NEKTAR THERAPEUTICS
Form 10-K
March 01, 2019

UNITED STATES

SECURITIES AND EXCHANGE COMMISSION

Washington, DC 20549

Form 10-K

ANNUAL REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934.
For the fiscal year ended December 31, 2018

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 No

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

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 No

Indicate by check mark whether the registrant has submitted electronically every Interactive Data File required to be submitted 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 such files). Yes No

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

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

Large accelerated filer	Accelerated filer
Non-accelerated filer	Smaller reporting company
Emerging growth company	

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act.

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

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 29, 2018, as reported on The NASDAQ Global Select Market, was approximately $8,366,439,130. This calculation excludes approximately 1,076,518 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 22, 2019, the number of outstanding shares of the registrant's common stock was 174,104,459.

DOCUMENTS INCORPORATED BY REFERENCE

Portions of registrant's definitive Proxy Statement to be filed for its 2019 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

2018 ANNUAL REPORT ON FORM 10-K

TABLE OF CONTENTS

		Page
	PART I	
Item 1.	Business	4
Item 1A.	Risk Factors	30
Item 1B.	Unresolved Staff Comments	45
Item 2.	Properties	45
Item 3.	Legal Proceedings	46
Item 4.	Mine Safety Disclosures	46
	PART II	
Item 5.	Market for Registrant's Common Equity, Related Stockholder Matters and Issuer Purchases of Equity Securities	47
Item 6.	Selected Financial Data	49
Item 7.	Management's Discussion and Analysis of Financial Condition and Results of Operations	51
Item 7A.	Quantitative and Qualitative Disclosures About Market Risk	64
Item 8.	Financial Statements and Supplementary Data	65
Item 9.	Changes in and Disagreements With Accountants on Accounting and Financial Disclosure	98
Item 9A.	Controls and Procedures	98
Item 9B.	Other Information	99
	PART III	
Item 10.	Directors, Executive Officers and Corporate Governance	100
Item 11.	Executive Compensation	100
Item 12.	Security Ownership of Certain Beneficial Owners and Management and Related Stockholder Matters	100
Item 13.	Certain Relationships and Related Transactions and Director Independence	100
Item 14.	Principal Accountant Fees and Services	100
	PART IV	
Item 15.	Exhibits and Financial Statement Schedules	101
Signatures		105

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 market size, 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 initiation, formation or 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, any statements related to potential, anticipated, or ongoing litigation 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

Nektar Therapeutics is a research-based biopharmaceutical company focused on discovering and developing innovative medicines in areas of high unmet medical need. Our research and development pipeline of new investigational drugs includes potential therapies for cancer, autoimmune disease and chronic pain. We leverage our proprietary and proven chemistry platform to discover and design new drug candidates. These drug candidates utilize our advanced polymer conjugate technology platforms, which are designed to enable the development of new molecular entities that target known mechanisms of action. We continue to make significant investments in building and advancing our pipeline of proprietary drug candidates as we believe that this is the best strategy to build long-term stockholder value. We refer to our drug candidates where we retain at least U.S. commercial rights as "proprietary programs" and our other drug candidate programs that we have licensed U.S. and potentially other commercial rights to collaboration partners as "collaboration partner programs."

Our Proprietary Programs

Immuno-oncology (I-O)

In the area of I-O, we are developing medicines that target biological pathways, which stimulate and sustain the body's immune response in order to fight cancer. We are developing medicines designed to directly or indirectly modulate the activity of key immune cells, such as cytotoxic T cells and natural killer (NK) cells, to increase their numbers and improve their function to recognize and attack cancer cells.

NKTR-214 (also known as bempegaldesleukin), our lead I-O candidate, is a biologic with biased signaling through one of the Interleukin-2 (IL-2) receptor subunits (CD 122) that can stimulate proliferation and growth of tumor-killing immune cells in the tumor micro-environment and increase expression of PD-1 on these immune cells. We are executing a comprehensive clinical development program for NKTR-214, including through a broad clinical collaboration with the Bristol-Myers Squibb Company (BMS), clinical collaborations with other third parties with pharmacological agents that have potential complementary mechanisms to NKTR-214, as well as pursuing our own independent clinical studies.

On February 13, 2018, we entered into a Strategic Collaboration Agreement (BMS Collaboration Agreement) with BMS, pursuant to which we and BMS are jointly developing NKTR-214, including combinations with BMS's Opdivo® (nivolumab), Opdivo® plus Yervoy® (ipilimumab), and certain other agents. The key economic components of the collaboration transaction included BMS making a non-refundable up-front payment of $1 billion to Nektar and an $850 million equity investment in our common stock at a premium over the 20-day VWAP for each share of common stock, BMS being responsible for a majority of the costs of the collaboration development plan, our annual funding obligation for collaboration development being limited to $125 million, Nektar retaining a 65% profit interest in NKTR-214, and recording global revenue for NKTR-214 commercial sales. We and BMS are jointly developing NKTR-214 under an expansive joint development plan (the Collaboration Development Plan) that encompasses more than 20 indications across nine tumor types. Together, we have started registrational studies in first-line melanoma, first-line renal cell carcinoma, cisplatin ineligible, locally advanced or metastatic urothelial cancer, second-line metastatic non-small cell lung cancer (post- checkpoint inhibitor and chemotherapy). Many other registrational studies in additional tumor types and indications are planned to begin in 2019.

We are also conducting a broad array of development activities evaluating NKTR-214 in combination with other agents that have potential complementary mechanisms of action. Our strategic objective is to establish NKTR-214 as a key component of many I-O combination regimens with the potential to improve the standard of care in multiple oncology settings. On November 6, 2018, we entered into a clinical trial collaboration with Pfizer, Inc. (Pfizer) to evaluate several combination regimens in multiple cancer settings, including metastatic castration-resistant prostate cancer and squamous cell carcinoma of the head and neck. The combination regimens in this collaboration will

evaluate NKTR-214 with avelumab, a human anti-PD-L1 antibody in development by Merck KGaA, and Pfizer; talazoparib, a poly (ADP-ribose) polymerase (PARP) inhibitor developed by Pfizer; or enzalutamide, an androgen receptor inhibitor in development by Pfizer and Astellas Pharma Inc. In February 2019, we started a Phase 1 dose-escalation study with Takeda Pharmaceutical Company Ltd. (Takeda) to evaluate NKTR-214 with Takeda's investigational medicine, TAK-659, a dual inhibitor of both spleen tyrosine kinase (SYK) and FLT-3, in up to 40 patients with advanced non-hodgkin lymphoma. We are also planning a Phase 1 study this year in pancreatic cancer patients in collaboration with BioXcel Therapeutics to evaluate a triplet combination of NKTR-214, BXCL-701 (a small molecule immune-modulator, DPP 8/9), and avelumab being supplied to BioXcel by Pfizer and Merck KGaA. We are also working in collaboration with Vaccibody AS to evaluate NKTR-214 in combination with Vaccibody's personalized cancer neoantigen vaccine in a Phase 1 proof-of-concept study.

Another key program in I-O, NKTR-262 is a small molecule agonist that targets toll-like receptors (TLRs) found on innate immune cells in the body. NKTR-262 is designed to stimulate the innate immune system and promote maturation and activation of antigen-presenting cells (APC), such as dendritic cells, which are critical to induce the body's adaptive immunity and create antigen-

specific cytotoxic T cells. NKTR-262 is being developed as an intra-tumoral injection in combination with systemic NKTR-214 in order to induce an abscopal response and achieve the goal of complete tumor regression in cancer patients treated with both therapies. The Phase 1 dose-escalation trial is currently ongoing.

NKTR-255 is a biologic that targets the interleukin-15 pathway in order to activate the body's innate and adaptive immunity. Signaling of the IL-15 pathway enhances the survival and activity of natural killer (NK) cells and enhances survival of both effector and CD8 memory T cells. Preclinical findings suggest NKTR-255 has the potential to synergistically combine with antibody-dependent cellular toxicity molecules as well as enhance CAR-T therapies. NKTR-255 is currently advancing through preclinical development and we plan to file an investigational new drug (IND) application for NKTR-255 this year and begin the first Phase 1 dose-escalation trial in multiple myeloma.

Immunology

We are currently developing NKTR-358, which is an investigational drug designed to correct the underlying immune system imbalance in the body that occurs in patients with autoimmune disease. The breakdown of mechanisms assuring recognition of self and non-self is what underlies all autoimmune diseases. A failure of the body's self-tolerance mechanisms is known to result from pathogenic auto reactive T lymphocytes. By increasing the number of regulatory T cells (which are specific immune cells in the body that modulate the immune system and prevent autoimmune disease by maintaining self-tolerance), these pathogenic auto reactive T cells can be reduced and the proper balance of effector and regulatory T cells can be achieved to restore the body's self-tolerance mechanisms. There is consistent evidence that suboptimal regulatory T cell numbers and their lack of activity play a significant role in a myriad of autoimmune diseases. NKTR-358 is designed to optimally target the IL-2 receptor complex in order to stimulate proliferation and growth of regulatory T cells. NKTR-358 is being developed as a once or twice monthly self-administered injection for a number of autoimmune diseases.

On July 23, 2017, we entered into a worldwide license agreement with Eli Lilly and Company (Lilly) to co-develop NKTR-358. We received an initial payment of $150.0 million in September 2017 and are eligible for up to an additional $250.0 million for development and regulatory milestones. We are responsible for completing Phase 1 clinical development and certain drug product development and supply activities. We also share Phase 2 development costs with Lilly, with 75% of those costs borne by Lilly and 25% of the costs borne by us. We will have the option to contribute funding to Phase 3 development on an indication-by-indication basis, ranging from zero to 25% of the global Phase 3 development costs. We are eligible for tiered royalties on global sales up to the low twenties that escalate based upon our level of contribution to Phase 3 development costs and the level of global product annual sales. Lilly will be responsible for all costs of global commercialization and we will have an option to co-promote in the U.S. under certain conditions. In February 2017, we filed an IND for NKTR-358. We have completed a Phase 1 dose-finding trial to evaluate single-ascending doses of NKTR-358 in approximately 100 healthy patients. Results from this study demonstrated a multiple-fold increase in regulatory T cells with no change in CD8 positive or natural killer (NK) cell levels and no dose-limiting toxicities observed. Data from this study are currently planned for presentation at the 2019 European Congress of Rheumatology Conference. The Phase 1 multiple-ascending dose trial to evaluate NKTR-358 in patients with systemic lupus erythematosus (SLE) was initiated in May 2018 and is currently enrolling patients.

Pain - NKTR-181

NKTR-181 (also known as oxycodegol) is a novel mu-opioid analgesic drug candidate that we are developing for chronic pain conditions. We have filed the new drug application (NDA) for NKTR-181 for the treatment of chronic low back pain in opioid-naïve adult patients and the current Prescription Drug User Fee Act (PDUFA) target action date is August 29, 2019. If approved, we plan to commercialize NKTR-181 through a separate subsidiary company, optionally with one or more partners with commercialization infrastructure and expertise and one or more strategic capital partners.

NKTR-181 met its primary and key secondary endpoints in the SUMMIT-07 Phase 3 efficacy study that compared twice-daily dosing of NKTR-181 tablets to placebo in the treatment of over 600 patients with moderate to severe chronic low back pain who were opioid-naïve. SUMMIT-07 evaluated four analgesic doses of NKTR-181 (100 mg, 200 mg, 300 mg and 400 mg). Patients in the trial achieved an average pain score reduction of over 65% (from 6.73 at screening to 2.32 at randomization) during the dose titration period. The primary efficacy endpoint of the study demonstrated significantly improved chronic back pain relief with NKTR-181 compared to placebo (p=0.0019). Key secondary endpoints of the study also achieved high statistical significance. The study demonstrated that NKTR-181 had a favorable safety profile and was well tolerated. The 52-week long-term safety study, which we call SUMMIT-LTS, was completed in December 2017, and evaluated the long-term safety and tolerability of NKTR-181 in 638 patients (opioid-naïve and opioid-experienced) with moderate to severe chronic low pain or chronic non-cancer pain. The study showed that NKTR-181 had a favorable safety profile with analgesic effect maintained over 52-weeks.

Additionally, on July 18, 2017, we announced positive top-line data for our pivotal human abuse potential study (HAP) for NKTR-181. The HAP study was designed to confirm and assess the relative oral abuse potential of NKTR-181, at its maximum analgesic therapeutic, dose (400 mg) studied in the SUMMIT-07 trial and at a supratherapeutic dose (3 times to 12 times greater than the

analgesic dose range of 100 mg to 400 mg used in the SUMMIT-07 trial), compared to common therapeutic doses of oxycodone (40 mg and 60 mg) in 54 healthy non-dependent recreational drug users. For the primary endpoint of Drug Liking, NKTR-181 (400 mg and 600 mg) rated less likable compared to oxycodone 40 mg and 60 mg ($p<0.0001$), and a supratherapeutic dose of NKTR-181 (1200 mg) rated less likable than oxycodone 60 mg ($p=0.0071$). Key secondary endpoints of Area Under Effect for Drug Liking (0-1 hours, 0-2 hours, 0-3 hours), Drug High and Take Drug Again scores also met statistical significance for all doses of NKTR-181 (1200 mg, 600 mg, 400 mg) compared to oxycodone (60 mg).

Oncology - ONZEALD™

ONZEALD™ (also known as NKTR-102, etirinotecan pegol) is our next-generation topoisomerase I inhibitor proprietary drug candidate. In March 2015, we announced top-line data from a Phase 3 clinical study for ONZEALD™, which we called the BEACON study, evaluating ONZEALD™ as a single-agent therapy for women with advanced metastatic breast cancer. The BEACON study compared ONZEALD™ 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 top-line analysis of 852 patients from the trial, ONZEALD™ provided a 2.1 month improvement in median overall survival over TPC (12.4 months for patients receiving ONZEALD™ 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 ONZEALD™ 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.

Based on meetings with the European Union (EU) health authorities, in June 2016, we filed a Marketing Authorization Application (MAA) with the European Medicines Agency (EMA) for conditional approval of ONZEALD™ for adult patients with advanced breast cancer who have brain metastases and began enrolling in the ATTAIN study, which compared the overall survival in patients with breast cancer and brain metastases treated with ONZEALD™ versus physicians treatment of choice. On July 21, 2017, we were informed by the EMA's Committee for Medicinal Products for Human Use (CHMP) that it had adopted a negative opinion for the conditional marketing authorization application for ONZEALD™ in the European Union. The Phase 3 study (ATTAIN) in breast cancer patients having brain metastases is ongoing.

Collaboration Partner Programs

In 2014, we achieved the first approval of one of our proprietary drug candidates, MOVANTIK® (naloxegol), under a global license agreement with AstraZeneca AB (AstraZeneca). MOVANTIK® is an oral peripherally-acting opioid antagonist, for the treatment of opioid-induced constipation, a side effect caused by chronic administration of prescription opioid pain medicines. AstraZeneca markets and sells MOVANTIK® in the United States in collaboration with Daiichi Sankyo, Inc. (Daiichi Inc.). Kyowa Hakko Kirin Co. Ltd. (Kirin) has exclusive marketing rights to MOVENTIG® (the naloxegol brand name in the EU) in the EU, Iceland, Liechtenstein, Norway and Switzerland.

We have a collaboration with Baxalta Incorporated (a wholly-owned subsidiary of Takeda) to develop and commercialize PEGylated drug candidates with the objective of providing new long-acting therapies for hemophilia patients. Under this collaboration, we worked with Baxalta to develop ADYNOVATE®, an extended half-life recombinant factor VIII (rFVIII) treatment for Hemophilia A based on ADVATE® [Antihemophilic Factor (Recombinant)]. ADYNOVATE®, was first approved by the United States Food and Drug Administration (FDA) in late 2015 for Hemophilia A. ADYNOVATE® has also been approved in the European Union, Japan, Korea, Canada, and certain other countries.

We also have a number of license, manufacturing and supply agreements with other leading biotechnology and pharmaceutical companies, including Amgen, Inc., Pfizer and UCB Pharma (UCB). More than 10 products using our PEGylation technology have received regulatory approval in the U.S. or the EU. There are also a number of other products in clinical development that incorporate our advanced polymer conjugate technologies.

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 on Form 10-K.

Our Technology Platform

As a leader in the polymer conjugation field, we have advanced our technology platform to include new advanced 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. Polymer conjugation or PEGylation has been a highly effective technology platform for the development of therapeutics with significant commercial success, such as Amgen's Neulasta® (pegfilgrastim) and UCB's CIMZIA (certolizumab pegol). 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. For example, 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 polymer conjugation, we have created the next generation of PEGylation technology. Our advanced polymer conjugation 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.

Our 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.

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-preferential IL-2 pathway agonist designed to provide rapid activation and proliferation of cancer-killing CD8+ effector T cells and natural killer (NK) cells, without over-activating the immune system, with an every two or every three-week dosing schedule.

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®, 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. In December 2016, the FDA expanded the approval of ADYNOVATE® for use in surgical settings for both adults and pediatric patients, and also for the treatment of Hemophilia A in pediatric patients under 12 years of age.

More recently, our scientists have shown that we can also optimize relative receptor binding characteristics of large molecule conjugates. For instance, the cytokine IL-2 has two different receptor complexes in the body that cause opposing effects on the immune system. We have engineered different novel conjugates of IL-2 with optimized differential receptor binding to the IL-2 receptor categories in the immune system. By biasing the receptor binding of these molecules in complementary ways, we have made two different drug candidates: NKTR-214, which selectively activates effector T cells, which kill tumors; and NKTR-358, which selectively activates regulatory T cells, which can reduce the pathological immune activation that underlies many autoimmune diseases.

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 the EU. 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 for which an NDA for the treatment of chronic low back pain in opioid-naïve adult patients was accepted by the FDA for review.

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.

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 and is approved for the treatment of

Crohn’s Disease and ankylosing spondylitis in the U.S., axial spondyloarthritis in the EU and psoriatic arthritis 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 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 research, 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 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.

Selectively Enter into Strategic Collaboration Agreements

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 evaluate the potential combination of that partner's drug with our own and to selectively access a partner's development, regulatory, or commercial capabilities with the structure of the collaboration depending on factors such as economic risk sharing, the cost and complexity of development, marketing and commercialization needs, therapeutic areas, potential for combination of drug programs, and geographic capabilities.

Transition to a Fully-Integrated Specialty Biotechnology Company with a Commercial Capability in the I-O Therapeutic Area

If we are successful with the development of NKTR-214 or one of our I-O drug candidates and one or more of them is approved, we plan to establish a commercial capability in the U.S. and other select major markets to market, sell and distribute these proprietary I-O therapies. Under our BMS Collaboration Agreement, we retained significant global commercial rights to NKTR-214 including global co-promotion rights for all combinations of NKTR-214 with any BMS proprietary therapy and we lead global commercialization for all other NKTR-214 combination regimens. We will also record all worldwide sales and revenue for NKTR-214 and we have final decision-making authority regarding the pricing of NKTR-214.

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

We are committed to continuing to build on our intellectual property position in the field of 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 Programs

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]
NKTR-181 (orally-available mu-opioid analgesic molecule)	Moderate to severe chronic pain	Phase 3/NDA Filed
ONZEALD™ (next-generation topoisomerase I inhibitor)	Advanced metastatic breast cancer in patients with brain metastases	Phase 3
NKTR-214 (CD122-preferential IL-2 pathway agonist)	Immuno-oncology	Phase 1, Phase 2, and Phase 3 studies ongoing in multiple indications
NKTR-358 (cytokine Treg stimulant)	Autoimmune Disease	Phase 1
NKTR-262 (toll-like receptor agonist)	Solid Tumors	Phase 1
NKTR-255 (IL-15 receptor agonist)	Immuno-oncology	Preclinical

(1) Status definitions are:
Phase 3 or Pivotal — drug candidate 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

Overview of Nektar Proprietary Programs

Immuno-oncology (I-O)

NKTR-214 (bempegaldesleukin, cytokine immunostimulatory therapy)

NKTR-214 (also known as bempegaldesleukin) is a CD122-preferential IL-2 pathway agonist designed to provide rapid activation and proliferation of cancer-killing CD8+ effector T cells and natural killer (NK) cells, without over-activating the immune system. NKTR-214 stimulates these cancer-killing immune cells in the body by targeting CD122-specific receptors found on the surface of these immune cells. CD122, which is also known as the Interleukin-2 receptor beta subunit, is a key signaling receptor that is known to increase proliferation of these CD8+ effector T cells. This receptor selectivity is intended to increase efficacy and improve safety over existing immunostimulatory cytokine drugs.

Under a research collaboration with The University of Texas MD Anderson Cancer Center, in December 2015 we commenced a Phase 1 study to evaluate NKTR-214 as a monotherapy in a variety of tumor types to evaluate safety and efficacy, and define the recommended Phase 2 dose of NKTR-214 in patients with solid tumors. In addition, the study also assessed the safety profile of NKTR-214, the immunologic effect of NKTR-214 on tumor-infiltrating lymphocytes and other immune activation markers in both blood and tumor tissue, the pharmacokinetic and pharmacodynamic profile of NKTR-214.

The development program for NKTR-214 includes combinations with a number of therapeutic approaches where we believe there is a strong biologic rationale for complementary mechanisms of action. On September 21, 2016, we entered into a Clinical Trial Collaboration Agreement with BMS, pursuant to which we and BMS collaborated to conduct Phase 1/2 clinical trials evaluating NKTR-214 and BMS' human monoclonal antibody that binds PD-1, known as Opdivo® (nivolumab), as a potential combination treatment regimen in five tumor types and eight potential indications (each, a Combined Therapy Trial). In the first phase of the PIVOT-02 study, we evaluated the clinical benefit, safety, and tolerability of combining NKTR-214 with Opdivo® in thirty-eight patients. Interim data from the dose-escalation phase of the trial was presented at the 2017 SITC meeting in November 2017. We identified the recommended Phase 2 dose for NKTR-214 in combination with Opdivo®. The second phase of the expansion cohorts, which now falls under the BMS Collaboration Agreement entered into on February 13, 2018, and described below, is evaluating the safety and efficacy of combining NKTR-214 with Opdivo®. Under the initial Clinical Trial Collaboration Agreement, BMS was responsible for 50% of all out-of-pocket costs reasonably incurred in connection with third party contract research organization, laboratories, clinical sites and institutional review boards. Each party was otherwise be responsible for its own internal costs, including internal personnel costs, incurred in connection with each Combined Therapy Trial.

On February 13, 2018, we entered into the second agreement with BMS (the BMS Collaboration Agreement), pursuant to which we and BMS are jointly developing NKTR-214, including, without limitation, in combination with BMS's Opdivo® (nivolumab) and Opdivo® plus Yervoy® (ipilimumab), and other compounds of BMS, us or any third party. The parties have agreed to jointly commercialize NKTR-214 on a worldwide basis. On April 3, 2018, the closing date of the transaction, BMS paid us a non-refundable upfront cash payment of $1.0 billion and purchased $850.0 million of our common stock at a purchase price of $102.60 per share pursuant to a Share Purchase Agreement (Purchase Agreement). We are eligible to receive additional cash payments of a total of up to $1.43 billion upon achievement of certain development and regulatory milestones and a total of up to $350.0 million upon achievement of certain sales milestones. We will record all worldwide sales and revenue for NKTR-214. We will share global commercialization profits and losses with BMS for NKTR-214, with Nektar sharing 65% and BMS sharing 35% of the net profits and losses. BMS will lead commercialization for combinations of NKTR-214 with BMS proprietary medicines, and we will lead all other commercialization efforts for NKTR-214. We will have the final decision-making authority regarding the pricing for NKTR-214. NKTR-214 will be sold on a stand-alone basis and there will be no fixed-dose combinations or co-packaging without the consent of both parties.

