June 6, 2014, the FDA approved Biogen Idec's ELOCTATE™ for the control and prevention of bleeding episodes, perioperative (surgical) management and routine prophylaxis in adults and children with Hemophilia A, and Bayer Healthcare and Novo Nordisk have ongoing Phase 3 clinical development programs for longer acting Factor VIII proteins based on pegylation technology approaches. For NKTR-181, there are numerous companies developing pain therapies designed to have less abuse potential primarily through formulation technologies and techniques applied to existing pain therapies. For NKTR-102 there are a number of chemotherapies and cancer therapies approved today and in various stages of clinical development for breast cancer, including, but not limited to: Abraxane® (paclitaxel protein-bound particles for injectable suspension (albumin bound)), Xeloda® (capecitabine), Afinitor® (everolimus), Doxil® (doxorubicin HCl), Ellence® (epirubicin), Gemzar® (gemcitabine), Halaven® (eribulin), Herceptin® (trastuzumab), Hycamtin® (topotecan), Ibrance® (palbociclib), Ixempra® (ixabepilone), Navelbine® (vinolrebine), Iniparib, Paraplatin® (carboplatin), Taxol® (paclitaxel) and Taxotere® (docetaxel). Major

pharmaceutical or biotechnology companies with approved drugs or drugs in development for breast cancers include, but are not limited to, Bristol-Meyers Squibb Company, Eli Lilly & Co., Roche, GlaxoSmithKline plc, Johnson and Johnson, Pfizer Inc., Eisai Inc., and Sanofi Aventis S.A. There are numerous companies engaged in developing immunotherapies to be used alone, or in combination, to treat a wide range of oncology indications targeting both solid and liquid tumors. In particular, we expect to compete with therapies with tumor infiltrating lymphocytes, or TILS, chimeric antigen receptor-expressing T cells, or CAR-T, cytokine-based therapies, and checkpoint inhibitors. Potential competitors in the TIL and CAR-T space include Kite Pharma/NCI, Adaptimmune LLC, Celgene Corporation, Juno Therapeutics, and Novartis, Alkermes, Altor, and Armo in the cytokine-based therapies space, and Tesaro, Macrogenics, Merck, BMS, and Roche in the checkpoint inhibitor space.

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

may succeed in developing competing technologies, obtaining regulatory approval or gaining market acceptance for products before we do. These developments could make our products or technologies uncompetitive or obsolete.

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

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

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

Our business strategy requires us to manage our business to provide for the continued development and potential commercialization of our proprietary and partnered drug candidates. Our strategy also calls for us to undertake increased research and development activities and to manage an increasing number of relationships with partners and other third parties, while simultaneously managing the capital necessary to support this strategy. If we make a decision to bear a majority or all of the clinical development costs of NKTR-102 this will substantially increase our future capital requirements. If we are unable to manage effectively our current operations and any growth we may experience, our business, financial condition and results of operations may be adversely affected. If we are unable to effectively manage our expenses, we may find it necessary to reduce our personnel-related costs through reductions in our workforce, which could harm our operations, employee morale and impair our ability to retain and recruit talent. Furthermore, if adequate funds are not available, we may be required to obtain funds through arrangements with partners or other sources that may require us to relinquish rights to certain of our technologies, products or future economic rights that we would not otherwise relinquish or require us to enter into other financing arrangements on unfavorable terms.

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

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

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

We must attract and retain experts in the areas of clinical testing, manufacturing, research, regulatory and finance, and may need to attract and retain marketing and distribution experts and develop additional expertise in our existing personnel. We face intense competition from other biopharmaceutical companies, research and academic institutions and other organizations for qualified personnel. Many of the organizations with which we compete for qualified

personnel have greater resources than we have. Because competition for skilled personnel in our industry is intense, companies such as ours sometimes experience high attrition rates with regard to their skilled employees. Further, in making employment decisions, job candidates often consider the value of the stock options they are to receive in connection with their employment. Our equity incentive plan and employee benefit plans may not be effective in motivating or retaining our employees or attracting new employees, and significant volatility in the price of our stock may adversely affect our ability to attract or retain qualified personnel. If we fail to attract new personnel or to retain and motivate our current personnel, our business and future growth prospects could be severely harmed.

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

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

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

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

- establishment of a classified board of directors such that not all members of the board may be elected at one time;
- lack of a provision for cumulative voting in the election of directors, which would otherwise allow less than a majority of stockholders to elect director candidates;
- the ability of our board to authorize the issuance of “blank check” preferred stock to increase the number of outstanding shares and thwart a takeover attempt;
- prohibition on stockholder action by written consent, thereby requiring all stockholder actions to be taken at a meeting of stockholders;
- establishment of advance notice requirements for nominations for election to the board of directors or for proposing matters that can be acted upon by stockholders at stockholder meetings; and
- limitations on who may call a special meeting of stockholders.

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

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

Our stock price is volatile. During the year ended December 31, 2015, based on closing prices on The NASDAQ Global Select Market, our stock price ranged from $9.50 to $17.41 per share. We expect our stock price to remain volatile. A variety of factors may have a significant effect on the market price of our common stock, including the risks described in this section titled “Risk Factors” and the following:

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

commercial launch;
- announcements by collaboration partners as to their plans or expectations related to drug candidates and approved drugs in which we have a substantial economic interest;
- announcements regarding terminations or disputes under our collaboration agreements;
- fluctuations in our results of operations;
- developments in patent or other proprietary rights, including intellectual property litigation or entering into intellectual property license agreements and the costs associated with those arrangements;

- announcements of technological innovations or new therapeutic products that may compete with our approved products or products under development;
- announcements of changes in governmental regulation affecting us or our competitors;
- litigation brought against us or third parties to whom we have indemnification obligations;
- public concern as to the safety of drug formulations developed by us or others;
- our financing needs and activities; and
- general market conditions.