Under the BMS Collaboration Agreement, we and BMS will collaborate to develop and conduct clinical studies of NKTR-214 pursuant to a joint development plan, which includes a series of registration-enabling trials in more than 20 indications in nine tumor types and may be revised only upon mutual agreement of the parties. The parties share the development costs for NKTR-214 in combination regimens, with BMS generally responsible of 67.5% and Nektar generally responsible for 32.5% of the development costs, based on each party's relative ownership interest in the compounds included in the regimens. For costs of producing NKTR-214, however, BMS is responsible for 35% and Nektar is responsible for 65% of costs. Our share of such development costs are limited to an annual cap of $125.0 million. Neither party will develop a therapy using an IL-2 agonist in combination with a small or large molecule that binds to the PD(L)-1 target (and in certain indications the anti-CTLA4 target), in indications included in the joint development plan (each, a Competing Combination), whether alone or in collaboration with any third party, during a limited exclusivity period from the closing date under the BMS Collaboration Agreement until the later of (i) the first commercial sale of NKTR-214 or (ii) the third anniversary of the closing date, but each party may develop a Competing Combination on its own (but not in collaboration with any third party) during the three years after the end of the foregoing limited exclusivity period. If a registration-enabling study included in the joint development plan does not have the first patient enrolled prior to the date which is 14 months from the closing date, subject to allowable delays, the indication covered by that study is no longer subject to the above exclusivity. Other

than as described above, Nektar may independently develop and commercialize NKTR-214 either alone or in combination with other Nektar proprietary compounds or third party compounds.

Outside of the Collaboration Development Plan with BMS, we are also conducting a broad array of development activities evaluating NKTR-214 in combination with other agents that have potential complementary mechanisms of action. Our strategic objective is to establish NKTR-214 as a key component with many immuno-oncology combination regimens with the potential to raise the standard of care in multiple oncology settings:

- On November 6, 2018, we entered into a clinical collaboration with Pfizer, Inc. to evaluate several combination regimens in multiple cancer settings, including metastatic castration-resistant prostate cancer and squamous cell carcinoma of the head and neck. The combination regimens in this collaboration will evaluate NKTR-214 with avelumab, a human anti-PD-L1 antibody in development by Merck KGaA and Pfizer; talazoparib, a poly (ADP-ribose) polymerase (PARP) inhibitor developed by Pfizer; or enzalutamide, an androgen receptor inhibitor in development by Pfizer and Astellas Pharma Inc.
- In February 2019, we started a Phase 1 dose-escalation study with Takeda to evaluate NKTR-214 with Takeda's investigational medicine, TAK-659, a dual inhibitor of both spleen tyrosine kinase (SYK) and FLT-3, in up to 40 patients with advanced non-hodgkin lymphoma.
- We are planning a Phase 1 study this year in pancreatic cancer patients in collaboration with BioXcel to evaluate a triplet combination of NKTR-214, BXCL-701 (a small molecule immune-modulator, DPP 8/9), and avelumab (being supplied to BioXcel by Pfizer and Merck KGaA).
- We are also working in collaboration with Vaccibody AS to evaluate NKTR-214 with Vaccibody's personalized cancer neoantigen vaccine in a Phase 1 proof-of-concept study.

With our non-BMS clinical collaborations for NKTR-214, we generally share clinical development costs on a substantially pro-rata basis. We expect to continue to make significant and increasing investments exploring the potential of NKTR-214 with mechanisms of action that we believe are synergistic with NKTR-214 based on emerging scientific findings in cancer biology and preclinical development work

In addition to these non-BMS clinical collaborations for NKTR-214, we intend to initiate further clinical development programs, on our own or in collaboration with other potential partners, to explore the potential of combining NKTR-214 with other therapies such as cancer vaccines (other than Vaccibody's personalized cancer neoantigen vaccine), adoptive cell therapy, and other small molecules and biological agents in order to generate novel immuno-oncology approaches.

NKTR-262

NKTR-262 is a small molecule agonist that targets toll-like receptors (TLRs) found on innate immune cells in the body. NKTR-262 is designed to overcome the body's dysfunction of antigen-presenting cells (APC), such as dendritic cells, which are critical to induce the body's adaptive immunity and create antigen-specific cytotoxic T cells. NKTR-262 is being developed as a single intra-tumoral injection to be administered at the start of therapy with NKTR-214 in order to induce an abscopal response and achieve the goal of complete tumor regression in cancer patients treated with both therapies. We initiated enrollment of patients in the initial Phase 1/2 clinical study in April 2018, which we call the REVEAL study, and the dose-escalation portion of this clinical study is ongoing.

NKTR-255

NKTR-255 is a biologic that targets the interleukin-15 pathway in order to activate the body's innate and adaptive immunity. Signaling of the IL-15 pathway enhances the survival and function of natural killer (NK) cells and induces survival of both effector and CD8 memory T cells. Native rhIL-15 is rapidly cleared from the body and must be administered frequently and in high doses limiting its utility due to toxicity. NKTR-255 is designed with IL-15 receptor alpha specificity to optimize biological activity and is uniquely engineered to provide optimal exposure and an improved safety profile. Preclinical findings suggest NKTR-255 has the potential to synergistically combine with

antibody dependent cellular toxicity molecules as well as enhance CAR-T therapies. NKTR-255 is currently advancing through preclinical development and we plan to file an IND for NKTR-255 this year and begin the first Phase 1 dose-escalation study in multiple myeloma.

Immunology

NKTR-358 is designed to correct the underlying immune system imbalance in the body which occurs in patients with autoimmune disease. Current systemic treatments for autoimmune disease, including corticosteroids and anti-TNF agents, suppress the immune system broadly and come with severe side effects. NKTR-358 targets the CD25 sub-receptor in the interleukin-2 pathway in order to stimulate proliferation and growth of regulatory T cells, which are specific immune cells in the body that modulate the immune system and prevent autoimmune disease by maintaining self-tolerance.

On July 23, 2017, we entered into the Lilly Agreement, pursuant to which we and Lilly will co develop NKTR-358. Under the terms of the Lilly Agreement, we received an initial payment of $150.0 million in September 2017 and are eligible for up to $250.0 million in additional development and regulatory milestones. We are responsible for completing Phase 1 clinical development and certain drug product development and supply activities. We will also share Phase 2 development costs with Lilly, with 75% of those costs borne by Lilly and 25% of the costs borne by us. We will have the option to contribute funding to Phase 3 development on an indication-by-indication basis, ranging from zero to 25% of the global Phase 3 development costs. We are eligible to receive up to double-digit sales royalty rates that escalate based upon our contribution to Phase 3 development cost and the level of global product annual sales. Lilly will be responsible for all costs of global commercialization and we will have an option to co-promote in the U.S. under certain conditions.

In February 2017, we filed an IND for NKTR-358. We have completed a Phase 1 dose-finding trial of NKTR-358 to evaluate single-ascending doses of NKTR-358 in approximately 100 healthy patients. Results from this study demonstrated a multiple-fold increase in regulatory T cells with no change in CD8 positive or natural killer cell levels and no dose-limiting toxicities were observed. Data from this study is currently planned for presentation at the 2019 European Congress of Rheumatology Conference. The Phase 1 multiple-ascending dose trial to evaluate NKTR-358 in patients with systemic lupus erythematosus (SLE) was initiated in May 2018 and is currently enrolling patients.

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

NKTR-181 (also known as oxycodegol) 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. The abuse deterrent properties of NKTR-181 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 nine 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. We enrolled the first patient in the first Phase 3 efficacy study, which we call SUMMIT-07 in February 2015 and we completed enrollment in the study in the fourth quarter of 2016. In this study, we randomized patients with chronic low back pain in an enriched enrollment randomized withdrawal design which included a qualifying screening period, an open-label titration period where NKTR-181 was given to all patients, followed by a 12-week double-blind randomized period where subjects were randomized on a 1:1 basis to receive either NKTR-181 or placebo. In January 2017, we started enrollment in a second human abuse liability study where we are assessing abuse liability of supra-therapeutic doses of NKTR-181 in order to further evaluate NKTR-181 for labeling and scheduling purposes. On March 20, 2017, we announced that NKTR-181 met its primary and key secondary endpoints in the SUMMIT-07 Phase 3 efficacy study that compared twice-daily dosing of NKTR-181 tablets to placebo in the treatment of over 600 patients with moderate to severe chronic low back pain who were new to opioid therapy (opioid-naïve).

SUMMIT-07 evaluated four analgesic doses of NKTR-181 (100 mg, 200 mg, 300 mg and 400 mg). Patients in the trial achieved an average pain score reduction of over 65% (from 6.73 at screening to 2.32 at randomization) during the dose titration period. The primary efficacy endpoint of the study demonstrated significantly improved chronic back pain relief with NKTR-181 compared to placebo (p=0.0019). Key secondary endpoints of the study also achieved high statistical significance. The study demonstrated that NKTR-181 had a favorable safety profile and was well tolerated.

Additionally, on July 18, 2017, we announced positive top-line data for our pivotal human abuse potential study (HAP) for NKTR-181. The HAP study was designed to confirm and assess the relative oral abuse potential of NKTR-181, at its maximum analgesic therapeutic, dose (400 mg) studied in the SUMMIT-07 trial and at a supratherapeutic dose (3 times to 12 times greater than the analgesic dose range of 100 mg to 400 mg used in the SUMMIT-07 trial), compared to common therapeutic doses of oxycodone (40 mg and 60 mg) in 54 healthy non-dependent recreational drug users. For the primary endpoint of Drug Liking, NKTR-181 (400 mg and 600 mg) rated less likable compared to oxycodone 40 mg and 60 mg (p<0.0001), and a supratherapeutic dose of NKTR-181 (1200 mg) rated less likable than oxycodone 60 mg (p=0.0071). Key secondary endpoints of Area Under Effect for Drug Liking (0-1 hours, 0-2 hours, 0-3 hours), Drug High and Take Drug Again scores met statistical significance for all doses of NKTR-181 (1200 mg, 600 mg, 400 mg) compared to oxycodone (60 mg).

The SUMMIT Phase 3 program also included a 52-week long-term safety study, which we call SUMMIT-LTS. This study evaluated the long-term safety and tolerability of NKTR-181 in 638 patients (opioid-naïve and opioid-experienced) with moderate to severe chronic low pain or chronic non-cancer pain. The study showed that NKTR-181 had a favorable safety profile and analgesic effect maintained over 52-weeks. On July 30, 2018, we announced that the NDA for NKTR-181 for the treatment of chronic low back pain in adult patients new to opioid therapy was accepted by the FDA for review. In February 2019, the FDA informed us it had adjusted the Prescription Drug User Fee Act (PDUFA) target action date from May 29, 2019 to August 29, 2019. If approved, we are evaluating several strategic alternatives to commercialize NKTR-181 including, without limitation, establishing a separate subsidiary company or joint venture with one or more partners with commercial capabilities and/or strategic capital partners. Since we have not yet established a commercial launch capability for NTKR-181, if approved, there remains substantial risk and uncertainties related to successful and timely completion of this process.

According to a 2013 report from the World Health Organization, approximately 149 million work days are lost every year because of low back pain, with total costs estimated to be $100 to $200 billion a year (of which two-thirds is due to lost wages and lower 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.

Oncology - ONZEALD™ (next generation, long-acting topoisomerase I inhibitor)

ONZEALD™ (previously known as NKTR-102 or etirinotecan pegol) is our next-generation topoisomerase I inhibitor proprietary drug candidate. In 2015, we announced top-line data from a Phase 3 clinical study for ONZEALD™, which we call the BEACON study (BrEAst Cancer Outcomes with ONZEALD™), as a single-agent therapy for women with advanced metastatic breast cancer. The BEACON study compared ONZEALD™ 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 top-line analysis of 852 patients from the trial, ONZEALD™ provided a 2.1 month improvement in median overall survival over TPC (12.4 months for patients receiving ONZEALD™ compared to 10.3 months for patients receiving TPC). Based on a stratified log-rank analysis, the primary endpoint measuring the hazard ratio for survival in the ONZEALD™ 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.

Based on meetings with European Union (EU) health authorities, in June 2016, we filed a Marketing Authorization Application (MAA) with the European Medicines Agency (EMA) for conditional approval of ONZEALD™ for adult patients with advanced breast cancer who have brain metastases and began enrolling patients in the ATTAIN study, which is comparing the overall survival in patients with breast cancer and brain metastases treated with ONZEALD™ versus physicians treatment of choice. On July 21, 2017, we were informed by the EMA's Committee for Medicinal Products for Human Use (CHMP) that it had adopted a negative opinion for the conditional marketing authorization application for ONZEALD™ in the EU. The Phase 3 study (ATTAIN) in breast cancer patients having brain metastases is ongoing.

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 (approximately 12%). In 2017, the American Cancer Society estimated there will be 252,710 new cases of invasive breast cancer diagnosed in the U.S. and about 40,610 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.

Collaboration Partner Programs

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. More than 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.

	Primary or Target	Drug	
Drug	Indications	Marketer/Partner	Status(1)
ADYNOVATE® (previously referred to as BAX 855, PEGylated rFVIII) and ADYNOVI® (brand name for ADYNOVATE® in Europe)	Hemophilia A	Takeda	Approved 2015
MOVANTIK® (naloxegol tablets) and MOVENTIG® (brand name for MOVANTIK® in Europe)	Opioid-induced constipation in adult patients with chronic non-cancer pain (US); Opiod-induced constipation in adult patients who have and inadequate response to laxatives (EU).	AstraZeneca AB	Approved 2014
CIMZIA® (certolizumab pegol)	Crohn's disease, Rheumatoid arthritis, and Psoriasis/ Ankylosing Spondylitis	UCB Pharma	Approved 2008*
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 2007*
Macugen® (pegaptanib sodium injection)	Age-related macular degeneration	Bausch Health Companies Inc. (formerly, Valeant Pharmaceuticals	Approved 2004

		International, Inc.)	
Somavert® (pegvisomant)	Acromegaly	Pfizer Inc.	Approved 2003
Neulasta® (pegfilgrastim)	Neutropenia	Amgen Inc.	Approved 2002
Dapirolizumab Pegol	Systemic Lupus Erythematosus	UCB Pharma (Biogen)	Phase 2
PEGPH20	Pancreatic, Non-Small Cell Lung Cancer, and other multiple tumor types	Halozyme Therapeutics, Inc.	Phase 1, 2, and 3
Longer-acting blood clotting proteins	Hemophilia	Takeda	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. Year indicates first regulatory approval.

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

Phase 3 or Pivotal — drug candidate 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® and MIRCERA® effective as of January 1, 2012.

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 Collaboration Partner Programs

We have a number of product candidates in clinical development and approved products in collaboration with our partners where we invented the drug candidate or where our collaboration partners have licensed our proprietary intellectual property to enable one of their drug candidates. Our agreements with collaboration partners may involve several elements including a technology license as well as the development, commercialization, and manufacturing and supply obligations. We typically receive consideration from our collaboration partners in the form of upfront payments, or milestone payments and royalties on sales. In certain cases, we also manufacture and supply our proprietary polymer materials to our partners.

ADYNOVATE® (previously referred to as BAX 855), ADYNOVI® (brand name for ADYNOVATE® in Europe) and Longer-Acting Blood Clotting Proteins for Hemophilia A, Agreement with Subsidiaries of Baxalta Incorporated

In September 2005, we entered into an exclusive research, development, license, manufacturing and supply agreement (Baxalta License Agreement) with certain subsidiaries of Baxalta (which has been acquired by Takeda), 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). ADYNOVATE® was first approved by the FDA on November 30, 2015. Since then it has been approved in one or more indications for Hemophilia A in the EU, Japan, and other countries around the world.

We are entitled to $35.0 million of 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 October 2017, we entered into a right to sublicense agreement with Baxalta, under which we granted to Baxalta the right to grant a nonexclusive sublicense to certain patents to a third party that were previously exclusively licensed to Baxalta under the Baxalta License Agreement. Under the right to sublicense agreement, Baxalta paid us $12.0 million in November 2017 and agreed to pay us single digit royalty payments based upon net sales of the third party products covered under the sublicense throughout the term of the right to sublicense agreement.

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 and 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 $6.0 billion globally.

MOVANTIK® and MOVENTIG® (brand name for MOVANTIK® in Europe), License Agreement with AstraZeneca AB

In September 2009, we entered into a global license agreement with AstraZeneca AB (AstraZeneca) pursuant to which we granted AstraZeneca a worldwide, exclusive, perpetual, royalty-bearing license under our patents and other intellectual property to develop, market and sell MOVANTIK®. 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 which is a medication 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 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. AstraZeneca launched the commercial sales of MOVANTIK® in the U.S. in March 2015 and MOVENTIG® in Germany, the first EU member country, in August 2015. Under the terms of our license agreement with AstraZeneca, 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®. 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 the EMA, respectively, in 2013. We received an additional developmental 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 and 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. On March 1, 2016, AstraZeneca announced that it had entered into an agreement with Kyowa Hakko Kirin Co. Ltd. (Kirin), granting Kirin exclusive marketing rights to MOVENTIG® in the EU, Iceland, Liechtenstein, Norway and Switzerland. Nektar's receipt of a 40% share of royalty payments made by Kirin to AstraZeneca will be financially equivalent to Nektar receiving high single-digit to low double-digit royalties depending on Kirin's annual net sales levels. 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.

CIMZIA®, Agreement with UCB

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 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 our Consolidated Financial Statements. Our agreement with UCB Pharma 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 and Hoffmann-La Roche Inc.

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. In 2013, we delivered additional quantities of PEGylation materials used by Roche to produce PEGASYS® and MIRCERA® for total consideration of approximately $18.6 million. 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 our Consolidated Financial Statements. As of December 31, 2016, we no longer had any continuing manufacturing or supply obligations under this MIRCERA® agreement.

Macugen®, Agreement with Bausch Health Companies Inc., formerly 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. 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. Our agreement with Valeant 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.

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.

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.

Dapirolizumab Pegol

In 2010, we entered into a license, manufacturing and supply agreement with UCB Pharma S.A., (UCB) under which we granted UCB a worldwide, exclusive license to certain of our proprietary PEGylation technology to develop, manufacture and commercialize an anti-CD40L PEGylated 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. In 2016, UCB initiated a multi-center, randomized, double-blind, placebo-controlled, parallel-group, dose-ranging Phase 2 clinical study followed by an observational period to evaluate the efficacy and safety of patients with moderately to severely active SLE receiving stable standard of care medications. In October 2018, UCB announced that the primary endpoint of the study to demonstrate a dose response at 24 weeks on the British Isles Lupus Assessment Group (BILAG) based Composite Lupus Assessment (BICLA) was not met and stated that it and Biogen will continue to further evaluate these data while assessing potential next steps.

PEGPH20, Agreement with Halozyme Therapeutics, Inc.

In December 2006, we entered into a license agreement with Halozyme pursuant to 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 3 clinical study combining PEGPH20 with ABRAXANE® (nab-paclitaxel) and gemcitabine in stage IV pancreatic ductal adenocarcinoma (PDA) (HALO 301), in Phase 1b clinical testing for PEGPH20 with KEYTRUDA® (pembrolizumab) in non-small cell lung cancer and gastric cancer (HALO 101), in Phase 1b/2 clinical testing for PEGPH20 with HALAVEN® (eribulin) in patients treated with up to two lines of prior therapy for HER2-negative metastatic breast cancer, in Phase 1b/2 clinical testing for PEGPH20 with Tecentriq® (atezolizumab) in patients with previously treated metastatic PDA, in Phase 1b/2 clinical testing for PEGPH20 with Tecentriq in patients with gastric cancer and in Phase 1b/2 clinical testing for PEGPH20 with Tecentriq in patients with cholangiocarcinoma and gall bladder cancer (HALO 110-101/MATRIX). 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.

Government Regulation

Product Development and Approval Process

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 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.

In situations where our partners are responsible for clinical and regulatory approval procedures, we may still 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 polymer conjugation 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.

Coverage, Reimbursement, and Pricing

Sales of any products for which we may obtain regulatory approval depend, in part, on the coverage and reimbursement status of those products. In the U.S., sales of any products for which we may receive regulatory approval for commercial sale will depend in part on the availability of coverage and reimbursement from third-party payors. Third-party payors include government programs such as Medicare, Medicaid, TRICARE and the Veterans Administration, as well as managed care providers, private health insurers and other organizations.

The process for determining whether a payor will provide coverage for a product is typically separate from the process for setting the reimbursement rate that the payor will pay for the product. Third-party payors may limit coverage to specific products on an approved list or formulary which might not include all of the FDA-approved products for a particular indication. Third-party payors may also refuse to include a particular branded drug on their formularies or otherwise restrict patient access to a branded drug when a less costly generic equivalent or other alternative is available. Further, private payors often follow the coverage and payment policies established by certain government programs, such as Medicare and Medicaid, which require manufacturers to comply with certain rebate, price reporting, and other obligations. For example, the Medicaid Drug Rebate Program, which is part of the Medicaid program (a program for financially needy patients, among others), requires pharmaceutical manufacturers to enter into and have in effect a national rebate agreement with the Secretary of the Department of Health and Human Services under which the manufacturer agrees to report certain prices to the government and pay rebates to state Medicaid programs on outpatient drugs furnished to Medicaid patients, as a condition for receiving federal reimbursement for the manufacturer's outpatient drugs furnished to Medicaid patients. Further, in order for a pharmaceutical product to receive federal reimbursement under Medicare Part B and Medicaid programs or to

be sold directly to U.S. government agencies, the manufacturer must extend discounts to entities eligible to participate in the Public Health Service's 340B drug pricing program.

Third-party payors are increasingly challenging the prices charged for medical products and services, and examining the medical necessity and cost- effectiveness of medical products and services, in addition to their safety and efficacy. Additionally, the containment of healthcare costs has become a priority of federal and state governments, and the price of therapeutics have been a focus in this effort. The U.S. government and state legislatures have shown significant interest in implementing cost-containment programs, including price controls and restrictions on reimbursement, among other controls. Adoption of price controls or other cost-containment measures could limit coverage for or the amounts that federal and state governments or private payors will pay for health care products and services, which could also result in reduced demand for our drug candidates or additional pricing pressures and affect our ultimate profitability. If third-party payors do not consider a product to be cost-effective compared to other available therapies, they may not cover an approved product or, if they do, the level of payment may not be sufficient to allow us to sell our products at a profit.

The marketability of any products for which we receive regulatory approval for commercial sale may suffer if the government and third-party payors fail to provide adequate coverage and reimbursement. Coverage policies and third-party reimbursement rates may change at any time. Even if favorable coverage and reimbursement status is attained for one or more products for which we receive regulatory approval, less favorable coverage policies and reimbursement rates may be implemented in the future.

Other Healthcare Laws and Regulations

If we obtain regulatory approval of our products, we may be subject to various federal and state laws targeting fraud and abuse in the healthcare industry. These laws may impact, among other things, our proposed sales and marketing programs. In addition, we may be subject to patient privacy regulation by both the federal government and the states in which we conduct our business. The laws that may affect our ability to operate include:

- the federal Anti-Kickback Statute, which prohibits, among other things, persons from knowingly and willfully soliciting, receiving, offering, or paying remuneration (a term interpreted broadly to include anything of value, including, for example, gifts, discounts, and credits), directly or indirectly, in cash or in kind, to induce or reward, or in return for, either the referral of an individual for, or the purchase, order, or recommendation of, an item or service reimbursable under a federal healthcare program, such as the Medicare and Medicaid programs;
- federal civil and criminal false claims laws and civil monetary penalty laws, which prohibit, among other things, individuals or entities from knowingly presenting, or causing to be presented, claims for payment to Medicare, Medicaid, or other third-party payors that are false or fraudulent, or making a false statement or record material to payment of a false claim or avoiding, decreasing, or concealing an obligation to pay money owed to the federal government;
- provisions of the federal Health Insurance Portability and Accountability Act of 1996, or HIPAA, which created new federal criminal statutes, referred to as the "HIPAA All-Payor Fraud Prohibition," that prohibit knowingly and willfully executing a scheme to defraud any healthcare benefit program and making false statements relating to healthcare matters;
- federal transparency laws, including the federal Physician Payment Sunshine Act, which require manufacturers of certain drugs and biologics to track and disclose payments and other transfers of value they make to U.S. physicians and teaching hospitals as well as physician ownership and investment interests in the manufacturer, and that such information is subsequently made publicly available in a searchable format on a CMS website;
- provisions of HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act and its implementing regulations, which imposes certain requirements relating to the privacy, security and transmission of individually identifiable health information; and
- state law equivalents of each of the above federal laws, such as anti-kickback and false claims laws which may apply to items or services reimbursed by any third-party payor, including commercial insurers, state transparency reporting

and compliance laws; and state laws governing the privacy and security of health information in certain circumstances, many of which differ from each other in significant ways and which may not have the same effect, thus complicating compliance efforts.

The Patient Protection and Affordable Care Act, as amended by the Health Care Education Reconciliation Act (collectively, the "Affordable Care Act"), enacted in 2010, expanded the reach of the fraud and abuse laws by, among other things, amending the intent

requirement of the federal Anti-Kickback Statute and the applicable criminal fraud statutes contained within 42 U.S.C. § 1320a-7b. Pursuant to the Affordable Care Act, a person or entity no longer needs to have actual knowledge of this statute or specific intent to violate it in order to have committed a violation. In addition, the Affordable Care Act provides that the government may assert that a claim including items or services resulting from a violation of the federal Anti-Kickback Statute constitutes a false or fraudulent claim for purposes of the civil False Claims Act or the civil monetary penalties statute. Many states have adopted laws similar to the federal Anti-Kickback Statute, some of which apply to the referral of patients for healthcare items or services reimbursed by any source, not only the Medicare and Medicaid programs.

The federal False Claims Act prohibits anyone from, among other things, knowingly presenting, or causing to be presented, for payment to federal programs (including Medicare and Medicaid) claims for items or services that are false or fraudulent. Although we would not submit claims directly to payors, manufacturers can be held liable under these laws if they are deemed to "cause" the submission of false or fraudulent claims by, for example, providing inaccurate billing or coding information to customers or promoting a product off-label. In addition, our future activities relating to the reporting of wholesaler or estimated retail prices for our products, the reporting of prices used to calculate Medicaid rebate information and other information affecting federal, state, and third-party reimbursement for our products, and the sale and marketing of our products, are subject to scrutiny under this law. For example, pharmaceutical companies have been prosecuted under the federal False Claims Act in connection with their alleged off-label promotion of drugs, purportedly concealing price concessions in the pricing information submitted to the government for government price reporting purposes, and allegedly providing free product to customers with the expectation that the customers would bill federal health care programs for the product. Penalties for a False Claims Act violation include three times the actual damages sustained by the government, plus mandatory civil penalties of between $10,781 and $21,916 for each separate false claim, the potential for exclusion from participation in federal healthcare programs, and, although the federal False Claims Act is a civil statute, conduct that results in a False Claims Act violation may also implicate various federal criminal statutes. In addition, private individuals have the ability to bring actions under the federal False Claims Act and certain states have enacted laws modeled after the federal False Claims Act.

Legislative and Regulatory Landscape

From time to time, legislation is drafted, introduced and passed in Congress that could significantly change the statutory provisions governing the testing, approval, manufacturing, marketing, coverage and reimbursement of products regulated by the FDA or other government agencies. In addition to new legislation, FDA and healthcare fraud and abuse and coverage and reimbursement regulations and policies are often revised or interpreted by the agency in ways that may significantly affect our business and our products. Further, the 2016 Presidential and Congressional elections and subsequent developments have caused the future state of many core aspects of the current health care marketplace to be uncertain, as the new Presidential Administration and Congress have repeatedly expressed a desire to repeal all or portions of the Affordable Care Act. While specific changes and their timing are not yet apparent, there may be significant changes to the healthcare environment in the future that could have an adverse effect on anticipated revenues from therapeutic candidates that we may successfully develop and for which we may obtain regulatory approval. Furthermore, federal agencies, Congress, state legislatures, and the privacy sector have shown significant interest in implementing cost containment programs to limit the growth of health care costs, including price controls, restrictions on reimbursement and other fundamental changes to the healthcare delivery system. Any proposed or actual changes could limit coverage for or the amounts that federal and state governments will pay for health care products and services, which could also result in reduced demand for our products or additional pricing pressures and affect our ultimate profitability.

Patents and Proprietary Rights

We own more than 275 U.S. and 850 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 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 advanced polymer conjugate technology platforms. 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.

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, 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 a combination of revenue elements including up-front payments for licensing agreements, milestone payments based on clinical progress, regulatory progress or net sales achievements, royalties or product sales revenue. Our revenues are concentrated among a limited number of collaboration partners under long-term arrangements. In particular, our

collaboration arrangements with BMS and Lilly represent 89% of our revenues for the year ended December 31, 2018 and 42% of our revenues for the year ended December 31, 2017, respectively, and these arrangements provide for the most significant portion of our potential future development and regulatory milestones. The relative portion of such revenues in any particular year, however, is dependent upon the mix of any milestone or other license revenues recognized and volume of recurring royalty revenues and product sales. Additionally, we derive substantially all of our cash royalty revenue from our collaboration arrangements with Takeda for ADYNOVATE®/ADYNOVI™ and AstraZeneca for MOVANTIK®/MOVENTIG® and we derive the significant majority of our product sales from two other partners.

Backlog

Pursuant to our collaboration agreements, we manufacture and supply our proprietary polymer conjugation materials. Inventory is produced and sales are made pursuant to customer purchase orders for delivery generally based on rolling four to eight quarter forecasts, of which at least two quarters are generally binding. Our backlog is not significant. 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 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 advanced polymer conjugate technologies, our competitors include Biogen Idec Inc., Crealta Pharma, 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 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

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., Eli Lilly & Co., Pfizer, Purdue Pharma L.P., and Teva Pharmaceutical Industries Ltd.

NKTR-214 (bempegaldesleukin)(CD122-preferential IL-2 pathway agonist)

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 Gilead Sciences, Inc. (through its acquisition of Kite Pharma)/NCI, Apeiron Biologics, Philogen S.p.A., IRX Therapeutics, Anaveon AG, and Adaptimmune LLC. In the cytokine-based therapies space, potential competitors include Novartis, Alkermes, Altor Bioscience, Eli Lilly & Co. (through its acquisition of Armo Biosciences), Roche, and Synthorx, Inc., and in the checkpoint inhibitor space potential competitors include Tesaro, Inc., Macrogenics, Inc., Merck, Bristol-Myers Squibb, and Roche.

NKTR-358 (IL-2 conjugate regulator T Cell stimulator)

There are a number of competitors in various stages of clinical development that are working on programs which are designed to correct the underlying immune system imbalance in the body due to autoimmune disease. In particular, we expect to compete with therapies that could be cytokine-based therapies (Symbiotix, LLC and Tizona Therapeutics), regulatory T cell therapies (Targazyme, Inc., Caladrius BioSciences, Inc., and Tract Therapeutics, Inc.), or IL-2 based therapies (Amgen, Inc.).

ONZEALD™ (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 advanced breast cancer. These therapies are only partially effective in treating advanced or metastatic breast cancer and none of them have a specific indication in either the U.S. or Europe for treatment of patients with advanced breast cancer and co-existing brain metastases. These therapies include but are not limited to: Abraxane® (paclitaxel protein-bound particles for injectable suspension (albumin bound)), Afinitor® (everolimus), Ellence® (epirubicin), Gemzar® (gemcitabine), Halaven® (eribulin), Herceptin®

(trastuzumab), Ixempra® (ixabepilone), Navelbine® (vinolrebine), Xeloda® (capecitabine) and Taxotere® (docetaxel). Major pharmaceutical or biotechnology companies with approved drugs or drugs in development for these cancers include Bristol-Myers Squibb Company, Eisai, Inc., Roche Holding Group (including its Genentech subsidiary), GlaxoSmithKline plc, Pfizer, Inc., Eli Lilly & Co., Sanofi Aventis S.A., and others.

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 and an oral treatment known as RELISTOR® which is marketed by Bausch Health Companies Inc. (formerly, Valeant Pharmaceuticals International, Inc., which previously acquired 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 July 22, 2016, Relistor (methylnaltrexone bromide) oral tablets for the treatment of OCI in adult patients with chronic non-cancer pain was approved by FDA. 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, GlaxoSmithKline plc, Ironwood Pharmaceuticals, Inc. in collaboration with Actavis plc, Purdue Pharma L.P. in collaboration with Shionogi & Co., Ltd., 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. On August 31, 2018, Bayer Healthcare received FDA approval for JIVI® (antihemophilic factor (recombinant) PEGylated-aucl), an extended half-life Factor VIII for Hemophilia A treatment in patients 12 and older which became commercially available in the third quarter of 2018. In addition, on February 19, 2019, Novo Nordisk received FDA approval for ESPEROCT® [antihemophilic factor (recombinant), glycoPEGylated-exei] a glycoPEGylated Factor VIII product with an extended half-life for use in adults and children with Hemophilia A, and is expected to be commercially available in 2020. The Bayer product and the Novo Nordisk product (upon launch) are competitors in the extended half-life Factor VIII market.

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,		
	2018	2017	2016
Third party and direct materials costs	$206.9	$125.4	$98.2
Personnel, overhead and other costs	130.8	113.5	84.6
Stock-based compensation and depreciation	61.8	29.6	21.0
Research and development expense	$399.5	$268.5	$203.8

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 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 biologics nor finished drug products for our development programs, we primarily utilize contract manufacturers to manufacture biologics and finished drug product for us. We

also utilize the services of contract manufacturers to manufacture APIs and finished drug products required for later phases of clinical development and eventual commercialization under all applicable laws and regulations.

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 for early phase clinical development products and enter into long-term supply arrangements only for late stage products nearing regulatory approval for marketing authorization.

Environment

As a manufacturer of PEG reagents for the U.S. market, we are subject to inspections by the FDA and EPA 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, 2018, we had 618 employees, of which 493 employees were engaged in research and development, manufacturing, commercial operations and quality activities and 125 employees in general administration and business development. Of the 618 employees, 547 were located in the U.S. and 71 were located in India. We have a number of employees who hold advanced degrees, such as Ph.D. 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 and clinical 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 22, 2019:

Name	Age	Position
Howard W. Robin	66	Director, President and Chief Executive Officer

Stephen K. Doberstein, Ph.D.	60	Senior Vice President, Research & Development and Chief Research & Development Officer
Maninder Hora, Ph.D	65	Senior Vice President, Pharmaceutical Development and Chief Technical Operations Officer
Gil M. Labrucherie, J.D.	47	Senior Vice President and Chief Financial Officer
John Nicholson	67	Senior Vice President and Chief Operating Officer
Jillian B. Thomsen	53	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.

Stephen K. Doberstein, Ph.D. has served as our Senior Vice President, Research & Development and Chief Research & Development Officer since November 2017. Dr. Doberstein served as Senior Vice President and Chief Scientific Officer from January 2010 to November 2017 when he was promoted to Senior Vice President, Research & Development and Chief Research & Development Officer. 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.

Maninder Hora, Ph.D. has served as our Senior Vice President, Pharmaceutical Development and Chief Technical Operations Officer since November 2017 and served as Senior Vice President, Pharmaceutical Development and Manufacturing from August 2010 to November 2017. 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.

Gil M. Labrucherie has served as our Senior Vice President and Chief Financial Officer since June 2016. Mr. Labrucherie served as our Vice President, Corporate Legal from October 2005 through April 2007 and served as our Senior Vice President, General Counsel and Secretary from April 2007 through June 2016 when he was promoted to Senior Vice President and Chief Financial Officer. 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 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.

John Nicholson has served as our Senior Vice President and Chief Operating Officer since June 2016. 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 and served as our Chief Financial Officer until June 2016 when he was promoted to Senior Vice President and Chief Operating Officer.

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.

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 began her career as a certified public accountant 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.

29

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

We are highly dependent on the success of NKTR-214, our lead I-O candidate. We are executing a broad development program for NKTR-214 and clinical and regulatory outcomes for NKTR-214, if not successful, will significantly harm our business.

Our future success is highly dependent on our ability to successfully develop, obtain regulatory approval for, and commercialize NKTR-214. In general, most early stage investigatory drugs, including oncology drug candidates such as NKTR-214, do not become approved drugs. Accordingly, there is a very meaningful risk that NKTR-214 will not succeed in one or more clinical trials sufficient to support one or more regulatory approvals. To date, reported clinical outcomes from NKTR-214 have had a significant impact on our market valuation, financial position, and business prospects and we expect this to continue in future periods. If one or more clinical studies of NKTR-214 are delayed or not successful, it would materially harm our market valuation, prospects, financial condition and results of operations. For example, under the BMS Collaboration Agreement, we are entitled to up to $1.43 billion in development milestones that are based upon clinical and regulatory successes from the NKTR-214 development program. One or more failures in NKTR-214 studies could jeopardize such milestone payments, and any product sales or royalty revenue or commercial milestones that we would otherwise be entitled to receive could be reduced, delayed or eliminated.

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 have ongoing trials evaluating NKTR-214 including a trial evaluating NKTR-214 as a potential combination treatment with BMS's Opdivo® (nivolumab) as well as other ongoing and planned combination trials. We also have an ongoing Phase 1 multiple-ascending dose trial to evaluate NKTR-358 in patients with systemic lupus erythematosus. We also continue to enroll patients in a Phase 1/2 study evaluating NKTR-214 in combination with NKTR-262. 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. Clinical study delays could also shorten any commercial periods during which our products have patent protection and may allow our competitors to bring products to market before we do, which could impair our ability to successfully commercialize our product candidates and may harm our business and results of operations.

The outcomes from competitive I-O and combination therapy clinical trials, and the discovery and development of new potential oncology therapies, could have a material and adverse impact on the value of our I-O research and development pipeline.

The research and development of I-O therapies is a very competitive global segment in the biopharmaceutical industry attracting billions of dollars of investment each year. Our clinical trial plans for NKTR-214, NKTR-262, and NKTR-255 face substantial competition from other I-O combination regimens already approved, and many more combination therapies that are either ahead of or in parallel development in patient populations where we are studying our drug candidates. I-O drug development entails substantial risks and uncertainties that include rapidly changing standards of care, patient enrollment competition, evolving regulatory frameworks to evaluate combination regimens, and varying risk-benefit profiles of competing therapies, any or all of which could have a material and adverse impact on the probability of success of I-O drug candidates.

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 (including commercialization of a competing therapy in the same or similar indication for which our drug candidate is being studied) and other variables (such as commercial supply challenges). 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-214, NKTR-358, NKTR-262, NKTR-255, NKTR-181, ONZEALD®, and other drug candidates currently in discovery research or preclinical development. The failure of one or more of our drug candidates could have a material adverse effect on our business, financial condition and results of operations.

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, an independent Institutional Review Board (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 patients 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.

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 most cases, we rely on contract manufacturing organizations to manufacture and supply drug product for our clinical studies and those of our collaboration partners. The manufacturing of drugs 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, 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 API and drug product 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 API or drug products 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. 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.

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.

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 drug products, 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 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 our BEACON study for ONZEALD® in 2015 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 is conducting a post-marketing, observational epidemiological study comparing MOVANTIK® to other treatments of opioid-induced constipation (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 and 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.

The NKTR-181 program is subject to important risks and uncertainties related to likelihood of FDA approval, commercial potential, and nonconvertibility of NKTR-181, any of which could significantly and negatively impact the economic value of NKTR-181.

On May 31, 2018, we announced that we submitted an NDA for NKTR-181 and on July 30, 2018, we announced that the NDA for NKTR-181 for the treatment of chronic low back pain in opioid-naïve adult patients was accepted by the FDA for review. The FDA has assigned a PDUFA target action date of August 29, 2019. While the results from the Phase 3 study of NKTR-181 were positive, and NKTR-181 has Fast Track designation, the regulatory pathway for NKTR-181 remains subject to substantial uncertainty including the amount of data required to support an approval of NKTR-181. In addition, regulations concerning and controlling the access to opioid-based pharmaceuticals are strict and there is no guarantee which scheduling category will apply to NKTR-181 if regulatory approval is achieved. The commercial potential of NKTR-181 remains difficult to predict due to factors that include, for example, the safety and efficacy compared to other available treatments, changing standards of care, third party payer reimbursement standards, scope and contents of the NKTR-181 label, constraints on marketing, patient and physician preferences, drug scheduling status, current and future litigation involving analgesic pharmaceuticals, perceived or actual resistance to the introduction of new controlled substances to the market, the availability of competitive alternatives that may emerge either during or after approval, the availability of generic versions of our NKTR-181, and the countries in which we receive regulatory approvals. If the market potential for NKTR-181 is lower than we anticipated, it could significantly and negatively impact the commercial potential and value of NKTR-181. In the event that we commercialize and market NKTR-181 products, we would be required to build, either internally or through third-party contracts, 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. 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, thereby having 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.

If NKTR-181 is approved by FDA, the ability to market and promote NKTR-181 will depend on the scope and content of the final FDA-approved labeling, which could have a material and adverse impact on the market potential of NKTR-181.

If NKTR-181 is approved by the FDA, the commercial success of NKTR-181 will be materially impacted by the FDA-approved label which will set forth the patient population covered by the approved indication in the label, the required warnings, a description of efficacy outcomes, and the human abuse potential profile of NKTR-181, among other matters, for healthcare providers and patients. FDA approval is required to make safety and efficacy claims regarding a product. As a result, there is substantial risk and uncertainty regarding the content of the final label and package insert for NKTR-181, if approved by FDA, which could materially and adversely impact the commercial potential of NKTR-181.

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 (other than the BMS Collaboration Agreement), 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 impact on our business. 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 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, 2018, we had cash and investments in marketable securities valued at approximately $1.9 billion and had debt of $250.0 million in principal of senior secured notes. Our cash and investments balance at December 31, 2018 reflects $1.85 billion received from BMS. As described above and in Note 10 to our Consolidated Financial Statements, in February 2018, we entered into the BMS Collaboration Agreement under which BMS paid us a non-refundable upfront cash payment of $1.0 billion on April 3, 2018. We also entered into the Share Purchase Agreement under which BMS purchased $850.0 million of shares of our common stock on April 3, 2018. 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 NKTR-214 in collaboration with BMS and NKTR-358 licensed to Lilly;
- 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® by AstraZeneca in the U.S. and ADYNOVATE® by Baxalta (a wholly-owned subsidiary of Takeda) globally, as well as MOVENTIG® (the naloxegol brand name in the EU) by Kirin in the EU;
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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.

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 potential of the drug candidate, 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 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 coverage and payment or reimbursement from third-party payers, such as government programs, including Medicare and Medicaid, managed care providers, private health insurers and other organizations. However, eligibility for coverage does not necessarily signify that a drug candidate will be adequately

reimbursed in all cases or at a rate that covers costs related to research, development, manufacture, sale, and distribution. Third-party payers are increasingly challenging the price and cost effectiveness of medical products and services. Therefore, significant uncertainty exists as to the coverage and 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 coverage or pricing approvals for, and reimbursement of, our products from government authorities and third-party payers. For example, Congress passed the Affordable Care Act in 2010 which enacted a number of reforms to expand access to health insurance while also reducing or constraining the growth of healthcare spending, enhancing remedies against fraud and abuse, adding new transparency requirements for healthcare industries, and imposing new taxes

on fees on healthcare industry participants, among other policy reforms. Federal agencies, Congress and state legislatures have continued to show interest in implementing cost containment programs to limit the growth of health care costs, including price controls, restrictions on reimbursement and other fundamental changes to the healthcare delivery system. In addition, in recent years, Congress has enacted various laws seeking to reduce the federal debt level and contain healthcare expenditures, and the Medicare and other healthcare programs are frequently identified as potential targets for spending cuts. New government legislation or regulations related to pricing or other fundamental changes to the healthcare delivery system as well as a government or third-party payer decision not to approve pricing for, or provide adequate coverage or reimbursement of, our products hold the potential to severely limit market opportunities of such products.

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.

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 product sales. Significant variations in the timing of receipt of cash payments and our recognition of revenue can result from 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.

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, substantially all of our revenue from collaboration agreements with biotechnology and pharmaceutical companies. These collaboration agreements contain complex commercial terms, including:

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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 numerous significant collaboration agreements and other strategic transaction agreements (e.g., financings and asset divestitures) that contain complex representations and warranties, covenants and indemnification obligations. If we are found to have materially breached such agreements, it could subject us to substantial liabilities and harm our financial condition.

From time to time, we are involved in litigation matters involving the interpretation and application of complex terms and conditions of our agreements. One or more disputes may arise or escalate in the future regarding our collaboration agreements, transaction documents, or third-party license agreements that may ultimately result in costly litigation and unfavorable interpretation of contract terms, which would have a material adverse effect on our business, financial condition and results of operations.

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 (a wholly-owned subsidiary of Takeda). In the event that we market our products without a partner, we would be required to build, either internally or through third-party contracts, 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.

If we are unable to create robust 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 or distribution capabilities. To commercialize any of our drugs that receive regulatory approval for commercialization, we must develop robust internal sales, marketing and distribution capabilities, and manage inventory, supply, labeling, storage, record keeping, and advertising and promotion 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 through partnerships 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 successfully educate adequate numbers of physicians about the potential benefits associated with the use of, and to subsequently 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.

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 the 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.

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

Due to the recognition of $1,059.8 million of revenue from the upfront payment of our BMS Collaboration Agreement as described in Note 10 to our Consolidated Financial Statements, for the year ended December 31, 2018, we reported net income of $681.3 million. Excluding this revenue item, 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 biotechnology companies;
- effectively estimate and manage clinical development costs, particularly the cost of the clinical studies for NKTR-214, NKTR-358, NKTR-262, NKTR-255, and ONZEALD®;
- 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.