At times, our stock price has been volatile even in the absence of significant news or developments. The stock prices of biotechnology companies and securities markets generally have been subject to dramatic price swings in recent years.

The indenture governing our 7.75% senior secured notes imposes significant operating and financial restrictions on us and our subsidiaries that may prevent us from pursuing certain business opportunities and restrict our ability to operate our business.

On October 5, 2015, we issued $250.0 million in aggregate principal amount of 7.75% senior secured notes due October 2020. The indenture governing the senior secured notes contains covenants that restrict our and our subsidiaries' ability to take various actions, including, among other things:

- incur or guarantee additional indebtedness or issue disqualified capital stock or cause certain of our subsidiaries to issue preferred stock;
- pay dividends or distributions, redeem equity interests or subordinated indebtedness or make certain types of investments;
- create or incur liens;
- transfer, sell, lease or otherwise dispose of assets and issue or sell equity interests in certain of our subsidiaries;
- incur restrictions on certain of our subsidiaries' ability to pay dividends or other distributions to the Company or to make intercompany loans, advances or asset transfers;
- enter into transactions with affiliates;
- engage in any business other than businesses which are the same, similar, ancillary or reasonably related to our business as of the date of the indenture; and
- consummate a merger, consolidation, reorganization or business combination, sell, lease, convey or otherwise dispose of all or substantially all of our assets or other change of control transaction.

This indenture also requires us to maintain a minimum cash balance of $60.0 million. We have certain reporting obligations under the indenture regarding cash position and royalty revenue. The indenture specifies a number of events of default, some of which are subject to applicable grace or cure periods, including, among other things, non-payment defaults, covenant defaults, cross-defaults to other material indebtedness, bankruptcy and insolvency defaults, non-payment of material judgments, loss of any material business license, criminal indictment of the Company, and certain civil forfeiture proceedings involving material assets of the Company. Our ability to comply with these covenants will likely be affected by many factors, including events beyond our control, and we may not satisfy those requirements. Our failure to comply with our obligations could result in an event of default under our other indebtedness and the acceleration of our other indebtedness, in whole or in part, could result in an event of default under the indenture governing the senior secured notes.

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

Item 1B. Unresolved Staff Comments

None.

Item 2. Properties

California

We lease a 126,285 square foot facility in the Mission Bay Area of San Francisco, California (Mission Bay Facility), under an operating lease which expires in 2020. The Mission Bay Facility is our corporate headquarters and also includes our research and development operations.

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

Alabama

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

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

India

We own a research and development facility consisting of approximately 88,000 square feet, near Hyderabad, India. In addition, we lease approximately 1,600 square feet of office space in Hyderabad, India, under a three-year operating lease that will expire in 2018.

Item 3. Legal Proceedings

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

Item 4. Mine Safety Disclosures

Not applicable.

PART II

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

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

	High	Low
Year Ended December 31, 2014:		
1st Quarter	$14.96	$11.68
2nd Quarter	14.31	10.53
3rd Quarter	14.48	10.55
4th Quarter	17.05	12.07
Year Ended December 31, 2015:		
1st Quarter	$15.70	$10.91
2nd Quarter	13.84	9.52
3rd Quarter	13.92	9.50
4th Quarter	17.41	9.98

Holders of Record

As of February 19, 2016, there were approximately 198 holders of record of our common stock.

Dividend Policy

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

There were no sales of unregistered securities and there were no common stock repurchases made during the year ended December 31, 2015.

Securities Authorized for Issuance Under Equity Compensation Plans

Information regarding our equity compensation plans as of December 31, 2015 is disclosed in Item 12 "Security Ownership of Certain Beneficial Owners and Management and Related Stockholder Matters" of this Annual Report on Form 10-K and is incorporated herein by reference from our proxy statement for our 2016 annual meeting of stockholders to be filed with the SEC pursuant to Regulation 14A not later than 120 days after the end of the fiscal year covered by this Annual Report on Form 10-K.

Performance Measurement Comparison

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

The following graph compares, for the five year period ended December 31, 2015, the cumulative total stockholder return (change in stock price plus reinvested dividends) of our common stock with (i) the NASDAQ Composite Index, (ii) the NASDAQ Pharmaceutical Index, (iii) the RDG SmallCap Pharmaceutical Index, (iv) the NASDAQ Biotechnology Index and (v) the RDG SmallCap Biotechnology Index. Measurement points are the last trading day of each of our fiscal years ended December 31, 2011, December 31, 2012, December 31, 2013, December 31, 2014 and December 31, 2015. The graph assumes that $100 was invested on December 31, 2010 in the common stock of the Company, the NASDAQ Composite Index, the Nasdaq Pharmaceutical Index, the RDG SmallCap Pharmaceutical Index, the NASDAQ Biotechnology Index and the RDG SmallCap Biotechnology Index and assumes reinvestment of any dividends. The stock price performance in the graph is not intended to forecast or indicate future stock price performance.

Item 6. Selected Financial Data

SELECTED CONSOLIDATED FINANCIAL INFORMATION

(In thousands, except per share information)

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

	Year Ended December 31,				
	2015	2014	2013	2012	2011
Statements of Operations Data:					
Revenue:					