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 advanced polymer conjugate chemistry platforms and our partnered and proprietary products and product candidates compete with various pharmaceutical and biotechnology companies. Competitors of our 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 polymer conjugation 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 NKTR-214, 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 Gilead Sciences, Inc. (through its acquisition of Kite Pharma, Inc.)/NCI, Apeiron Biologics, Philogen S.p.A., IRX Therapeutics, Anaveon AG, Adaptimmune LLC, and Novartis AG, Alkermes plc, Altor Bioscience, Roche, Synthorx, Inc., and Eli Lilly & Co. (through its acquisition of Armo BioSciences) in the cytokine-based therapies space, and Tesaro, Inc., Macrogenics, Inc., Merck, Bristol-Myers Squibb Company, and Roche in the checkpoint inhibitor space. For NKTR 358, there are a number of competitors in various stages of clinical development that are working on programs which are designed to correct the underlying immune system imbalance in the body due to autoimmune disease. In particular, we expect to compete with therapies that could be cytokine-based therapies (Symbiotix, LLC and Tizona Therapeutics), regulatory T cell therapies (Targazyme, Inc., Caladrius BioSciences, Inc., and Tract Therapeutics, Inc.), or IL-2-based-therapies (Amgen Inc.). For MOVANTIK®, there are currently several alternative

therapies used to address opioid-induced constipation (OIC) and opioid-induced bowel dysfunction (OBD), including RELISTOR® Subcutaneous Injection (methylnaltrexone bromide), oral therapy AMITIZA® (lubiprostone), and oral and rectal over-the-counter laxatives and stool softeners such as docusate sodium, senna and milk of magnesia. For ADYNOVATE®, there is substantial competition from Sanofi's Fc fusion protein ELOCTATE™ for Hemophilia A treatment, JIVI® (antihemophilic factor (recombinant) PEGylated-aucl, an extended half-life Factor VIII for Hemophilia A treatment, approved in the U.S. in August 2018, and marketed by Bayer Healthcare, and Novo Nordisk which is expected to launch an extended half-life product in 2020. In addition, technologies other than those based on Fc fusion and polymer conjugation approaches (such as gene therapy approaches being developed by BioMarin Pharmaceutical Inc. and others) are being pursued to treat patients with Hemophilia A. 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. Potential competitors include Acura

Pharmaceuticals, Inc., Cara Therapeutics, Inc., Collegium Pharmaceutical, Inc., Egalet Ltd, Elite Pharmaceuticals, Inc., Endo Health Solutions Inc., KemPharm, Inc., Pfizer/Eli Lilly & Co., Purdue Pharma L.P., and Regeneron Pharmaceuticals, Inc./Teva Pharmaceutical Industries Ltd. For ONZEALD® 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), Ellence® (epirubicin), Gemzar® (gemcitabine), Halaven® (eribulin), Herceptin® (trastuzumab), Ixempra® (ixabepilone), Navelbine® (vinolrebine), 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-Myers Squibb Company, Eli Lilly & Co., Roche, GlaxoSmithKline plc, Pfizer Inc., Eisai Inc., and Sanofi Aventis S.A. 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.

We may not be able to manage our growth effectively, which could adversely affect our operations and financial performance.

The ability to manage and operate our business as we execute our development and growth strategy will require effective planning. Significant rapid growth could strain our management and internal resources, and other problems may arise that could adversely affect our financial performance. We expect that our efforts to grow will place a significant strain on personnel, management systems, infrastructure and other resources. Our ability to effectively manage future growth will also require us to successfully attract, train, motivate, retain and manage new employees and continue to update and improve our operational, financial and management controls and procedures. If we do not manage our growth effectively, our operations and financial performance could be adversely affected.

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 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.

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 commercial, 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.

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.

The price of our common stock has, and may continue to fluctuate significantly, which could result in substantial losses for investors and securities class action litigation.

Our stock price is volatile. During the year ended December 31, 2018, based on closing prices on The NASDAQ Global Select Market, the closing price of our common stock ranged from $30.43 to $108.44 per share. Plaintiffs' securities litigation firms have recently publicly announced that they are investigating a potential breach of fiduciary duty claim involving our board of directors. Additionally, on October 30, 2018, the Company and its CEO and CFO were named in a putative securities class action entitled, Mulquin v. Nektar Therapeutics et. al., N.D. Cal. Also, on February 13, 2019, and February 18, 2019, shareholder derivative complaints were filed in the U.S. District Court for the District of Delaware naming the CEO, CFO and certain members of Nektar's board. Both the class action and shareholder derivative actions assert, among other things, that for a period beginning at least from November 11, 2017 through October 2, 2018, the Company's stock was inflated due to alleged misrepresentations about the efficacy and safety of NKTR-214. 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 – in particular, data from clinical studies of NKTR-214 has had a significant impact on our stock price;
- 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.

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 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 and investments in marketable securities 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.

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.

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 275 U.S. and 850 foreign patents and have 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, inter partes review 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 post grant or inter parties review before 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 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.

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.

If we or current or future collaborators or service providers fail to comply with healthcare laws and regulations, we or they could be subject to enforcement actions and civil or criminal penalties.

Although we do not currently have any products on the market, once we begin commercializing our drug candidates, we will be subject to additional healthcare statutory and regulatory requirements and enforcement by the federal and state governments of the jurisdictions in which we conduct our business. Healthcare providers, physicians and third-party payers play a primary role in the recommendation and prescription of any drug candidates for which we obtain marketing approval. Our future arrangements with third-party payers and customers may expose us to broadly applicable fraud and abuse and other healthcare laws and regulations that may constrain the business or financial arrangements and relationships through which we market, sell and distribute our therapeutic candidates for which we obtain marketing approval. Restrictions under applicable federal and state healthcare laws and regulations, include the following:

- the federal Anti-Kickback Statute, which prohibits, among other things, persons from knowingly and willfully soliciting, receiving, offering, or paying remuneration (a term interpreted broadly to include anything of value, including, for example, gifts, discounts, and credits), directly or indirectly, in cash or in kind, to induce or reward, or in return for, either the referral of an individual for, or the purchase, order, or recommendation of, an item or service reimbursable under a federal healthcare program, such as the Medicare and Medicaid programs;
- federal civil and criminal false claims laws and civil monetary penalty laws, which prohibit, among other things, individuals or entities from knowingly presenting, or causing to be presented, claims for payment to Medicare, Medicaid, or other third-party payers that are false or fraudulent, or making a false statement or record material to payment of a false claim or avoiding, decreasing, or concealing an obligation to pay money owed to the federal government;
- provisions of the federal Health Insurance Portability and Accountability Act of 1996 (HIPAA), which created new federal criminal statutes, referred to as the “HIPAA All-Payer Fraud Prohibition,” that prohibit knowingly and willfully executing a scheme to defraud any healthcare benefit program and making false statements relating to healthcare matters;
- federal transparency laws, including the federal Physician Payment Sunshine Act, which require manufacturers of certain drugs and biologics to track and disclose payments and other transfers of value they make to U.S. physicians and teaching hospitals as well as physician ownership and investment interests in the manufacturer, and that such information is subsequently made publicly available in a searchable format on a CMS website;
- provisions of HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act and its implementing regulations, which imposes certain requirements relating to the privacy, security and transmission of individually identifiable health information; and
- state law equivalents of each of the above federal laws, such as anti-kickback and false claims laws which may apply to items or services reimbursed by any third-party payer, including commercial insurers, state transparency reporting and compliance laws; and state laws governing the privacy and security of health information in certain circumstances, many of which differ from each other in significant ways and which may not have the same effect, thus complicating compliance efforts.

Ensuring that our future business arrangements with third-parties comply with applicable healthcare laws and regulations could involve substantial costs. If our operations are found to be in violation of any such requirements, we may be subject to penalties, including civil or criminal penalties, monetary damages, the curtailment or restructuring of our operations, or exclusion from participation in government contracting, healthcare reimbursement or other

government programs, including Medicare and Medicaid, any of which could adversely affect financial results. Although effective compliance programs can mitigate the risk of investigation and prosecution for violations of these laws, these risks cannot be entirely eliminated. Any action against us for an alleged or suspected violation could cause us to incur significant legal expenses and could divert our management's attention from the operation of our business, even if our defense is successful. In addition, achieving and sustaining compliance with applicable laws and regulations may be costly to us in terms of money, time and resources.

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.

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 proceedings 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 (a wholly-owned subsidiary of Takeda). The subject matter of our patent filings in this proceeding relates to Bayer's PEGylated recombinant Factor VIII compound, BAY 94-9027, now commercially marketed as JIVI®. 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. In addition, Nektar has filed claims in Germany seeking ownership rights of certain Bayer patent applications. In the U.S., Bayer filed a complaint against Baxalta and Nektar alleging the ADYNOVATE® product infringes a Bayer patent. Although the U.S. court dismissed all of Bayer's claims against Nektar and Nektar was removed as a defendant, a jury found the Bayer patent was valid and infringed, and awarded Bayer damages, the responsibility of which are borne fully by Baxalta. This damages award does not impact our royalties from sales of ADYNOVATE® under our collaboration with Baxalta. In other U.S. proceedings, Nektar and Baxalta filed complaints against Bayer Healthcare alleging Bayer's JIVI® product infringes a total of twelve Nektar patents. In addition, in response to notices AstraZeneca and we received from the generic companies, Apotex (Apotex Inc. and Apotex Corp.) and MSN Laboratories Pvt. Ltd., alerting us that they had filed abbreviated new drug applications (ANDAs) with the FDA to market a generic version of MOVANTIK® ("Paragraph IV Certifications"), AstraZeneca and we together filed patent infringement suits against each of these generic companies in December 2018. In the Paragraph IV Certifications, both generic companies only alleged one patent, U.S. Patent No. 9,012,469, was either invalid, unenforceable and/or not infringed by the manufacture, use or sale of their respective genetic products. At this time, none of the other five Orange Book listed patents associated with MOVANTIK® are being challenged by these generics companies. 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. 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 internal computer systems, or those of our partners, vendors, CROs or other contractors or consultants, may fail or suffer security breaches, which could result in a material disruption of our product development programs or the theft of our confidential information or patient confidential information.

Despite the implementation of security measures, our internal computer systems and those of our partners, vendors, contract research organizations (CROs) and other contractors and consultants are vulnerable to damage from computer viruses, unauthorized access, natural disasters, terrorism, war and telecommunication and electrical failures. Such events could cause interruptions of our operations. For instance, the loss of preclinical data or data from any future

clinical trial involving our product candidates could result in delays in our development and regulatory filing efforts and significantly increase our costs. To the extent that any disruption or security breach were to result in a loss of, or damage to, our data, or inappropriate disclosure of confidential or proprietary information of our company or clinical patients, we could suffer or be subject to reputational harm, monetary fines, civil suits, civil penalties or criminal sanctions and requirements to disclose the breach, and other forms of liability, and the development of our product candidates could be delayed.

Global economic conditions may negatively affect us and may magnify certain risks that affect our business.

Our operations and performance have been, and may continue to be, affected by global economic conditions. As a result of global economic conditions, some third-party payers may delay or be unable to satisfy their reimbursement obligations. Job losses or other economic hardships may also affect patients' ability to afford healthcare as a result of increased co-pay or deductible obligations, greater cost sensitivity to existing co-pay or deductible obligations, lost healthcare insurance coverage or for other reasons. We believe

such conditions have led and could continue to lead to reduced demand for our and our collaboration partners' drug products, which could have a material adverse effect on our product sales, business and results of operations.

Further, rising international trade tensions, new or increased tariffs and changes in the U.S. trade policy may increase the costs of materials and products imported into the U.S. and may adversely affect our business. Tariffs, trade restrictions or sanctions imposed by the U.S. or other countries could increase the prices of our and our collaboration partners' drug products, affect our and our collaboration partners' ability to commercialize such drug products, or create adverse tax consequences in the U.S. or other countries. As a result, changes in international trade policy, changes in trade agreements and the imposition of tariffs or sanctions by the U.S. or other countries could materially adversely affect our results of operations and financial condition.

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 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.

Item 1B. Unresolved Staff Comments

None.

Item 2. Properties

California

We lease a 134,356 square foot facility in the Mission Bay Area of San Francisco, California (Mission Bay Facility), under an operating lease which expires in 2030. The Mission Bay Facility is our corporate headquarters and also includes our research and development operations.

In May 2018, we entered into a lease agreement for 135,936 square feet of office space in San Francisco (the Third Street Facility), under an operating lease which expires in 2030. A total of 68,831 square feet was delivered for our use as of the end of 2018, and the remaining space will be delivered in phases during 2019. The Third Street Facility will allow us to expand personnel to support our expanding research and development activities.

Alabama

We currently own facilities consisting of approximately 124,000 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 June 2018, we completed the sale of one of our buildings located in Huntsville that we had ceased using for research activities.

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 2021.

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, 2017:		
1st Quarter	$24.20	$11.75
2nd Quarter	22.57	17.54
3rd Quarter	24.00	17.79
4th Quarter	60.50	23.02
Year Ended December 31, 2018:		
1st Quarter	$108.44	$57.40
2nd Quarter	104.45	46.25
3rd Quarter	68.49	46.46
4th Quarter	56.65	30.43

Holders of Record

As of February 22, 2019, there were approximately 164 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, 2018.

Securities Authorized for Issuance Under Equity Compensation Plans

Information regarding our equity compensation plans as of December 31, 2018 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 2019 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, 2018, 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, 2014, December 31, 2015, December 31, 2016, December 31, 2017 and December 31, 2018. The graph assumes that $100 was invested on December 31, 2013 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,				
	2018	2017	2016	2015	2014
Statements of Operations Data:					
Revenue:					
Product sales	$20,774	$32,688	$55,354	$40,155	$25,152
Royalty revenue	41,976	33,527	19,542	2,967	329
Non-cash royalty revenue related to sale of future royalties[1]	33,308	30,531	30,158	22,058	21,937
License, collaboration and other revenue	1,097,265	210,965	60,382	165,604	153,289
Total revenue	1,193,323	307,711	165,436	230,784	200,707
Operating costs and expenses:					
Research and development	399,536	268,461	203,801	182,787	147,734
Other operating expenses[2]	105,855	98,892	74,490	77,368	69,458
Total operating costs and expenses[2]	505,391	367,353	278,291	260,155	217,192
Income (loss) from operations	687,932	(59,642)	(112,855)	(29,371)	(16,485)
Non-cash interest expense on liability related to sale of future royalties[1]	(21,196)	(18,869)	(19,712)	(20,619)	(20,888)
Interest income (expense) and other income (expense), net	15,989	(17,565)	(20,081)	(16,602)	(17,055)
Loss on extinguishment of debt	—	—	—	(14,079)	—
Provision (benefit) for income taxes	1,412	616	876	506	(512)
Net income (loss)	$681,313	$(96,692)	$(153,524)	$(81,177)	$(53,916)
Net income (loss) per share[3]					
Basic	$4.02	$(0.62)	$(1.10)	$(0.61)	$(0.42)
Diluted	$3.78	$(0.62)	$(1.10)	$(0.61)	$(0.42)
Weighted average shares outstanding used in computing net income (loss) per share[3]					
Basic	169,600	155,953	139,596	132,458	126,783
Diluted	180,119	155,953	139,596	132,458	126,783

	As of December 31,				
	2018	2017	2016	2015	2014
Balance Sheet Data:					
Cash, cash equivalents and investments in marketable securities	$1,918,239	$353,220	$389,102	$308,944	$262,824

Working capital	$1,355,685	$270,657	$353,730	$288,805	$224,153
Total assets	$2,150,172	$508,866	$568,871	$498,642	$441,621
Deferred revenue	$24,636	$37,970	$66,239	$83,854	$101,384
Senior secured notes, net	$246,950	$245,207	$243,464	$241,699	$125,000
Liability related to the sale of future royalties[1]	$82,911	$94,655	$105,950	$116,029	$120,471
Other long-term liabilities	$9,990	$5,992	$7,223	$10,813	$18,204
Accumulated deficit	$(1,424,051)	$(2,117,941)	$(2,021,010)	$(1,867,486)	$(1,786,309)
Total stockholders' equity	$1,717,575	$87,828	$88,125	$6,429	$36,332

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

royalties from UCB and Roche are remitted directly to the purchaser of these royalty interests starting in the second quarter of 2012, we will continue to record non-cash revenue for these royalties and related non-cash interest expense.

(2) Operating costs and expenses in 2017 includes $16.0 million for the impairment of equipment and related costs resulting from the termination of the Amikacin Inhale development program.

(3) Basic net income (loss) per share is based upon the weighted average number of common shares outstanding. Diluted net income (loss) per share is based on the weighted-average number of shares of common stock outstanding, including potentially dilutive securities.

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

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

Overview

Strategic Direction of Our Business

Nektar Therapeutics is a research-based biopharmaceutical company focused on discovering and developing innovative new medicines in areas of high unmet medical need. Our research and development pipeline of new investigational drugs includes treatments for cancer, autoimmune disease and chronic pain. We leverage our proprietary and proven chemistry platform to discover and design new drug candidates. These drug candidates utilize our advanced polymer conjugate technology platforms, which are designed to enable the development of new molecular entities that target known mechanisms of action. We continue to make significant investments in building and advancing our pipeline of proprietary drug candidates as we believe that this is the best strategy to build long-term stockholder value.

In immuno-oncology, we are executing a broad clinical development for NKTR-214 in collaboration with BMS as well as other independent development work evaluating NKTR-214 in combination with other agents with potential complementary mechanisms of action. We expect our research and development expense to continue to grow over the next few years as we expand and execute a very broad clinical development program for NKTR-214. For development work within our collaboration development plan, we share development costs based on each party's relative ownership interest in the compounds included in the regimen. For example, we share development costs for NKTR-214 in combination with Opdivo®, BMS 67.5% and Nektar 32.5%, and for NKTR-214 in a triplet combination with Opdivo® and Yervoy®, BMS 78% and Nektar 22%. For costs of producing NKTR-214, however, BMS is responsible for 35% and Nektar is responsible for 65% of costs. Under our collaboration development plan, we have started registration enabling studies in first line melanoma, first line renal cell carcinoma, cisplatin ineligible, locally advanced or metastatic urothelial cancer, second line metastatic non-small cell lung cancer (post-checkpoint inhibitor and chemotherapy), and several more registrational studies in additional tumor types and indications are planned to begin in 2019. Our share of such development costs under the collaboration development plan is limited to an annual cap of $125 million. To the extent this annual cap is exceeded, we will recognize our full share of the research and development expense and BMS will reimburse us for the amount over the annual cap and it will be recorded as a contingent liability. This contingent liability will be paid to BMS only if NKTR-214 is approved and solely by reducing our share of a portion of our net profits following the first commercial sale of NKTR-214. In addition, under the BMS collaboration agreement, we are entitled to $1.43 billion of regulatory and commercial launch milestones, $650 million of which are associated with approval and launch of NKTR-214 in its first indication in the U.S., EU and Japan. As a result, whether and when NKTR-214 is approved in any indication will have a significant impact on our future results of operations and financial condition.

Outside of the collaboration development plan with BMS, we are conducting a broad array of development activities evaluating NKTR-214 in combination with other agents that have potential complementary mechanisms of action. Our strategic objective is to establish NKTR-214 as a key component of many immuno-oncology combination regimens with the potential to enhance the standard of care in multiple oncology settings. On November 6, 2018, we entered into a clinical collaboration with Pfizer to evaluate several combination regimens in multiple cancer settings, including metastatic castration-resistant prostate cancer and squamous cell carcinoma of the head and neck. The combination regimens in this collaboration will evaluate NKTR-214 with avelumab, a human anti-PD-L1 antibody in

development by Merck KGaA, and Pfizer; talazoparib, a poly (ADP-ribose) polymerase (PARP) inhibitor developed by Pfizer; or enzalutamide, an androgen receptor inhibitor in development by Pfizer and Astellas Pharma Inc. In February 2019, we started a Phase 1 dose-escalation study with Takeda to evaluate NKTR-214 with Takeda's investigational medicine, TAK-659, a dual inhibitor of both spleen tyrosine kinase (SYK) and FLT-3, in up to 40 patients with advanced non-hodgkin lymphoma. We are planning a Phase 1 study this year in pancreatic cancer patients in collaboration with BioXcel to evaluate a triplet combination of NKTR-214, BXCL-701 (a small molecule immune-modulator, DPP 8/9), and avelumab being supplied to BioXcel by Pfizer and Merck KGaA. We are also working in collaboration with Vaccibody AS to evaluate in a Phase 1 proof-of-concept study combining NKTR-214 with Vaccibody's personalized cancer neoantigen vaccine. With our non-BMS clinical collaborations for NKTR-214, we generally equally share clinical development costs on a substantially pro-rata basis. We expect to continue to make significant and increasing investments exploring the potential of NKTR-214 with mechanisms of action that we believe are synergistic with NKTR-214 based on emerging scientific findings in cancer biology and preclinical development work.

We are also advancing other molecules in our immuno-oncology portfolio. NKTR-262 is a small molecule agonist that targets toll-like receptors found on innate immune cells in the body. NKTR-262 is designed to stimulate the innate immune system and promote maturation and activation of antigen-presenting cells (APC), such as dendritic cells, which are critical to induce the body's adaptive immunity and create antigen-specific cytotoxic T cells. NKTR-262 is being developed as an intra-tumoral injection in combination with systemic NKTR-214 in order to induce an abscopal response and achieve the goal of complete tumor regression in cancer patients treated with both therapies. The Phase 1 dose-escalation trial is currently ongoing. NKTR-255 is a biologic that targets

the interleukin-15 (IL-15) pathway in order to activate the body's innate and adaptive immunity. Signaling of the IL-15 pathway enhances the survival and function of natural killer (NK) cells and induces survival of both effector and CD8 memory T cells. Preclinical findings suggest NKTR-255 has potential to synergistically combine with antibody dependent cellular toxicity molecules as well as enhance CAR-T therapies. NKTR-255 is currently advancing through preclinical development and we plan to file an IND for NKTR-255 this year and begin a Phase 1 dose-escalation study in multiple myeloma. Over the next several years, we plan to continue to make significant investments to advance our early drug candidate pipeline.

In immunology, we are developing NKTR-358, which is designed to correct the underlying immune system imbalance in the body that occurs in patients with autoimmune disease. NKTR-358 is designed to optimally target the IL-2 receptor complex in order to stimulate proliferation and growth of regulatory T cells. NKTR-358 is being developed as a once or twice monthly self-administered injection for a number of autoimmune diseases. In 2017, we entered into a worldwide license agreement with Eli Lilly and Company (Lilly) to co-develop NKTR-358. We received an initial payment of $150.0 million in September 2017 and are eligible for up to an additional $250.0 million for development and regulatory milestones. We are responsible for completing Phase 1 clinical development and certain drug product development and supply activities. We also share Phase 2 development costs with Lilly, with 75% of those costs borne by Lilly and 25% of the costs borne by us. We will have the option to contribute funding to Phase 3 development on an indication-by-indication basis, ranging from zero to 25% of the Phase 3 development costs. Lilly will be responsible for all costs of global commercialization and we will have an option to co-promote in the U.S. under certain conditions. We have completed the first Phase 1 dose-finding trial of NKTR-358 to evaluate single-ascending doses of NKTR-358 in approximately 100 healthy patients. The study has completed enrollment. The Phase 1 multiple-ascending dose trial to evaluate NKTR-358 in patients with systemic lupus erythematosus (SLE) was initiated in May of 2018 and is currently enrolling patients. Over the next several years, we plan to continue to fund our share of the development costs under this collaboration.

In pain, we have filed the NDA for NKTR-181 for the treatment of chronic low back pain in adult opioid-naïve patients and the FDA's current Prescription Drug User Fee Act target action date is August 29, 2019. NKTR-181 met its primary and key secondary endpoints in the SUMMIT-07 Phase 3 efficacy study in opioid-naïve patients with chronic low back pain and also demonstrated positive results in a pivotal human abuse potential study, long-term safety study, and several other clinical and non-clinical studies included in the NDA data package. If approved, we plan to commercialize NKTR-181 through a separate subsidiary company with one or more partners with commercial infrastructure and expertise and one or more strategic capital partners. Since we have not yet completed our work to establish a commercial launch capability for NTKR-181, there remains substantial risk and uncertainties related to successful and timely completion of establishing this commercialization infrastructure for NKTR-181.

The level of our future research and development investment will depend on a number of trends and uncertainties including clinical outcomes, future studies required to advance programs to regulatory approval, and the economics related to potential future collaborations that may include up-front payments, development funding, milestones, and royalties.

We have historically derived all of our revenue and substantial amounts of operating capital from our collaboration agreements including the BMS collaboration for NKTR-214 that was completed on April 3, 2018, pursuant to which we recognized $1.06 billion in revenue and recorded $790.2 million in additional paid in capital for shares of our common stock issued in the transaction. While in the near-term we continue to expect to generate substantially all of our revenue from collaboration arrangements, including the potential $1.43 billion in development and regulatory milestones under the BMS collaboration, in the medium- to long-term our plan is to generate significant revenue from proprietary products including NKTR-181 and NKTR-214. Since we do not have experience commercializing products or an established commercialization organization, there will be substantial risks and uncertainties in future years as we build commercial, organizational, and operational capabilities.

We also receive royalties and milestone from two approved drugs. We have a collaboration with AstraZeneca for MOVANTIK®, an oral peripherally-acting mu-opioid antagonist for the treatment of opioid-induced constipation in adult patients with non-cancer pain which was approved and subsequently launched in March 2015 and MOVENTIG®, for the treatment of opioid-induced constipation in adult patients who have an inadequate response to laxatives, which was approved by health authorities in the European Union and many other countries beginning in 2014. We have a collaboration with Baxalta (a wholly-owned subsidiary of Takeda) for ADYNOVATE®, that was approved by the FDA in late 2015 for use in adults and adolescents, aged 12 years and older, who have Hemophilia A. ADYNOVI™ was approved by health authorities in Europe in January 2018, and has also been approved in many other countries.

Our business is subject to significant risks, including the risks inherent in our development efforts, the results of our clinical trials, our dependence on the marketing efforts by our collaboration partners, uncertainties associated with obtaining and enforcing patents, the lengthy and expensive regulatory approval process and competition from other products. For a discussion of these and some of the other key risks and uncertainties affecting our business, see Item 1A "Risk Factors" of this Annual Report on Form 10-K.

While the approved drugs and clinical development programs described above are key elements of our future success, we believe it is critically important that we continue to make substantial investments in our earlier-stage drug candidate pipeline. We have

several drug candidates in earlier stage clinical development or being explored in research that we are preparing to advance into the clinic in future years. We are also advancing several other drug candidates in preclinical development in the areas of cancer immunotherapy, immunology, and other therapeutic indications. We believe that our substantial investment in research and development has the potential to create significant value if one or more of our drug candidates demonstrates positive clinical results, receives regulatory approval in one or more major markets and achieves commercial success, drug research and development is an inherently uncertain process and there is a high risk of failure at every stage prior to approval and the timing and outcome of clinical trial results are extremely difficult to predict. Clinical development successes and failures can have a disproportionately positive or negative impact on our scientific and medical prospects, financial condition and prospects, results of operations and market value.

Key Developments and Trends in Liquidity and Capital Resources

We estimate that we have working capital to fund our current business plans through at least March 1, 2020. At December 31, 2018, we had approximately $1.9 billion in cash and investments in marketable securities and had debt of $250.0 million in principal of senior secured notes due in October 2020.

Results of Operations

Years Ended December 31, 2018, 2017, and 2016

Revenue (in thousands, except percentages)

	Year Ended December 31,			Increase/ (Decrease) 2018 vs. 2017	Increase/ (Decrease) 2017 vs. 2016	Percentage Increase/ (Decrease) 2018 vs. 2017	Percentage Increase/ (Decrease) 2017 vs. 2016
	2018	2017	2016				
Product sales	$20,774	$32,688	$55,354	$(11,914)	$(22,666)	(36)%	(41)%
Royalty revenue	41,976	33,527	19,542	8,449	13,985	25 %	72 %
Non cash royalty revenue related to sale of future royalties	33,308	30,531	30,158	2,777	373	9 %	1 %
License, collaboration and other revenue	1,097,265	210,965	60,382	886,300	150,583	> 100 %	> 100 %
Total revenue	$1,193,323	$307,711	$165,436	$885,612	$142,275	> 100 %	86 %

As described in Note 1 to our Consolidated Financial Statements, on January 1, 2018, we adopted Accounting Standards Codification (ASC) 606, Revenue Recognition - Revenue from Contracts with Customers. ASC 606 supersedes the guidance in ASC 605, Revenue Recognition. We adopted ASC 606 on a modified retrospective basis under which we recognized the $12.7 million cumulative effect of adoption as a reduction to opening accumulated deficit. Revenue for the year ended December 31, 2017 and 2016 was recorded under ASC 605, while revenue for the year ended December 31, 2018 was recorded under ASC 606. If we had continued to use ASC 605 during 2018,

revenue would have been $1.18 billion for the year ended December 31, 2018. The primary difference between revenue recognition under ASC 605 and ASC 606 during 2018 relates to the recognition of royalty revenue for certain of our royalty programs. Under ASC 605, we recognized certain of our royalty arrangements on a cash basis, generally one quarter in arrears. Under ASC 606, we recognize royalty revenue and related sales milestones when the underlying sales occur based on our best estimates of sales of the drugs.

Our revenue is derived from our collaboration agreements, under which we may receive product sales revenue, royalties, and license fees, as well as development and sales milestones and other contingent payments. Under ASC 606, revenue is recognized when we transfer promised goods or services to our collaboration partners. The amount of upfront fees received under our license and collaboration agreements allocated to continuing obligations, such as manufacturing and supply commitments, is generally recognized as we deliver products or provide development services. As a result, there may be significant variations in the timing of receipt of cash payments and our recognition of revenue. We make our best estimate of the timing and amount of products and services expected to be required to fulfill our performance obligations. Given the uncertainties in research and development collaborations, significant judgment is required to make these estimates.

Product sales

Product sales include predominantly fixed price manufacturing and supply agreements with our collaboration partners and are the result of firm purchase orders from those partners. The timing of shipments is based solely on the demand and requirements of our collaboration partners and is not ratable throughout the year.

Product sales decreased for the years ended December 31, 2018 and 2017 compared to the years ended December 31, 2017 and 2016, respectively, primarily due to decreased product demand from our collaboration partner Ophthotech related to its drug candidate Fovista®. In the year ended December 31, 2017, we recognized $10.4 million of product sales to Ophthotech based on prior binding purchase commitments. Our agreement with Ophthotech was terminated in October 2017 following Ophthotech's announcement that the third and final Fovista® Phase 3 trial also failed to meet its primary endpoint, following previous failures of the first two studies.

We expect product sales in 2019 to be consistent with 2018. However, if NKTR-181 receives regulatory approval and commercial sales begin in 2019, we expect an increase in product sales in 2019 compared to 2018.

Royalty revenue

We receive royalty revenue from certain of our collaboration partners based on their net sales of commercial products. Royalty revenue increased for the years ended December 31, 2018 and 2017 compared to the years ended December 31, 2017 and 2016, respectively, due primarily to the annual sales growth of ADYNOVATE® /ADYNOVI™ in 2018 and 2017 and MOVANTIK®/ MOVENTIG® in 2017. We expect royalty revenue in 2019 to increase marginally as compared to 2018.

As part of its approval of MOVANTIK®, the FDA required AstraZeneca to perform a post-marketing, observational epidemiological study comparing MOVANTIK® to other treatments of OIC in patients with chronic, non-cancer pain. As a result, the royalty rate payable to us from net sales of MOVANTIK® in the U.S. by AstraZeneca can be reduced by up to two percentage points to fund 33% of the external costs incurred by AstraZeneca to fund such post approval study, subject to a $35.0 million aggregate cap. As of December 31, 2018, our cumulative share of the post-approval study expenses since 2015 has been $1.3 million. Any costs incurred by AstraZeneca can only be recovered by the reduction of the royalty paid to us. In no case can amounts be recovered by the reduction of a contingent payment due from AstraZeneca to us or through a payment from us to AstraZeneca.

Non-cash royalty revenue related to sale of future royalties

In February 2012, we sold all of our rights to receive future royalty payments on CIMZIA® and MIRCERA®. As described in Note 7 to our Consolidated Financial Statements, this royalty sale transaction has been recorded as a liability that amortizes over the estimated royalty payment period. As a result of this liability accounting, even though the royalties from UCB and Roche are remitted directly to the purchaser of these royalty interests, we will continue to record revenue for these royalties. We expect non-cash royalties from net sales of CIMZIA® and MIRCERA® in 2019 to increase marginally compared to 2018.

License, collaboration and other revenue

License, collaboration and other revenue includes the recognition of upfront payments, milestone and other contingent payments received in connection with our license and collaboration agreements and certain research and development activities. The level of license, collaboration and other revenue depends in part upon the estimated recognition period of the upfront payments allocated to continuing performance obligations, the achievement of milestones and other contingent events, the continuation of existing collaborations, the amount of research and development work, and entering into new collaboration agreements, if any.

License, collaboration and other revenue increased for the year ended December 31, 2018 compared to the year ended December 31, 2017 primarily due to the recognition of $1,059.8 million from the BMS Collaboration Agreement as described in Note 10 to our Consolidated Financial Statements. In addition, we recognized a $10.0 million milestone payment received in March 2018 as a result of the marketing authorization of ADYNOVI™ in the EU in January 2018, and we recognized an additional $10.0 million milestone in the fourth quarter of 2018 for annual sales of ADYNOVATE® reaching a certain specified amount. For the years ended December 31, 2018 and 2017, we

recognized $11.6 million and $130.1 million, respectively, of the $150.0 million upfront payment we received in September 2017 from our collaboration agreement with Eli Lilly for NKTR-358 as described in Note 10 to our Consolidated Financial Statements.

License, collaboration and other revenue increased for the year ended December 31, 2017 compared to the year ended December 31, 2016 primarily due to the recognition of revenue from the Lilly collaboration described above. In addition, for the year ended December 31, 2017, we recognized $34.7 million related to the termination of our collaboration agreements with Bayer and Ophthotech as described in Note 10 to our Consolidated Financial Statements. These increases in 2017 were partially offset by the recognition of $28.0 million in March 2016 for our 40% share of the $70.0 million sublicense payment received by AstraZeneca from Kirin for sublicense rights to MOVENTIG® in Europe.

We expect that our license, collaboration and other revenue will decrease significantly in 2019 compared to 2018 as a result of the revenue recognized in 2018 for the BMS Collaboration Agreement.

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

Revenue by geography (in thousands)

Revenue by geographic area is based on the headquarters or shipping locations of our partners. The following table sets forth revenue by geographic area:

	Year Ended December 31,		
	2018	2017	2016
United States	$1,090,794	$190,810	$39,147
Europe	102,529	116,901	126,289
Total revenue	$1,193,323	$307,711	$165,436

The increase in revenue attributable to the U.S. for the year ended December 31, 2018 compared to the year ended December 31, 2017 is primarily attributable to the recognition of $1,059.8 million from the BMS Collaboration Agreement as described above. The increase in revenue attributable to the U.S. for the year ended December 31, 2017 compared to the year ended December 31, 2016 is primarily attributable to the recognition of $130.1 million of the $150.0 million upfront payment we received from Lilly, as described above.

Cost of goods sold (in thousands, except percentages)

	Year Ended December 31,			Increase/ (Decrease) 2018 vs. 2017	Increase/ (Decrease) 2017 vs. 2016	Percentage Increase/ (Decrease) 2018 vs. 2017	Percentage Increase/ (Decrease) 2017 vs. 2016
	2018	2017	2016				
Cost of goods sold	$24,412	$30,547	$30,215	$ (6,135)	$ 332	(20)%	1 %
Product gross profit	(3,638)	2,141	25,139	(5,779)	(22,998)	(270)%	(91)%
Product gross margin	(18)%	7 %	45 %				

Our strategy is to manufacture and supply polymer reagents to support our proprietary drug candidates or our third-party collaborators where we have a strategic development and commercialization relationship or where we derive substantial economic benefit. We have elected to only enter into and maintain those manufacturing relationships associated with long-term collaboration agreements which include multiple sources of revenue, which we view holistically and in aggregate. We have a predominantly fixed cost base associated with our manufacturing activities. As a result, our product gross profit and margin are significantly impacted by the mix and volume of products sold in each period.

Cost of goods sold decreased for the year ended December 31, 2018 compared to the year ended December 31, 2017 primarily due to decreased product sales. Cost of goods sold during the year ended December 31, 2017 was consistent

with the year ended December 31, 2016. The decreases in product gross profit and product gross margin during the years ended December 31, 2018 and 2017 compared to the years ended December 31, 2017 and 2016, respectively, are primarily due to decreased product sales as well as a less favorable product mix in 2018 and 2017 compared to 2017 and 2016, respectively. In particular, we have a manufacturing arrangement with a partner that includes a fixed price which is less than the fully burdened manufacturing cost for the reagent, and we expect this situation to continue with this partner in future years. There were more shipments to this partner relative to shipments to other customers during 2018 and 2017 compared to 2017 and 2016, respectively. In addition to product sales from reagent materials supplied to the partner where our sales are less than our fully burdened manufacturing cost, we also receive royalty revenue from this collaboration. In the years ended December 31, 2018, 2017 and 2016, the royalty revenue from this collaboration exceeded the related negative gross profit.

We expect product gross margin to continue to fluctuate in future periods depending on the level and mix of manufacturing orders from our customers. We currently expect product gross margin to be negative in 2019 as a result of the anticipated unfavorable product mix described above. However, if NKTR-181 receives regulatory approval and commercial sales begin, we expect an increase in product sales, which would improve our margin.

Research and development expense (in thousands, except percentages)

	Year Ended December 31,			Increase/ (Decrease)	Increase/ (Decrease)	Percentage Increase/ (Decrease)	Percentage Increase/ (Decrease)
	2018	2017	2016	2018 vs. 2017	2017 vs. 2016	2018 vs. 2017	2017 vs. 2016
Research and development expense	$399,536	$268,461	$203,801	$131,075	$64,660	49 %	32 %

Research and development expense consists primarily of clinical study costs, contract manufacturing costs, direct costs of outside research, materials, supplies, licenses and fees as well as personnel costs (including salaries, benefits, and stock-based compensation). Research and development expense also includes certain overhead allocations consisting of support and facilities-related costs. Where we perform research and development activities under a clinical joint development collaboration, such as our collaboration with BMS, we record the expense reimbursement from our partners as a reduction to research and development expense, and we record our share of our partners' expenses as an increase to research and development expense.

Research and development expense increased for the year ended December 31, 2018 compared to the year ended December 31, 2017 primarily due to our expanded clinical development of NKTR-214, NKTR-262, NKTR-358, and preclinical activities for NKTR-255, as well as pre-commercial manufacturing and costs related to our NDA filing for NKTR-181. In particular, we incurred significant contract manufacturing costs for NKTR-214 and other drug candidates for our broad clinical development for NKTR-214 under the BMS Collaboration Agreement, collaboration agreements with third parties and our own studies. In addition, the increase in research and development expense for the year ended December 31, 2018 compared with the year ended December 31, 2017 includes increases in non-cash stock-based compensation and other personnel costs. These increases were partially offset by cost reimbursements by BMS under our collaboration agreement. For the years ended December 31, 2018 and 2017, we recorded net reductions to research and development expense for BMS' reimbursements of our expenses of $62.5 million and $7.8 million, respectively. Under the BMS Collaboration Agreement, BMS bears 67.5% of expenses for development costs for NKTR-214 in combination with Opdivo® and 35% of costs for producing NKTR-214. No reimbursement amounts were recorded in 2016.

Research and development expense increased during the year ended December 31, 2017 compared to the year ended December 31, 2016 and included increased costs for our clinical development of NKTR-214, NKTR-358, NKTR-262, and preclinical activities for NKTR-255, as well as increased costs for personnel and outside services.

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

Clinical Study	Year Ended December 31, 2018	2017	2016

	Status[1]			
NKTR-214 (CD122-preferential IL-2 pathway agonist)[2]	Phase 1/2/3	$98,024	$33,834	$16,118
NKTR-181 (orally-available mu-opioid analgesic molecule)	Phase 3 / NDA filed	56,272	41,680	46,783
NKTR-358 (cytokine Treg stimulant)	Phase 1	17,002	10,607	5,695
NKTR-255 (IL-15 receptor agonist)	Pre-clinical	12,981	4,881	1,297
NKTR-262 (toll-like receptor agonist)	Phase 1	9,847	4,837	11
ONZEALD™ (next-generation topoisomerase I inhibitor)	Phase 3	9,205	15,052	14,940
Other product candidates	Various	3,608	14,477	13,353
Total clinical development, contract manufacturing and other third party costs		206,939	125,368	98,197
Personnel, overhead and other costs[3]		130,837	113,466	84,563
Stock-based compensation and depreciation		61,760	29,627	21,041
Research and development expense		$399,536	$268,461	$203,801

(1) Clinical Study Status definitions are provided in the chart found in Part I, Item 1. Business.

(2) The amounts for the years ended December 31, 2018 and 2017 includes $47.0 million and $7.8 million, respectively, of development cost reimbursements from BMS under our collaboration, net of our share of BMS' costs. No reimbursement amounts were recorded in 2016. Development expenses for NKTR-214 during 2018 include expenses under the BMS Collaboration Agreement, other collaboration agreements and our own studies.

(3) The amount for the year ended December 31, 2018 includes $15.6 million of employee cost reimbursements from BMS under our collaboration. No reimbursement amounts were recorded in 2017 or 2016.

We expect research and development expense to increase significantly for 2019 compared to 2018 primarily as a result of the development of NKTR-214 under the BMS Collaboration Agreement. Under the BMS Collaboration Agreement, we and BMS will jointly develop NKTR-214 in combination with BMS's Opdivo® (nivolumab) and Opdivo® plus Yervoy® (ipilimumab), with several more registrational studies in additional tumor types and indications planned to begin in 2019.

In addition, we are collaborating with Lilly to develop NKTR-358 and are continuing its Phase 1 clinical development program in 2019. We are continuing to enroll patients in a Phase 1/2 study for NKTR-262 in combination with NKTR-214 in 2019. We plan to file an IND for NKTR-255 in 2019 and begin a Phase 1 dose-escalation study in multiple myeloma. We will continue to incur contract manufacturing costs for NKTR-181 and will recognize such costs in research and development expense until NKTR-181 receives regulatory approval, if ever, and we will likely conduct additional development activities for NKTR-181 if NKTR-181 receives regulatory approval. The timing and amount of our future clinical investments will vary significantly based upon our evaluation of ongoing clinical results and the structure, timing, and scope of potential collaboration partnerships (if any) for these programs. In addition, we expect personnel and overhead costs to increase in 2019 due to increases in our employee workforce and facilities costs to support product development, and we also expect non-cash stock-based compensation expense to increase in 2019 due primarily to the increase in our employee workforce.

In addition to our drug candidates that we plan to evaluate in clinical development during 2019 and beyond, we believe it is vitally important to continue our substantial investment in a pipeline of new drug candidates to continue to build the value of our drug candidate pipeline and our business. Our discovery research organization is identifying new drug candidates by applying our polymer conjugation technology platform to a wide range of molecule classes, including small molecules and large proteins, peptides and antibodies, across multiple therapeutic areas. We plan to continue to advance our most promising early research drug candidates into preclinical development with the objective to advance these early stage research programs to human clinical studies over the next several years.

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

- the number of patients required for a given clinical study design;
- the length of time required to enroll clinical study participants;
- the number and location of sites included in the clinical studies;
- the clinical study designs required by the health authorities (i.e. primary and secondary endpoints as well as the size of the study population needed to demonstrate efficacy and safety outcomes);
- the potential for changing standards of care for the target patient population;
- the competition for patient recruitment from competitive drug candidates being studied in the same clinical setting;
- the costs of producing supplies of the drug candidates needed for clinical trials and regulatory submissions;
- the safety and efficacy profile of the drug candidate;
- the use of clinical research organizations to assist with the management of the trials; and
- the costs and timing of, and the ability to secure, approvals from government health authorities.

Furthermore, our strategy includes the potential of entering into collaborations with third parties to participate in the development and commercialization of some of our drug candidates such as those collaborations that we have already completed for NKTR-214, NKTR-358 and MOVANTIK®. In certain situations, the clinical development program and process for a drug candidate and the estimated completion date will largely be under the control of that third party and not under our control. We cannot forecast with any degree of certainty which of our drug candidates will be subject to

future collaborations or how such arrangements would affect our development plans or capital requirements.

The risks and uncertainties associated with our research and development projects are discussed more fully in Item 1A — Risk Factors. As a result of the uncertainties discussed above, we are unable to determine with any degree of certainty the duration and

completion costs of our research and development projects, anticipated completion dates or when and to what extent we will receive cash inflows from a collaboration arrangement or the commercialization of a drug candidate.

General and administrative expense (in thousands, except percentages)

	Year Ended December 31,			Increase/ (Decrease) 2018 vs. 2017	Increase/ (Decrease) 2017 vs. 2016	Percentage Increase/ (Decrease) 2018 vs. 2017	Percentage Increase/ (Decrease) 2017 vs. 2016
	2018	2017	2016				
General and administrative expense	$81,443	$52,364	$44,275	$ 29,079	$ 8,089	56 %	18 %

General and administrative expense includes the cost of administrative staffing, business development, marketing, finance, and legal activities. General and administrative expense increased for the year ended December 31, 2018 compared with the year ended December 31, 2017 primarily due to increased non-cash stock based compensation expense as well as other costs related to personnel, facilities and outside services. In particular, stock based compensation expense increased by $14.3 million from $13.0 million in 2017 to $27.3 million in 2018. General and administrative expense increased for the year ended December 31, 2017 compared with the year ended December 31, 2016 primarily due to increased costs related to personnel, facilities and outside services. We expect general and administrative expenses in 2019 to increase compared to 2018, due to costs related to personnel, facilities and outside services to support the continued expansion of our business. If NKTR-181 receives regulatory approval, we initially plan to commercialize NKTR-181 through a subsidiary and we expect significant increases in commercialization costs, including sales personnel and related costs to support that separate subsidiary organization.

Impairment of equipment and other costs for terminated program

As described in Note 4 to our Consolidated Financial Statements, in December 2017, Bayer terminated our collaboration to develop Amikacin Inhale. As a result of the termination of the program, in the year ended December 31, 2017, we expensed program-specific manufacturing equipment with a net book value of $15.1 million. In addition, in the year ended December 31, 2017, we incurred approximately $0.9 million of other program termination costs related to our manufacturing obligations.

Interest expense (in thousands, except percentages)

	Year Ended December 31,			Increase/ (Decrease) 2018 vs. 2017	Increase/ (Decrease) 2017 vs. 2016	Percentage Increase/ (Decrease) 2018 vs. 2017	Percentage Increase/ (Decrease) 2017 vs. 2016
	2018	2017	2016				

Interest expense	$21,582	$22,085	$22,468	$ (503)	$ (383)	(2)%	(2)%
Non-cash interest expense on liability related to sale of future royalties	$21,196	$18,869	$19,712	$ 2,327	$ (843)	12 %	(4)%

Interest expense for the years ended December 31, 2018, 2017 and 2016 primarily consists of interest from our senior secured notes which, as further described in Note 5 to our Consolidated Financial Statements, were issued in October 2015 for $250.0 million in aggregate principal amount at a rate of 7.75% and which are due in October 2020. Interest on the 7.75% senior secured notes is calculated based on actual days outstanding over a 360 day year. Interest expense for the years ended December 31, 2018 and 2017 decreased marginally compared with the years ended December 31, 2017 and 2016, respectively, due to decreased interest expense from our capital leases, which were fully repaid as of December 31, 2017. We expect interest expense in 2019 to be consistent with 2018.

Non-cash interest expense on the liability related to sale of future royalties for the year ended December 31, 2018 increased compared with the year ended December 31, 2017 as a result of the increase to our estimated interest rate. In February 2012, we sold all of our rights to receive future royalty payments on CIMZIA® and MIRCERA® in exchange for $124.0 million. As described in Note 7 to our Consolidated Financial Statements, this royalty sale transaction has been recorded as a liability that amortizes over the estimated royalty payment period as CIMZIA® and MIRCERA® royalties are remitted directly to the purchaser. We impute interest on the transaction and record interest expense at the effective interest rate, which we estimated to be approximately 17% from inception to 2017. During the three month period ended December 31, 2017, primarily as a result of increases in the forecasted sales of CIMZIA®, our estimate of the effective annual interest rate over the life of the agreement increased to approximately 17.6%, which resulted in a prospective interest rate of 21%. During the three month period ended December 31, 2018, primarily as a result of increases in the forecasted sales of MIRCERA®, our estimate of the effective annual interest rate over the life of the agreement

increased to approximately 18.7%, which results in a prospective interest rate of 29%. There are a number of factors that could materially affect the estimated interest rate, in particular, the amount and timing of royalty payments from future net sales of CIMZIA® and MIRCERA®, and we will assess this estimate on a periodic basis. As a result, future interest rates could differ significantly and any such change in interest rate will be adjusted prospectively. Unless we adjust our estimated interest rate, we expect non-cash interest expense on the liability related to sale of future royalties for the full year of 2019 to increase compared to 2018 as a result of the increase of the estimated prospective interest rate noted above.

Non-cash interest expense on the liability related to sale of future royalties for the year ended December 31, 2017 decreased marginally as compared to the year ended December 31, 2016 due to the decrease of the average balance of the related liability as that liability balance amortized in 2017.

Income Tax Expense

For the years ended December 31, 2017 and 2016, we recorded an income tax provision at an effective tax rate of approximately 35% as a result of taxable income at our Nektar India operations. For the year ended December 31, 2018, as a result of taxable income in India and the U.S. resulting primarily from income recognized from the upfront payment from BMS, we recorded a global income tax provision, resulting in an effective tax rate of approximately 0.2%. Our tax provision results from taxable income from our Nektar India operations and estimated tax liabilities in certain states where we do not have sufficient net operating losses to offset our estimated apportioned taxable income.

Our income tax expense in the U.S. is based on certain assumptions and other estimates regarding the apportionment of taxable income and the states in which we have nexus in 2018. Our apportionment of taxable income includes estimates of the apportionment of the BMS upfront payment based on estimates of activities to be carried out under the collaboration agreement with BMS, as well as the apportionment of other sources of income. Our income tax expense reflects the release of the valuation allowance of net operating loss carryforwards and other tax credits to offset U.S. federal and state taxable income. Our remaining deferred tax assets continue to be fully reserved, as we believe it is not more likely than not that the benefit of such assets will be realized in the future.

Due to our expected net loss in 2019, we expect income tax expense to decrease compared to 2018 and to reflect an income tax expense for our Nektar India operations at an effective rate of approximately 29%.

Liquidity and Capital Resources

We have financed our operations primarily through revenue from upfront and milestone payments under our strategic collaboration agreements, royalties and product sales, as well as public offering and private placements of debt and equity securities. At December 31, 2018, we had approximately $1.9 billion in cash and investments in marketable securities and had debt of $250.0 million in principal of senior secured notes due in October 2020.

We estimate that we have working capital to fund our current business plans through at least March 1, 2020. We expect the clinical development of our proprietary drug candidates including NKTR-214, NKTR-358, NKTR-262, NKTR-255, NKTR-181, and ONZEALD™ will continue to require significant investment in order to continue to advance in clinical development with the objective of entering into a collaboration partnership or obtaining regulatory approval, as well as for NKTR-181 commercialization activities. In the past, we have received a number of significant payments from collaboration agreements and other significant transactions. In April 2018, we received a total of $1.85 billion from BMS including a $1 billion upfront payment and an $850 million premium investment in our common stock. In July 2017, we entered into a collaboration agreement for NKTR-358 with Lilly, under which we received a $150.0 million upfront payment. In the future, we expect to receive substantial payments from our collaboration agreements with BMS and Lilly and other existing and future collaboration transactions if drug candidates in our pipeline achieve positive clinical or regulatory outcomes. In particular, under the BMS Collaboration Agreement, we are entitled to $1.43 billion of regulatory and commercial launch milestones, $650 million of which are associated

with approval and launch of NKTR-214 in its first indication in the U.S., EU and Japan. As a result, whether and when NKTR-214 is approved in any indication will have a significant impact on our future liquidity and capital resources. We have no credit facility or any other sources of committed capital.

Due to the potential for adverse developments in the credit markets, we may experience reduced liquidity with respect to some of our investments in marketable securities. These investments are generally held to maturity, which, in accordance with our investment policy, is less than two years. However, if the need arises to liquidate such securities before maturity, we may experience losses on liquidation. At December 31, 2018, the average time to maturity of the investments held in our portfolio was approximately eight months. To date we have not experienced any liquidity issues with respect to these securities. We believe that, even allowing for potential liquidity issues with respect to these securities, our remaining cash and investments in marketable securities will be sufficient to meet our anticipated cash needs for at least the next twelve months.

Our current business plan is subject to significant uncertainties and risks as a result of, among other factors, clinical and regulatory outcomes for NKTR-214, the sales levels of our products, if and when they are approved, the sales levels for those products for which we are entitled to royalties, clinical program outcomes, whether, when and on what terms we are able to enter into new collaboration transactions, expenses being higher than anticipated, unplanned expenses, cash receipts being lower than anticipated, and the need to satisfy contingent liabilities, including litigation matters and indemnification obligations.

The availability and terms of various financing alternatives, if required in the future, substantially depend on many factors including the success or failure of drug development programs in our pipeline. The availability and terms of financing alternatives and any future significant payments from existing or new collaborations depend on the positive outcome of ongoing or planned clinical studies, whether we or our partners are successful in obtaining regulatory authority approvals in major markets, and if approved, the commercial success of these drugs, as well as general capital market conditions. We may pursue various financing alternatives to fund the expansion of our business as appropriate.

Cash flows from operating activities

Cash flows provided by operating activities for the year ended December 31, 2018 totaled $718.2 million, which includes $1,059.8 million of the payments received under the BMS Collaboration Agreement in April 2018 and a $10.0 million milestone payment from our collaboration agreement with Baxalta, partially offset by $332.1 million of net operating cash uses as well as $19.5 million for interest payments on our senior secured notes.

Cash flows used in operating activities for the year ended December 31, 2017 totaled $80.4 million, which includes $237.8 million of net operating cash uses as well as $19.6 million for interest payments on our senior secured, partially offset by the receipt of $150.0 million upfront payment in September 2017 from our collaboration agreement with Lilly for NKTR-358, the receipt of $12.0 million in November 2017 related to our collaboration agreement with Baxalta and the receipt of $15.0 million in December 2017 resulting from a settlement agreement.

Cash flows used in operating activities for the year ended December 31, 2016 totaled $117.0 million, which includes $138.3 million of net operating cash uses as well as $19.7 million for interest payments on our senior secured notes, partially offset by the receipt of $31.0 million of payments from AstraZeneca related to its sub-license to Kirin and the receipt of a $10.0 million milestone in January 2016 from our Baxalta collaboration agreement.

We expect that cash flows used in operating activities, excluding upfront, milestone and other contingent payments received, if any, will increase in 2019 compared to 2018 primarily as a result of increased research and development expenses.

Cash flows from investing activities

We paid $14.2 million, $9.7 million, and $6.4 million to purchase property, plant and equipment in the years ended December 31, 2018, 2017, and 2016, respectively. For 2018, we also received $2.6 million from the sale of property, plant and equipment, primarily from the sale of a former research facility in Huntsville, Alabama. We expect our capital expenditures in 2019 to increase significantly compared to 2018, primarily due to construction of leasehold improvements at our new facilities lease as more fully described in Note 6 of our Consolidated Financial Statements (the Third Street Facility).

For the year ended December 31, 2018, we purchased $1.4 billion of investments in debt securities, net of maturities of investments, primarily as a result of the $1.85 billion received in April 2018 from BMS under the BMS Collaboration Agreement and the Share Purchase Agreement.

Cash flows from financing activities

As described in Note 10 to our Consolidated Financial Statements, we received $850.0 million for the issuance of our common stock to BMS under our Share Purchase Agreement in April 2018, of which we recorded $790.2 million in equity as a financing activity.

On October 24, 2016, we completed the issuance and sale of 14,950,000 shares of our common stock in an underwritten public offering with total proceeds of approximately $189.7 million after deducting the underwriting commissions and discounts of approximately $12.1 million. In addition, we incurred approximately $0.4 million in legal and accounting fees, filing fees, and other costs in connection with this offering.

We received proceeds from issuance of common stock related to our employee option and stock purchase plans of $61.7 million, $59.5 million, and $20.3 million in the years ended December 31, 2018, 2017, and 2016, respectively.

Contractual Obligations (in thousands)

	Payments Due by Period				
		<=1 Yr	2-3 Yrs	4-5 Yrs	
	Total	2019	2020-2021	2022-2023	2024+
Obligations[1]					
7.75% senior secured notes due October 2020, including interest	$288,750	$19,644	$269,106	$ —	$—
Operating leases[2]	183,616	8,494	26,615	31,065	117,442
Purchase commitments[3]	63,303	63,303	—	—	—
	$535,669	$91,441	$295,721	$ 31,065	$117,442

(1) The above table does not include certain commitments and contingencies which are discussed in Note 8 to our Consolidated Financial Statements.
(2) These amounts primarily result from our Mission Bay Facility and Third Street Facility leases, which both expire in 2030. The leases are discussed in Note 6 to our Consolidated Financial Statements. Our commitment for the Third Street Facility above includes fixed amounts payable for certain costs that we have excluded from our minimum lease payments as disclosed in Note 6 to our Consolidated Financial Statements.
(3) Substantially all of this amount was subject to open purchase orders as of December 31, 2018 that were issued under existing contracts. This amount does not represent minimum contract termination liabilities for our existing contracts.

Off Balance Sheet Arrangements

We do not utilize off-balance sheet financing arrangements as a source of liquidity or financing.

Critical Accounting Policies

The preparation and presentation of financial statements in conformity with U.S. generally accepted accounting principles (GAAP) requires management to make estimates and assumptions that affect the reported amounts of assets and liabilities and disclosure of contingent assets and liabilities at the date of the financial statements and the reported amounts of revenues and expenses during the reporting period.

We base our estimates on historical experience and on various other assumptions that we believe to be reasonable under the circumstances, the results of which form our basis for making judgments about the carrying value of assets and liabilities that are not readily apparent from other sources, and evaluate our estimates on an ongoing basis. Actual results may differ materially from those estimates under different assumptions or conditions. We have determined that for the periods in this report, the following accounting policies and estimates are critical in understanding our financial condition and the results of our operations.

Collaborative Arrangements

When we enter into collaboration agreements with pharmaceutical and biotechnology partners, we assess whether the arrangements fall within the scope of Accounting Standards Codification (ASC) 808, Collaborative Arrangements (ASC 808) based on whether the arrangements involve joint operating activities and whether both parties have active participation in the arrangement and are exposed to significant risks and rewards. To the extent that the arrangement falls within the scope of ASC 808, we assess whether the payments between us and our collaboration partner fall

within the scope of other accounting literature. If we conclude that payments from the collaboration partner to us represent consideration from a customer, such as license fees and contract research and development activities, we account for those payments within the scope of ASC 606, Revenue from Contracts with Customers. However, if we conclude that our collaboration partner is not a customer for certain activities and associated payments, such as for certain collaborative research, development, manufacturing and commercial activities, we record such payments as a reduction of research and development expense or general and administrative expense, based on where we record the underlying expense.

Revenue Recognition

We recognize license, collaboration and other research revenue based on the facts and circumstances of each contractual agreement and includes recognition of upfront fees and milestone payments. At the inception of each agreement, we determine which promises represent distinct performance obligations, for which management must use significant judgment. Additionally, at inception and at each reporting date thereafter, we must determine and update, as appropriate, the transaction price, which includes variable consideration such as development milestones. We must use judgment to determine when to include variable consideration in the transaction price such that inclusion of such variable consideration will not result in a significant reversal of revenue recognized when

the contingency surrounding the variable consideration is resolved. We must also allocate the arrangement consideration to performance obligations based on their relative standalone selling prices, which we generally base on our best estimates and which require significant judgment. For example, in estimating the standalone selling prices for granting licenses for our drug candidate, our estimates may include revenue forecasts, clinical development timelines and costs, discount rates and probabilities of clinical and regulatory success. For performance obligations satisfied over time, we recognize revenue based on our estimates of expected future costs or other measures of progress.

Clinical Trial Accruals

We record accruals for the estimated costs of our clinical study activities performed by third parties. The financial terms of these agreements are subject to negotiation, vary from contract to contract and may result in uneven payment flows to our vendors. Payments under the contracts depend on factors such as the achievement of certain events, successful enrollment of patients and completion of certain clinical trial activities. We generally accrue costs associated with the start-up and reporting phases of the clinical studies ratably over the estimated duration of the start-up and reporting phases. We generally accrue costs associated with the treatment phase of clinical studies based on the total estimated cost of the treatment phase on a per patient basis and we expense the per patient cost ratably over the estimated patient treatment period based on patient enrollment in the studies. In specific circumstances, such as for certain time-based costs, we recognize clinical trial expenses using a methodology that we consider to be more reflective of the timing of costs incurred. Advance payments for goods or services that will be used or rendered for future research and development activities are capitalized as prepaid expenses and recognized as expense as the related goods are delivered or the related services are performed. We base our estimates on the best information available at the time. However, additional information may become available to us which may allow us to make a more accurate estimate in future periods. In this event, we may be required to record adjustments to research and development expenses in future periods when the actual level of activity becomes more certain. Such increases or decreases in cost are generally considered to be changes in estimates and will be reflected in research and development expenses in the period identified.

Contract Manufacturing Accruals

We record accruals for the estimated costs of our contract manufacturing activities performed by third parties. The financial terms of these agreements are subject to negotiation, vary from contract to contract and may result in uneven payment flows to our vendors. Payments under the contracts include upfront payments and milestone payments, which depend on factors such as the achievement of the completion of certain stages of the manufacturing process. For purposes of recognizing expense, we assess whether we consider the production process sufficiently defined to be considered the delivery of a good, as evidenced by predictive or contractually required yields, or the delivery of a service, where processes and yields are developing and less certain. If we consider the process to be the delivery of a good, we recognize expense when the drug product is delivered, or we otherwise bear risk of loss. If we consider the process to be the delivery of a service, we recognize expense based on our best estimates of the contract manufacturer’s progress towards completion of the stages in the contract. We base our estimates on the best information available at the time. However, additional information may become available to us which may allow us to make a more accurate estimate in future periods. In this event, we may be required to record adjustments to research and development expenses in future periods when the actual level of activity becomes more certain. In certain circumstances, we may be entitled to reductions of amounts due under these arrangements if delivery is delayed or the yield from the production process is lower than expected. Given the uncertainties with such reductions, we may only recognize such decrease when the contract manufacturer agrees with such reduction. Such increases or decreases in cost are generally considered to be changes in estimates and will be reflected in research and development expenses in the period identified.

Stock-Based Compensation

We expense the estimated fair value of each stock award ratably over the expected service period of the award and recognize forfeitures as they occur. For stock options, we use the Black-Scholes option pricing model for each respective option grant to determine the estimated fair value on the date of grant (grant date fair value). The Black-Scholes option pricing model requires the input of highly subjective assumptions. These variables include, but are not limited to, our stock price volatility over the term of the awards, and actual and projected employee stock option exercise behaviors. Because our employee stock options have characteristics significantly different from those of traded options, and because changes in the subjective input assumptions can materially affect fair value estimates, in management's opinion, the existing models may not provide a reliable single measure of the fair value of our employee stock options. Management continually assesses the assumptions and methodologies used to calculate the estimated fair value of stock-based compensation. In addition, for awards that vest upon the achievement of performance milestones, we estimate whether the awards will vest and the vesting period based on our evaluation of the probability of achievement of each respective milestone and the related estimated date of achievement. Circumstances may change and additional data may become available over time, which could result in changes to the assumptions and methodologies, and which could materially impact our fair value determination, as well as our stock-based compensation expense.

Non-cash Interest Expense on Liability Related to Sale of Future Royalties

In February 2012, we sold all of our rights to receive future royalty payments from sales of the CIMZIA® and MIRCERA® drug products marketed by UCB and Roche, respectively. Although we are required to make payments to the purchaser (RPI) only in certain situations, including the event of our breach of a representation, warranty or covenant in the Purchase and Sale Agreement that gives rise to a liability in accordance with the terms and conditions of such agreement, this royalty sale transaction was recorded as a liability (Royalty Obligation) that we will amortize using the interest method over the estimated life of the Purchase and Sale Agreement. As a result, we impute interest on the transaction and record interest expense at the estimated interest rate. Our estimate of the interest rate under the agreement is based on the amount of royalty payments to be received by RPI over the life of the arrangement and payments we are required to make to RPI under the agreement. We will periodically assess the expected royalty payments to RPI from UCB and Roche using a combination of historical results and forecasts from market data sources. To the extent such payments are greater or less than our initial estimates or the timing of such payments is materially different than our original estimates, we will prospectively adjust the amortization of the Royalty Obligation. There are a number of factors that could materially affect the amount and timing of royalty payments from CIMZIA® and MIRCERA®, most of which are not within our control. Such factors include, but are not limited to, changing standards of care, the introduction of competing products, manufacturing or other delays, biosimilar competition, intellectual property matters, adverse events that result in health authority imposed restrictions on the use of the drug products, significant changes in foreign exchange rates as the royalties remitted to RPI are made in U.S. dollars (USD) while significant portions of the underlying sales of CIMZIA® and MIRCERA® are made in currencies other than USD, and other events or circumstances that result in reduced royalty payments from CIMZIA® and MIRCERA®, all of which would result in a reduction of non-cash royalty revenue and non-cash interest expense over the life of the Royalty Obligation. Conversely, if sales of CIMZIA® and MIRCERA® are higher than expected, non-cash royalty revenue and non-cash interest expense would be greater over the term of the Royalty Obligation. During the three month period ended December 31, 2017, as a result of increases in the forecasted sales of CIMZIA®, our estimate of the effective annual interest rate over the life of the agreement increased from 17% to approximately 17.6%, which resulted in a prospective interest rate of 21%. During the three month period ended December 31, 2018, primarily as a result of increases in the forecasted sales of MIRCERA®, our estimate of the effective annual interest rate over the life of the agreement increased to approximately 18.7%, which results in a prospective interest rate of 29%. If we had determined that the interest rate used in 2018 should have been one percentage point higher than our quarterly estimates during 2018, the non-cash interest expense recognized in the year ended December 31, 2018 and the Royalty Obligation balance as of December 31, 2018 would have increased by $1.0 million. If we had determined that the interest rate used in 2018 should have been 29% during 2018, the non-cash interest expense recognized in the year ended December 31, 2018 and the Royalty Obligation balance as of December 31, 2018 would have increased by $6.5 million.

Recent Accounting Pronouncements

In November 2018, the Financial Accounting Standards Board (FASB) issued Accounting Standards Update 2018-18: Clarifying the Interaction between Topic 808 and Topic 606 (ASU 2018-18). The guidance clarifies that certain transactions between collaborative arrangement participants should be accounted for as revenue under ASC 606 when the collaborative arrangement participant is a customer for a promised good or service that is distinct within the collaborative arrangement. The guidance also precludes entities from presenting amounts related to transactions with a collaborative arrangement participant that is not a customer as revenue, unless those transactions are directly related to third-party sales. ASU 2018-18 is effective in the first quarter of 2020 and should be applied retrospectively to January 1, 2018, when we adopted ASC 606. Early adoption is permitted. We are evaluating the effect of adoption, but we do not expect a material effect on our revenue.

In February 2016, the FASB issued guidance to amend a number of aspects of lease accounting, including requiring lessees to recognize almost all leases with a term greater than one year as a right-of-use asset and corresponding liability, measured at the present value of the lease payments. The guidance became effective for us beginning in the

first quarter of 2019 and is required to be adopted using a modified retrospective approach. The adoption of this guidance will have a material effect on our balance sheet. In particular, for our facilities leases described in Note 6 to our Consolidated Financial Statements, we expect to recognize right-of-use assets, estimated between $87 million and $97 million, and lease liabilities, estimated between $96 million and $106 million. We will recognize additional right-of-use assets and lease liabilities as additional space is delivered to us for our Third Street Facility lease

Item 7A. Quantitative and Qualitative Disclosures About Market Risk

Interest Rate and Market Risk

The primary objective of our investment activities is to preserve principal while at the same time maximizing yields without significantly increasing risk. To achieve this objective, we invest in liquid, high quality debt securities. Our investments in debt securities are subject to interest rate risk. To minimize the exposure due to an adverse shift in interest rates, we invest in securities with maturities of two years or less and maintain a weighted average maturity of one year or less.

A hypothetical 50 basis point increase in interest rates would result in an approximate $6.7 million decrease, less than 1%, in the fair value of our available-for-sale securities at December 31, 2018. This potential change is based on sensitivity analyses performed on our investment securities at December 31, 2018. Actual results may differ materially. The same hypothetical 50 basis point increase in interest rates would have resulted in an approximate $1.1 million decrease, less than 1%, in the fair value of our available-for-sale securities at December 31, 2017.

As of December 31, 2018, we held $1.8 billion of available-for-sale investments, excluding money market funds, with an average time to maturity of eight months. To date we have not experienced any liquidity issues with respect to these securities, but should such issues arise, we may be required to hold some, or all, of these securities until maturity. We believe that, even allowing for potential liquidity issues with respect to these securities, our remaining cash, cash equivalents, and investments in marketable securities will be sufficient to meet our anticipated cash needs for at least the next twelve months. Based on our available cash and our expected operating cash requirements, we currently do not intend to sell these securities prior to maturity and it is more likely than not that we will not be required to sell these securities before we recover the amortized cost basis. Accordingly, we believe there are no other-than-temporary impairments on these securities and have not recorded any provisions for impairment.

Foreign Currency Risk

The majority of our revenue, expense, and capital purchasing activities are transacted in U.S. dollars. However, we have contracts with contract manufacturing organizations in Europe, transacted in the British pound sterling or Euros. Additionally, a portion of our operations consists of research and development activities outside the United States, with transactions in the Indian Rupee. Finally, although our payments from our collaboration partners for our royalty revenues are in U.S. dollars, a portion of the payment is based on net sales in foreign currency translated into U.S. dollars for such period. Accordingly, we are subject to foreign currency exchange risk for these transactions.

Our international operations are subject to risks typical of international operations, including, but not limited to, differing economic conditions, changes in political climate, differing tax structures, other regulations and restrictions, and foreign exchange rate volatility. We do not utilize derivative financial instruments to manage our exchange rate risks. We do not believe that inflation has had a material adverse impact on our revenues or operations in any of the past three years.

Item 8. Financial Statements and Supplementary Data
NEKTAR THERAPEUTICS

INDEX TO CONSOLIDATED FINANCIAL STATEMENTS

	Page
Reports of Independent Registered Public Accounting Firm	66
Consolidated Balance Sheets at December 31, 2018 and 2017	68
Consolidated Statements of Operations for each of the three years in the period ended December 31, 2018	69
Consolidated Statements of Comprehensive Income (Loss) for each of the three years in the period ended December 31, 2018	70
Consolidated Statements of Stockholders' Equity for each of the three years in the period ended December 31, 2018	71
Consolidated Statements of Cash Flows for each of the three years in the period ended December 31, 2018	72
Notes to Consolidated Financial Statements	73

Report of Independent Registered Public Accounting Firm

To the Stockholders and the Board of Directors of Nektar Therapeutics

Opinion on the Financial Statements

We have audited the accompanying consolidated balance sheets of Nektar Therapeutics (the “Company”) as of December 31, 2018 and 2017, the related consolidated statements of operations, comprehensive income (loss), stockholders’ equity and cash flows for each of the three years in the period ended December 31, 2018, and the related notes. In our opinion, the consolidated financial statements present fairly, in all material respects, the financial position of the Company at December 31, 2018 and 2017, and the results of its operations and its cash flows for each of the three years in the period ended December 31, 2018, in conformity with U.S. generally accepted accounting principles.

We also have audited, in accordance with the standards of the Public Company Accounting Oversight Board (United States) (PCAOB), the Company’s internal control over financial reporting as of December 31, 2018, based on criteria established in Internal Control-Integrated Framework issued by the Committee of Sponsoring Organizations of the Treadway Commission (2013 framework) and our report dated February 28, 2019 expressed an unqualified opinion thereon.

Adoption of ASU No. 2014-09

As discussed in Note 1 to the consolidated financial statements, the Company changed its method for recognizing revenue as a result of the adoption of Accounting Standards Update (ASU) No. 2014-09, Revenue from Contracts with Customers (Topic 606), using the modified retrospective method effective January 1, 2018.

Basis for Opinion

These financial statements are the responsibility of the Company's management. Our responsibility is to express an opinion on the Company’s financial statements based on our audits. We are a public accounting firm registered with the PCAOB and are required to be independent with respect to the Company in accordance with the U.S. federal securities laws and the applicable rules and regulations of the Securities and Exchange Commission and the PCAOB.

We conducted our audits in accordance with the standards of the PCAOB. Those standards require that we plan and perform the audit to obtain reasonable assurance about whether the financial statements are free of material misstatement, whether due to error or fraud. Our audits included performing procedures to assess the risks of material misstatement of the financial statements, whether due to error or fraud, and performing procedures that respond to those risks. Such procedures included examining, on a test basis, evidence regarding the amounts and disclosures in the financial statements. Our audits also included evaluating the accounting principles used and significant estimates made by management, as well as evaluating the overall presentation of the financial statements. We believe that our audits provide a reasonable basis for our opinion.

/s/ Ernst & Young LLP

We have served as the Company’s auditor since 1993.

Redwood City, California
February 28, 2019

Report of Independent Registered Public Accounting Firm

To the Stockholders and the Board of Directors of Nektar Therapeutics

Opinion on Internal Control over Financial Reporting

We have audited Nektar Therapeutics' internal control over financial reporting as of December 31, 2018, based on criteria established in Internal Control—Integrated Framework issued by the Committee of Sponsoring Organizations of the Treadway Commission (2013 framework) (the COSO criteria). In our opinion, Nektar Therapeutics (the Company) maintained, in all material respects, effective internal control over financial reporting as of December 31, 2018, based on the COSO criteria.

We also have audited, in accordance with the standards of the Public Company Accounting Oversight Board (United States) (PCAOB), the consolidated balance sheets of the Company as of December 31, 2018 and 2017, the related consolidated statements of operations, comprehensive income (loss), stockholders' equity and cash flows for each of the three years in the period ended December 31, 2018, and the related notes and our report dated February 28, 2019 expressed an unqualified opinion thereon.

Basis for Opinion

The Company's management is responsible for maintaining effective internal control over financial reporting and for its assessment of the effectiveness of internal control over financial reporting included in the accompanying Management's Annual Report on Internal Control over Financial Reporting. Our responsibility is to express an opinion on the Company's internal control over financial reporting based on our audit. We are a public accounting firm registered with the PCAOB and are required to be independent with respect to the Company in accordance with the U.S. federal securities laws and the applicable rules and regulations of the Securities and Exchange Commission and the PCAOB.

We conducted our audit in accordance with the standards of the PCAOB. Those standards require that we plan and perform the audit to obtain reasonable assurance about whether effective internal control over financial reporting was maintained in all material respects.

Our audit included obtaining an understanding of internal control over financial reporting, assessing the risk that a material weakness exists, testing and evaluating the design and operating effectiveness of internal control based on the assessed risk, and performing such other procedures as we considered necessary in the circumstances. We believe that our audit provides a reasonable basis for our opinion.

Definition and Limitations of Internal Control Over Financial Reporting

A company's internal control over financial reporting is a process designed to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles. A company's internal control over financial reporting includes those policies and procedures that (1) pertain to the maintenance of records that, in reasonable detail, accurately and fairly reflect the transactions and dispositions of the assets of the company; (2) provide reasonable assurance that transactions are recorded as necessary to permit preparation of financial statements in accordance with generally accepted accounting principles, and that receipts and expenditures of the company are being made only in accordance with authorizations of management and directors of the company; and (3) provide reasonable assurance regarding prevention or timely detection of unauthorized acquisition, use, or disposition of the company's assets that could have a material effect on the financial statements.

Because of its inherent limitations, internal control over financial reporting may not prevent or detect misstatements. Also, projections of any evaluation of effectiveness to future periods are subject to the risk that controls may become inadequate because of changes in conditions, or that the degree of compliance with the policies or procedures may deteriorate.

/s/ Ernst & Young LLP

Redwood City, California
February 28, 2019

NEKTAR THERAPEUTICS

CONSOLIDATED BALANCE SHEETS

(In thousands, except par value information)

	December 31,	
	2018	2017
ASSETS		
Current assets:		
Cash and cash equivalents	$194,905	$4,762
Short-term investments	1,140,445	291,370
Accounts receivable	43,213	5,014
Inventory	11,381	10,726
Advance payments to contract manufacturers	26,450	7,155
Other current assets	21,293	7,793
Total current assets	1,437,687	326,820
Long-term investments	582,889	57,088
Property, plant and equipment, net	48,851	47,463
Goodwill	76,501	76,501
Other assets	4,244	994
Total assets	$2,150,172	$508,866
LIABILITIES AND STOCKHOLDERS' EQUITY		
Current liabilities:		
Accounts payable	$5,854	$4,782
Accrued compensation	9,937	8,263
Accrued contract manufacturing expenses	23,841	3,845
Accrued clinical trial expenses	14,700	9,461
Other accrued expenses	9,087	6,219
Interest payable	4,198	4,198
Deferred revenue, current portion	13,892	18,949
Other current liabilities	493	446
Total current liabilities	82,002	56,163
Senior secured notes, net	246,950	245,207
Liability related to the sale of future royalties, net	82,911	94,655
Deferred revenue, less current portion	10,744	19,021
Other long-term liabilities	9,990	5,992
Total liabilities	432,597	421,038
Commitments and contingencies		
Stockholders' equity:		
Preferred stock, $0.0001 par value; 10,000 shares authorized; no shares designated, issued or outstanding at December 31, 2018 or 2017	—	—
Common stock, $0.0001 par value; 300,000 shares authorized; 173,530 shares and 159,524 shares issued and outstanding at December 31, 2018 and 2017, respectively	17	15
Capital in excess of par value	3,147,925	2,207,865

Accumulated other comprehensive loss	(6,316)	(2,111)
Accumulated deficit	(1,424,051)	(2,117,941)
Total stockholders' equity	1,717,575	87,828
Total liabilities and stockholders' equity	$2,150,172	$508,866

The accompanying notes are an integral part of these consolidated financial statements.

NEKTAR THERAPEUTICS

CONSOLIDATED STATEMENTS OF OPERATIONS

(In thousands, except per share information)

	Year Ended December 31,		
	2018	2017	2016
Revenue:			
Product sales	$20,774	$32,688	$55,354
Royalty revenue	41,976	33,527	19,542
Non-cash royalty revenue related to sale of future royalties	33,308	30,531	30,158
License, collaboration and other revenue	1,097,265	210,965	60,382
Total revenue	1,193,323	307,711	165,436
Operating costs and expenses:			
Cost of goods sold	24,412	30,547	30,215
Research and development	399,536	268,461	203,801
General and administrative	81,443	52,364	44,275
Impairment of equipment and other costs for terminated program	—	15,981	—
Total operating costs and expenses	505,391	367,353	278,291
Income (loss) from operations	687,932	(59,642)	(112,855)
Non-operating income (expense):			
Interest expense	(21,582)	(22,085)	(22,468)
Non-cash interest expense on liability related to sale of future royalties	(21,196)	(18,869)	(19,712)
Interest income and other income (expense), net	37,571	4,520	2,387
Total non-operating expense, net	(5,207)	(36,434)	(39,793)
Income (loss) before provision for income taxes	682,725	(96,076)	(152,648)
Provision for income taxes	1,412	616	876
Net income (loss)	$681,313	$(96,692)	$(153,524)
Net income (loss) per share			
Basic	$4.02	$(0.62)	$(1.10)
Diluted	$3.78	$(0.62)	$(1.10)
Weighted average shares outstanding used in computing net income (loss) per share			
Basic	169,600	155,953	139,596
Diluted	180,119	155,953	139,596

The accompanying notes are an integral part of these consolidated financial statements.

NEKTAR THERAPEUTICS

CONSOLIDATED STATEMENTS OF COMPREHENSIVE INCOME (LOSS)

(In thousands)

	Year Ended December 31,		
	2018	2017	2016
Net income (loss)	$681,313	$(96,692)	$(153,524)
Other comprehensive income (loss):			
Net unrealized gain (loss) on available-for-sale investments, net of tax	(2,975)	(533)	79
Net foreign currency translation gain (loss)	(1,230)	785	(272)
Other comprehensive income (loss), net of tax	(4,205)	252	(193)
Comprehensive income (loss)	$677,108	$(96,440)	$(153,717)

The accompanying notes are an integral part of these consolidated financial statements.

NEKTAR THERAPEUTICS

CONSOLIDATED STATEMENTS OF STOCKHOLDERS' EQUITY

(In thousands)

	Common Shares	Par Value	Capital in Excess of Par Value	Accumulated Other Comprehensive Income/(Loss)	Accumulated Deficit	Total Stockholders' Equity
Balance at December 31, 2015	135,289	$ 13	$1,876,072	$ (2,170)	$(1,867,486)	$ 6,429
Sale of common stock, net of issuance costs of $439	14,950	2	189,274	—	—	189,276
Shares issued under equity compensation plans	2,973	—	20,287	—	—	20,287
Stock-based compensation	—	—	25,850	—	—	25,850
Other comprehensive loss	—	—	—	(193)	—	(193)
Net loss	—	—	—	—	(153,524)	(153,524)
Balance at December 31, 2016	153,212	15	2,111,483	(2,363)	(2,021,010)	88,125
Shares issued under equity compensation plans	6,312	—	59,528	—	—	59,528
Stock-based compensation	—	—	36,615	—	—	36,615
Other comprehensive loss	—	—	239	252	(239)	252
Net loss	—	—	—	—	(96,692)	(96,692)
Balance at December 31, 2017	159,524	15	2,207,865	(2,111)	(2,117,941)	87,828
Shares issued under equity compensation plans	5,721	1	61,728	—	—	61,729
Stock-based compensation	—	—	88,101	—	—	88,101
Sale of stock to Bristol-Myers Squibb (Note 10)	8,285	1	790,231	—	—	790,232
Adoption of new accounting standards					12,577	12,577
Other comprehensive loss	—	—	—	(4,205)	—	(4,205)
Net income	—	—	—	—	681,313	681,313
Balance at December 31, 2018	173,530	$ 17	$3,147,925	$ (6,316)	$(1,424,051)	$ 1,717,575

The accompanying notes are an integral part of these consolidated financial statements.

NEKTAR THERAPEUTICS

CONSOLIDATED STATEMENTS OF CASH FLOWS

(In thousands)

	Year Ended December 31,		
	2018	2017	2016
Cash flows from operating activities:			
Net income (loss)	$681,313	$(96,692)	$(153,524)
Adjustments to reconcile net income (loss) to net cash provided by (used in) operating activities:			
Non-cash royalty revenue related to sale of future royalties	(33,308)	(30,531)	(30,158)
Non-cash interest expense on liability related to sale of future royalties	21,196	18,869	19,712
Stock-based compensation	88,101	36,615	25,850
Depreciation and amortization	10,870	14,741	15,351
Impairment of equipment from terminated program	—	15,081	—
Accretion of discounts, net, and other non-cash transactions	(10,952)	(881)	(2,185)
Changes in operating assets and liabilities:			
Accounts receivable	(25,505)	10,664	4,269
Inventory	(655)	383	237
Other assets	(31,652)	(4,800)	(312)
Accounts payable	971	2,074	518
Accrued compensation	1,674	(10,017)	12,282
Other accrued expenses	27,947	7,277	(71)
Deferred revenue	(15,331)	(28,269)	(17,615)
Other liabilities	3,545	(14,928)	8,622
Net cash provided by (used in) operating activities	718,214	(80,414)	(117,024)
Cash flows from investing activities:			
Purchases of investments	(2,271,250)	(404,425)	(334,659)
Maturities of investments	890,957	347,743	253,682
Sales of investments	11,963	37,549	4,969
Purchases of property, plant and equipment	(14,239)	(9,676)	(6,392)
Sales of property and plant	2,633	—	—
Net cash used in investing activities	(1,379,936)	(28,809)	(82,400)
Cash flows from financing activities:			
Payment of capital lease obligations	—	(5,131)	(5,945)
Proceeds from shares issued under equity compensation plans	61,735	59,522	20,287
Issuance of common stock, net of issuance costs	790,231	—	189,276
Net cash provided by financing activities	851,966	54,391	203,618
Effect of exchange rates on cash and cash equivalents	(101)	(46)	(124)
Net increase (decrease) in cash and cash equivalents	190,143	(54,878)	4,070
Cash and cash equivalents at beginning of year	4,762	59,640	55,570
Cash and cash equivalents at end of year	$194,905	$4,762	$59,640
Supplemental disclosure of cash flow information:			
Cash paid for interest	$19,471	$20,116	$20,589
Cash paid for income taxes	$618	$556	$757

The accompanying notes are an integral part of these consolidated financial statements.

72

NEKTAR THERAPEUTICS

NOTES TO CONSOLIDATED FINANCIAL STATEMENTS

December 31, 2018

Note 1 — Organization and Summary of Significant Accounting Policies

Organization

We are a research-based biopharmaceutical company headquartered in San Francisco, California and incorporated in Delaware. We are developing a pipeline of drug candidates that utilize our advanced polymer conjugate technology platforms, which are designed to enable the development of new molecular entities that target known mechanisms of action. Our research and development pipeline of new investigational drugs includes treatments for cancer, autoimmune disease and chronic pain.

Our research and development activities have required significant ongoing investment to date and are expected to continue to require significant investment. As a result, with the exception of the income resulting from the upfront payment in April 2018 from our collaboration agreement with Bristol-Myers Squibb Company (BMS), we expect to continue to incur substantial losses and negative cash flows from operations in the future. We have financed our operations primarily through cash generated from licensing, collaboration and manufacturing agreements and financing transactions. At December 31, 2018, we had approximately $1.9 billion in cash and investments in marketable securities and had debt of $250.0 million in principal of senior secured notes due in October 2020.

Basis of Presentation, Principles of Consolidation and Use of Estimates

Our consolidated financial statements include the financial position, results of operations and cash flows of our wholly-owned subsidiaries: Nektar Therapeutics (India) Private Limited and Nektar Therapeutics UK Limited. All intercompany accounts and transactions have been eliminated in consolidation.

Our Consolidated Financial Statements are denominated in U.S. dollars. Accordingly, changes in exchange rates between the applicable foreign currency and the U.S. dollar will affect the translation of each foreign subsidiary’s financial results into U.S. dollars for purposes of reporting our consolidated financial results. Translation gains and losses are included in accumulated other comprehensive income (loss) in the stockholders’ equity section of the Consolidated Balance Sheets. To date, such cumulative translation adjustments have not been significant to our consolidated financial position. Aggregate gross foreign currency transaction gains (losses) recorded in operations for the years ended December 31, 2018, 2017, and 2016 were not significant.

The preparation of consolidated financial statements in conformity with U.S. generally accepted accounting principles (GAAP) requires management to make estimates and assumptions that affect the reported amounts of assets and liabilities and disclosure of contingent assets and liabilities at the date of the consolidated financial statements and the reported amounts of revenue and expenses during the reporting period. Accounting estimates and assumptions are inherently uncertain. Actual results could differ materially from those estimates and assumptions. Our estimates include those related to estimated selling prices of performance obligations and estimates of variable consideration in collaboration agreements, estimated royalty revenue, other estimates required for revenue recognition as described further below, the net realizable value of inventory, the impairment of investments, goodwill and long-lived assets, contingencies, accrued clinical trial, contract manufacturing and other expenses, estimated non-cash royalty revenue

and non-cash interest expense from our liability related to our sale of future royalties, stock-based compensation, and ongoing litigation, among other estimates. We base our estimates on historical experience and on other assumptions that management believes are reasonable under the circumstances. These estimates form the basis for making judgments about the carrying values of assets and liabilities when these values are not readily apparent from other sources. As appropriate, estimates are assessed each period and updated to reflect current information and any changes in estimates will generally be reflected in the period first identified.

Reclassifications

We have reclassified certain items previously reported in specific financial statement captions to conform to the current period presentation. Such reclassifications do not materially impact previously reported revenue, operating (income) loss, net (income) loss, total assets, liabilities or stockholders' equity.

Cash, Cash Equivalents, and Investments, and Fair Value of Financial Instruments

We consider all investments in marketable securities with an original maturity of three months or less when purchased to be cash equivalents. We classify investments in securities with remaining maturities of less than one year, or where our intent is to use the investments to fund current operations or to make them available for current operations, as short-term investments. We classify investments in securities with remaining maturities of over one year as long-term investments.

Investments are designated as available-for-sale and are carried at fair value, with unrealized gains and losses reported in stockholders' equity as accumulated other comprehensive income (loss). The disclosed fair value related to our cash equivalents and investments is based on market prices from a variety of industry standard data providers and generally represent quoted prices for similar assets in active markets or have been derived from observable market data.

We include interest on securities classified as available-for-sale, as well as amortization of premiums and accretion of discounts to maturity, in interest income. We include realized gains and losses and declines in value of available-for-sale securities judged to be other-than-temporary, if any, in other income (expense). The cost of securities sold is based on the specific identification method.

Our cash, cash equivalents, short-term investments and long-term investments are exposed to credit risk in the event of default by the third parties that hold or issue such assets. Our cash, cash equivalents, short-term investments and long-term investments are held by financial institutions that management believes are of high credit quality. Our investment policy limits investments to fixed income securities denominated and payable in U.S. dollars such as corporate bonds, corporate commercial paper, U.S. government obligations, and money market funds and places restrictions on maturities and concentrations by type and issuer.

Accounts Receivable and Significant Customer Concentrations

Our customers are primarily pharmaceutical and biotechnology companies that are located in the U.S. and Europe and with whom we have multi-year arrangements. Our accounts receivable balance contains billed and unbilled trade receivables from product sales, milestones, other contingent payments and royalties, and cost-sharing billings from collaborative research and development agreements. For the year ended December 31, 2018, our accounts receivable includes $24.2 million from contracts with customers and $19.0 million for net expense reimbursements from our collaboration partner. For the year ended December 31, 2017, our accounts receivable includes $3.3 million from contracts with customers and $1.7 million for expense reimbursements from our collaboration partner. We generally do not require collateral from our customers. We perform a regular review of our customers' credit risk and payment histories, including payments made subsequent to year-end. When appropriate, we provide for an allowance for doubtful accounts by reserving for specifically identified doubtful accounts, although historically we have not experienced credit losses from our accounts receivable. At December 31, 2018, three customers represented 44%, 36% and 12%, respectively, of our accounts receivable. At December 31, 2017, four different customers represented 43%, 20%, 19% and 14%, respectively, of our accounts receivable.

Inventory and Significant Supplier Concentrations

Inventory is generally manufactured upon receipt of firm purchase orders from our collaboration partners. Inventory includes direct materials, direct labor, and manufacturing overhead and cost is determined on a first-in, first-out basis for raw materials and on a specific identification basis for work-in-process and finished goods. Inventory is valued at the lower of cost or net realizable value and defective or excess inventory is written down to net realizable value based on historical experience or projected usage. Inventory related to our research and development activities is expensed as manufactured by us or when purchased.

We are dependent on our suppliers and contract manufacturers to provide raw materials and drug candidates of appropriate quality and reliability and to meet applicable contract and regulatory requirements. In certain cases, we rely on single sources of supply of one or more critical materials. Consequently, in the event that supplies are delayed or interrupted for any reason, our ability to develop and produce our drug candidates or our ability to meet our supply obligations could be significantly impaired, which could have a material adverse effect on our business, financial condition and results of operations.

Long-Lived Assets

Property, plant and equipment are stated at cost, net of accumulated depreciation. Major improvements are capitalized, while maintenance and repairs are expensed when incurred. Manufacturing, laboratory and other equipment are depreciated using the straight-line method generally over estimated useful lives of three to ten years. Buildings are depreciated using the straight-line method generally over the estimated useful life of twenty years. Leasehold improvements are amortized using the straight-line method over the shorter of the estimated useful life or the remaining term of the lease.

Goodwill represents the excess of the price paid for another entity over the fair value of the assets acquired and liabilities assumed in a business combination. We are organized in one reporting unit and evaluate the goodwill for the Company as a whole. Goodwill has an indefinite useful life and is not amortized, but instead tested for impairment at least annually in the fourth quarter of each year using an October 1 measurement date.

We assess the impairment of long-lived assets whenever events or changes in business circumstances indicate that the carrying amounts of the assets may not be fully recoverable. In the case of property, plant and equipment, we determine whether there has been an impairment by comparing the carrying value of the asset to the anticipated undiscounted net cash flows associated with the asset. If such cash flows are less than the carrying value, we write down the asset to its fair value, which may be measured as anticipated discounted net cash flows associated with the asset. In the case of goodwill impairment, we compare the carrying value of the reporting unit to its fair value, which we generally measure using market capitalization for our single reporting unit. If an impairment exists, we write down goodwill such that the carrying value of the reporting units equals its fair value.

Collaborative Arrangements

We enter into collaboration arrangements with pharmaceutical and biotechnology collaboration partners, under which we may grant licenses to our collaboration partners to further develop and commercialize one of our proprietary drug candidates, either alone or in combination with the collaboration partners' compounds, or grant licenses to partners to use our technology to research and develop their own proprietary drug candidates. We may also perform research, development, manufacturing and supply activities under our collaboration agreements. Consideration under these contracts may include an upfront payment, development milestones and other contingent payments, expense reimbursements, royalties based on net sales of approved drugs, and commercial sales milestone payments. Additionally, these contracts may provide options for the customer to purchase our proprietary PEGylation materials, drug candidates or additional contract research and development services under separate contracts.

When we enter into collaboration agreements, we assess whether the arrangements fall within the scope of Accounting Standards Codification (ASC) 808, Collaborative Arrangements (ASC 808) based on whether the arrangements involve joint operating activities and whether both parties have active participation in the arrangement and are exposed to significant risks and rewards. To the extent that the arrangement falls within the scope of ASC 808, we assess whether the payments between us and our collaboration partner fall within the scope of other accounting literature. If we conclude that payments from the collaboration partner to us represent consideration from a customer, such as license fees and contract research and development activities, we account for those payments within the scope of ASC 606, Revenue from Contracts with Customers. However, if we conclude that our collaboration partner is not a customer for certain activities and associated payments, such as for certain collaborative research, development, manufacturing and commercial activities, we present such payments as a reduction of research and development expense or general and administrative expense, based on where we present the underlying expense.

Revenue Recognition

For elements of those arrangements that we determine should be accounted for under ASC 606, we assess which activities in our collaboration agreements are performance obligations that should be accounted for separately and determine the transaction price of the arrangement, which includes the assessment of the probability of achievement of future milestones and other potential consideration. For arrangements that include multiple performance obligations, such as granting a license or performing contract research and development activities or participation on joint steering or other committees, we allocate upfront and milestone payments under a relative standalone selling price method. Accordingly, we develop assumptions that require judgment to determine the standalone selling price for each performance obligation identified in the contract. These key assumptions may include revenue forecasts, clinical development timelines and costs, discount rates and probabilities of clinical and regulatory success.

Product sales

Product sales are primarily derived from manufacturing and supply agreements with our collaboration partners. We have assessed our current manufacturing and supply arrangements and have generally determined that they provide the customer an option to purchase our proprietary PEGylation materials. Accordingly, we treat each purchase order as a discrete exercise of the customer's option (i.e. a separate contract) rather than as a component of the overall

arrangement. The pricing for the manufacturing and supply is generally at a fixed price and may be subject to annual producer price index (PPI) adjustments. We invoice and recognize product sales when title and risk of loss pass to the customer, which generally occurs upon shipment. Customer payments are generally due 30 days from receipt of an invoice. Our products are tested for adherence to technical specifications prior to shipment; accordingly, we have not experienced any significant returns from our customers.

Royalty revenue

Generally, we are entitled to royalties from our collaboration partners based on the net sales of their approved drugs that are marketed and sold in one or more countries where we hold royalty rights. For arrangements that include sales-based royalties, including commercial milestone payments based on the level of sales, we have concluded that the license is the predominant item to which the royalties relate. Accordingly, we recognize royalty revenue, including for our non-cash royalties, when the underlying sales occur based on our best estimates of sales of the drugs. Our partners generally pay royalties or commercial milestones after the end of

the calendar quarter in accordance with contractual terms. We present commercial milestone payments within license, collaboration and other revenue.

License, collaboration and other revenue

License Grants: For collaboration arrangements that include a grant of a license to our intellectual property, we consider whether the license grant is distinct from the other performance obligations included in the arrangement. Generally, we would conclude that the license is distinct if the customer is able to benefit from the license with the resources available to it. For licenses that are distinct, we recognize revenues from nonrefundable, upfront payments and other consideration allocated to the license when the license term has begun and we have provided all necessary information regarding the underlying intellectual property to the customer, which generally occurs at or near the inception of the arrangement.

Milestone Payments: At the inception of the arrangement and at each reporting date thereafter, we assess whether we should include any milestone payments or other forms of variable consideration in the transaction price, based on whether a significant reversal of revenue previously recognized is not probable upon resolution of the uncertainty. Since milestone payments may become payable to us upon the initiation of a clinical study or filing for or receipt of regulatory approval, we review the relevant facts and circumstances to determine when we should update the transaction price, which may occur before the triggering event. When we do update the transaction price for milestone payments, we allocate it on a relative standalone selling price basis and record revenue on a cumulative catch-up basis, which results in recognizing revenue for previously satisfied performance obligations in such period. Our partners generally pay development milestones subsequent to achievement of the triggering event.

Research and development services: For amounts allocated to our research and development obligations in a collaboration arrangement, we recognize revenue over time using a proportional performance model, representing the transfer of goods or services as we perform activities over the term of the agreement.

Shipping and Handling Costs

We recognize costs related to shipping and handling of product to customers in cost of goods sold.

Research and Development Expense

Research and development costs are expensed as incurred and include salaries, benefits and other operating costs such as outside services, supplies and allocated overhead costs. We perform research and development for our proprietary drug candidates and technology development and for certain third parties under collaboration agreements. For our proprietary drug candidates and our internal technology development programs, we invest our own funds without reimbursement from a third party. Where we perform research and development activities under a clinical joint development collaboration, such as our collaboration with Bristol-Myers Squibb, we record the partner’s share of collaboration expenses as a reduction to research and development expense when reimbursement amounts are due to us under the agreement.

We record an accrued expense for the estimated costs of our clinical trial activities performed by third parties. The financial terms of these agreements are subject to negotiation, vary from contract to contract and may result in uneven payment flows to our vendors. Payments under the contracts depend on factors such as the achievement of certain events, successful enrollment of patients, and completion of certain clinical trial activities. We generally accrue costs associated with the start-up and reporting phases of the clinical trials ratably over the estimated duration of the start-up and reporting phases. We generally accrue costs associated with the treatment phase of clinical trials based on the total estimated cost of the treatment phase on a per patient basis and we expense the per patient cost ratably over the estimated patient treatment period based on patient enrollment in the trials. In specific circumstances, such as for certain time-based costs, we recognize clinical trial expenses using a methodology that we consider to be more

reflective of the timing of costs incurred.

We record an accrued expense for the estimated costs of our contract manufacturing activities performed by third parties. The financial terms of these agreements are subject to negotiation, vary from contract to contract and may result in uneven payment flows to our vendors. Payments under the contracts include upfront payments and milestone payments, which depend on factors such as the achievement of the completion of certain stages of the manufacturing process. For purposes of recognizing expense, we assess whether we consider the production process is sufficiently defined to be considered the delivery of a good, as evidenced by predictive or contractually required yields in the production process, or the delivery of a service, where processes and yields are developing and less certain. If we consider the process to be the delivery of a good, we recognize expense when the drug product is delivered, or we otherwise bear risk of loss. If we consider the process to be the delivery of a service, we recognize expense based on our best estimates of the contract manufacturer’s progress towards completion of the stages in the contracts. We recognize and amortize upfront payments and accrue liabilities based on the specific terms of each arrangement. Certain arrangements may provide upfront payments for certain stages of the arrangement and milestone payments for the completion of certain stages, and, accordingly, we may record

advance payments for services that have not been completed or goods not delivered and liabilities for stages where the contract manufacturer is entitled to a milestone payment.

Advance payments for goods or services that will be used or rendered for future research and development activities are capitalized as prepaid expenses and recognized as expense as the related goods are delivered or the related services are performed. We base our estimates on the best information available at the time. However, additional information may become available to us which may allow us to make a more accurate estimate in future periods. In this event, we may be required to record adjustments to research and development expenses in future periods when the actual level of activity becomes more certain. Such increases or decreases in cost are generally considered to be changes in estimates and will be reflected in research and development expenses in the period identified.

Stock-Based Compensation

Stock-based compensation arrangements include stock option grants and restricted stock unit (RSU) awards under our equity incentive plans, as well as shares issued under our Employee Stock Purchase Plan (ESPP), through which employees may purchase our common stock at a discount to the market price.

We use the Black-Scholes option pricing model for the respective grant to determine the estimated fair value of the option on the date of grant (grant date fair value) and the estimated fair value of common stock purchased under the ESPP. The Black-Scholes option pricing model requires the input of highly subjective assumptions. These variables include, but are not limited to, our stock price volatility over the term of the awards, and actual and projected employee stock option exercise behaviors. Because our employee stock options have characteristics significantly different from those of traded options, and because changes in the subjective input assumptions can materially affect the fair value estimate, in management’s opinion, the existing models may not provide a reliable single measure of the fair value of our employee stock options or common stock purchased under the ESPP. The fair value of an RSU is equal to the closing price of our common stock on the grant date. Management will continue to assess the assumptions and methodologies used to calculate the estimated fair value of stock-based compensation. Circumstances may change and additional data may become available over time, which could result in changes to these assumptions and methodologies, and which could materially impact our fair value determination.

We expense the value of the portion of the option or award on a straight line basis over the requisite service periods in our Consolidated Statements of Operations and recognize forfeitures of options and awards as they occur. For options and awards that vest upon the achievement of performance milestones, we estimate the vesting period based on our evaluation of the probability of achievement of each respective milestone and the related estimated date of achievement. Stock-based compensation expense for purchases under the ESPP is recognized over the respective six-month purchase period. Expense amounts are recorded in cost of goods sold, research and development expense, and general and administrative expense based on the function of the applicable employee. Stock-based compensation charges are non-cash charges and as such have no impact on our reported cash flows.

Net Income (Loss) Per Share

For all periods presented in the Consolidated Statements of Operations, the net income (loss) available to common stockholders is equal to the reported net income (loss). Basic net income (loss) per share is calculated based on the weighted-average number of common shares outstanding during the periods presented. Diluted net income (loss) per share is calculated based on the weighted-average number of shares of common stock outstanding, including potentially dilutive securities, which consist of common shares underlying stock options and restricted stock units (RSUs). For 2018, the effect of these dilutive securities under the treasury stock method was approximately 10.5 million, and we excluded approximately 3.3 million of weighted-average shares of common stock underlying outstanding stock options from the computation of diluted net income per share because their effect was antidilutive. For 2017 and 2016, basic and diluted net loss per share are the same due to our net losses and the requirement to exclude potentially dilutive securities which would have an antidilutive effect on net loss per share. We excluded

weighted average outstanding stock options and RSUs totaling 20.6 million and 19.9 million during the years ended December 31, 2017 and 2016, respectively.

Income Taxes

We account for income taxes under the liability method. Under this method, we determine deferred tax assets and liabilities based on differences between the financial reporting and tax reporting bases of assets and liabilities, measured using enacted tax rates and laws that we expect to be in effect when we expect the differences to reverse. Realization of deferred tax assets is dependent upon future earnings, the timing and amount of which are uncertain. We record a valuation allowance against deferred tax assets to reduce their carrying value to an amount that is more likely than not to be realized. When we establish or reduce the valuation allowance related to the deferred tax assets, our provision for income taxes will increase or decrease, respectively, in the period we make such determination.

We utilize a two-step approach to recognize and measure uncertain tax positions. The first step is to evaluate the tax position for recognition by determining if the weight of available evidence indicates that it is more likely than not that the position will be sustained upon tax authority examination, including resolution of related appeals or litigation processes, if any. The second step is to measure the tax benefit as the largest amount of benefit, determined on a cumulative probability basis, that is more than 50% likely of being realized upon ultimate settlement.

Comprehensive income (loss)

Comprehensive income (loss) is the change in stockholders' equity from transactions and other events and circumstances other than those resulting from investments by stockholders and distributions to stockholders. Our other comprehensive income (loss) includes net income (loss), gains and losses from the foreign currency translation of the assets and liabilities of our India and UK subsidiaries, and unrealized gains and losses on investments in available-for-sale securities.

Adoption of New Accounting Principle

On January 1, 2018, we adopted ASC 606, Revenue Recognition - Revenue from Contracts with Customers. ASC 606 supersedes the guidance in ASC 605, Revenue Recognition. Under ASC 606, an entity recognizes revenue when its customer obtains control of promised goods or services, in an amount that reflects the consideration which the entity expects to receive in exchange for those goods or services. To determine revenue recognition for units of account that an entity determines are within the scope of ASC 606, the entity performs the following five steps: (i) identify the contract(s) with a customer; (ii) identify the performance obligations in the contract; (iii) determine the transaction price; (iv) allocate the transaction price to the performance obligations in the contract; and (v) recognize revenue when (or as) the entity satisfies a performance obligation. In our adoption, we used the practical expedients to analyze only those contracts that were still active contracts as of January 1, 2018 and evaluated those contracts based on the cumulative contract modifications through that date. We do not believe that the use of the practical expedients had or will have a material impact on our transition adjustment or our prospective accounting. We adopted ASC 606 on a modified retrospective basis under which we recognized the cumulative effect of adoption as a transition adjustment to opening accumulated deficit. Therefore, the periods prior to the adoption date of ASC 606 have not been restated.

The transition adjustment totaled $12.7 million, and included $10.7 million related to the recognition of royalty revenue. Previously, under ASC 605, we recognized certain of our royalty arrangements on a cash basis, generally one quarter in arrears. Beginning in the first quarter of 2018, we began to accrue our estimate of these royalties earned based on our collaboration partners' sales of the associated drug compounds. As a result, in the first quarter of 2018, we recognized $11.1 million of estimated royalty revenue associated with our partners' sales of MOVANTIK® and ADYNOVATE® in the first quarter of 2018. Previously, in the fourth quarter of 2017, we recognized $9.6 million in royalty revenue associated with sales of MOVANTIK® and ADYNOVATE® in the third quarter of 2017. The transition between the two accounting methods results in the $10.7 million in royalties for sales of MOVANTIK® and ADYNOVATE® in the fourth quarter of 2017 being recognized as a direct reduction of our accumulated deficit instead of being recognized in the statement of operations. The transition adjustment also includes $2.0 million for the reduction of deferred revenue related to one of our collaboration arrangements. The impact of the adoption of ASC 606 on our Consolidated Balance Sheet as of December 31, 2018 and Consolidated Statement of Operations data for the year ended December 31, 2018 was as follows (in thousands):

	As reported	Adjustments	Balances Without the Adoption of Topic 606

Consolidated Balance Sheet data as of December 31, 2018			
Accounts receivable, net	$43,213	$ (21,030)	$22,183
Deferred revenue, current portion	13,892	1,191	15,083
Deferred revenue, less current portion	10,744	(112)	10,632
Accumulated deficit	(1,424,051)	(22,109)	(1,446,160)
Consolidated Statement of Operations data for the year ended December 31, 2018			
Product sales	$20,774	$ (192)	$20,582
Royalty revenue	41,976	(286)	41,690
License, collaboration and other revenue	1,097,265	(8,934)	1,088,331
Total revenue	1,193,323	(9,412)	1,183,911

Recent Accounting Pronouncements

In November 2018, the Financial Accounting Standards Board (FASB) issued Accounting Standards Update 2018-18: Clarifying the Interaction between Topic 808 and Topic 606 (ASU 2018-18). The guidance clarifies that certain transactions between collaborative arrangement participants should be accounted for as revenue under ASC 606 when the collaborative arrangement participant is a customer for a promised good or service that is distinct within the collaborative arrangement. The guidance also precludes entities from presenting amounts related to transactions with a collaborative arrangement participant that is not a customer as revenue, unless those transactions are directly related to third-party sales. ASU 2018-18 is effective in the first quarter of 2020 and should be applied retrospectively to January 1, 2018, when we adopted ASC 606. Early adoption is permitted. We are evaluating the effect of adoption, but we do not expect a material effect on our revenue.

In February 2016, the FASB issued guidance to amend a number of aspects of lease accounting, including requiring lessees to recognize almost all leases with a term greater than one year as a right-of-use asset and corresponding liability, measured at the present value of the lease payments. The guidance will become effective for us beginning in the first quarter of 2019 and is required to be adopted using a modified retrospective approach. The adoption of this guidance will have a material effect on our balance sheet. In particular, for our facilities leases described in Note 6, we expect to recognize right-of-use assets, estimated between $87 million and $97 million and lease liabilities, estimated between $96 million and $106 million. The estimate for the right-of-use assets reflects the estimated lease liabilities, reduced by our historical deferred rent balance, which, as discussed in Note 6, totaled $9.3 million as of December 31, 2018.

Note 2 — Cash and Investments in Marketable Securities

Cash and investments in marketable securities, including cash equivalents, are as follows (in thousands):

	Estimated Fair Value at	
	December 31, 2018	December 31, 2017
Cash and cash equivalents	$194,905	$4,762
Short-term investments	1,140,445	291,370
Long-term investments	582,889	57,088
Total cash and investments in marketable securities	$1,918,239	$353,220

We invest in liquid, high quality debt securities. Our investments in debt securities are subject to interest rate risk. To minimize the exposure due to an adverse shift in interest rates, we invest in securities with maturities of two years or less and maintain a weighted average maturity of one year or less. All of our long-term investments as of December 31, 2018 and 2017 had maturities between one and two years.

Gross unrealized gains and losses were not significant at either December 31, 2018 or 2017. During the years ended December 31, 2018, 2017 and 2016, we sold available-for-sale securities totaling $12.0 million, $37.5 million, and $5.0 million, respectively, and realized gains and losses were not significant in any of those periods.

Under the terms of our 7.75% senior secured notes due October 2020, we are required to maintain a minimum cash and investments in marketable securities balance of $60.0 million.

79

Our portfolio of cash and investments in marketable securities includes (in thousands):

	Fair Value Hierarchy	Estimated Fair Value at December 31, 2018	December 31, 2017
	Level		
Corporate notes and bonds	2	$1,288,986	$216,253
Corporate commercial paper	2	498,048	128,096
Obligations of U.S. government agencies	2	12,977	2,977
Available-for-sale investments		1,800,011	347,326
Money market funds	1	105,656	302
Certificate of deposit	N/A	6,760	1,132
Cash	N/A	5,812	4,460
Total cash and investments in marketable securities		$1,918,239	$353,220

Level 1 ~~Q~~uoted prices in active markets for identical assets or liabilities.
Level 2 ~~In~~puts other than Level 1 that are observable, either directly or indirectly, such as quoted prices for similar assets or liabilities; quoted prices for identical or similar assets or liabilities in markets that are not active; or other inputs that are observable or can be corroborated by observable market data for substantially the full term of the assets or liabilities.
Level 3 ~~U~~nobservable inputs that are supported by little or no market activity and that are significant to the fair value of the assets or liabilities.
During the years ended December 31, 2018 and 2017, there were no transfers between Level 1 and Level 2 of the fair value hierarchy.

At December 31, 2018 and 2017, we had letter of credit arrangements in favor of our landlords and certain vendors totaling $6.6 million and $1.1 million, respectively. These letters of credit are secured by investments of similar amounts.

Note 3 — Inventory

Inventory consists of the following (in thousands):

	December 31,	
	2018	2017
Raw materials	$1,846	$1,796
Work-in-process	6,403	4,843
Finished goods	3,132	4,087
Total inventory	$11,381	$10,726

Note 4 — Property, Plant and Equipment

Property, plant and equipment consists of the following (in thousands):

	December 31,	
	2018	2017
Building and leasehold improvements	$77,771	$81,444
Laboratory equipment	33,806	31,214
Computers, furniture, and other	31,354	27,800
Manufacturing equipment	21,339	20,695
Depreciable property, plant and equipment at cost	164,270	161,153
Less: accumulated depreciation	(120,507)	(115,090)
Depreciable property, plant and equipment, net	43,763	46,063
Construction-in-progress	5,088	1,400
Property, plant and equipment, net	$48,851	$47,463

Building and leasehold improvements include our manufacturing, research and development and administrative facilities and the related improvements to these facilities. Laboratory and manufacturing equipment include assets that support both our manufacturing and research and development efforts. Construction-in-progress includes assets being built to enhance our manufacturing and research and development efforts.

Depreciation and amortization expenses on property, plant and equipment for the years ended December 31, 2018, 2017, and 2016 was $8.8 million, $12.6 million, and $13.2 million, respectively.

In November 2017, Bayer announced that the Phase 3 Amikacin Inhale clinical program did not meet its primary endpoint or key secondary endpoints and, in December 2017, Bayer terminated our related collaboration agreement. Under this collaboration, we were responsible for the development, manufacturing and supply of our proprietary nebulizer device included in the Amikacin product and had acquired specific manufacturing equipment for this purpose. As a result of the termination of the program, in the three months ended December 31, 2017, we expensed program specific manufacturing equipment with an original cost of $23.4 million and a net book value of $15.1 million. We completed the disposal of this equipment in the first quarter of 2018. In addition, in the three months ended December 31, 2017, we incurred approximately $0.9 million of other program termination costs related to our manufacturing obligations.

Note 5 — Senior Secured Notes

On October 5, 2015, we completed the sale and issuance of $250.0 million in aggregate principal amount of 7.75% senior secured notes due 2020 (the Notes). The Notes are secured by a first-priority lien on substantially all of our assets and bear interest at a rate of 7.75% per annum payable in cash quarterly in arrears on January 15, April 15, July 15, and October 15 of each year. Interest is calculated based on actual days outstanding over a 360 day year. The Notes will mature on October 5, 2020, at which time the outstanding principal will be due and payable.

In connection with the issuance of the Notes, we paid fees and expenses of $8.9 million, of which $8.7 million of transaction and facility fees paid directly to the purchasers of the Notes and other direct issuance costs were capitalized as a debt discount and issuance costs and are recorded as a reduction to the senior secured notes, net liability balance in our Consolidated Balance Sheet. The unamortized balance of these costs is $3.1 million at December 31, 2018 and will be amortized to interest expense over the remaining term of the Notes.

The agreement, pursuant to which the Notes were issued, contains customary covenants, including covenants that limit or restrict our ability to incur liens, incur indebtedness, declare or pay dividends, redeem stock, issue preferred stock, make certain investments, merge or consolidate, make dispositions of assets, or enter into certain new businesses or transactions with affiliates, but do not contain covenants related to future financial performance. In particular, the Notes agreement requires us to maintain a minimum cash and investments in marketable securities balance of $60.0 million during the term of the Notes. We may currently redeem some or all of these notes at a redemption price equal to 102% of the principal amount of the notes if the redemption date is prior to October 5, 2019, or 100% of the principal amount of the notes if the redemption date is on or after October 5, 2019, plus, in each case, accrued and unpaid interest to the applicable redemption date. If we experience certain change of control events, the holders of the Notes will have the right to require us to purchase all or a portion of the Notes at a purchase price in cash equal to 101% of the principal amount thereof, plus accrued and unpaid interest to the date of purchase. In addition, upon certain asset sales, we may be required to offer to use the net proceeds thereof to purchase some of the Notes at 100% of the principal amount thereof, plus accrued and unpaid interest to the date of purchase.

As of December 31, 2018, based on a discounted cash flow analysis using Level 3 inputs including financial discount rates, we estimate that the fair value of the Notes is approximately $258.0 million.

Note 6 — Leases

Operating Leases

In August 2017, we entered into a Lease Agreement (the Mission Bay Lease) with ARE-San Francisco No. 19, LLC (ARE) and terminated our sublease with Pfizer, Inc., effectively extending our lease term from 2020 to 2030 for our 134,356 square foot corporate office and R&D facility located at 455 Mission Bay Boulevard, San Francisco, California (the Mission Bay Facility).

The term of the Mission Bay Lease commenced on September 1, 2017, and will expire January 31, 2030, subject to our right to extend the term of the lease for two consecutive five-year periods. The monthly base rent for the Mission Bay Facility will escalate over the term of the lease at various intervals. During the term of the Mission Bay Lease, we are responsible for paying our share of operating expenses specified in the lease, including insurance costs and taxes. The Mission Bay Lease also obligates us to rent from ARE a total of an additional approximately 18,000 square feet of space at the Mission Bay Facility at specified delivery dates. The Mission Bay Lease includes various covenants, indemnities, defaults, termination rights, security deposits and other provisions customary for lease transactions of this nature.

In May 2018, we entered into a Lease Agreement (the Third Street Lease) with Kilroy Realty Finance Partnership, L.P. to lease 135,936 square feet of space located at 360 Third Street, San Francisco, California (the Third Street Facility) from June 2018 to January 31, 2030. An initial 1,726 square feet was delivered in June 2018, and a total of 67,105 square feet for two additional spaces was delivered in December 2018. The remaining space will be delivered in phases during 2019. The Third Street Lease will provide us additional facilities to support increased personnel for our San Francisco-based R&D activities. The lease term includes a right to extend the term for a consecutive five-year period. Our fixed annual base rent on an industrial gross lease basis includes certain expenses and property taxes paid directly by the landlord and will escalate each year over the term at specified intervals. We have a onetime right of first offer with respect to certain additional rental space at the Third Street Facility. The Third Street Lease includes various covenants, indemnities, defaults, termination rights, security deposits and other provisions customary for lease transactions of this nature.

We recognize rent expense on a straight-line basis over the lease period. For the years ended December 31, 2018, 2017 and 2016, rent expense totaled approximately $8.1 million, $4.7 million and $3.2 million, respectively. As of December 31, 2018 and 2017, we had total deferred rent balances of $9.3 million and $6.0 million, respectively, which we present in other long-term liabilities in our Consolidated Balance Sheets.

Our future minimum lease payments for our operating leases at December 31, 2018 are as follows (in thousands):

Year ending December 31,	
2019	$7,914
2020	10,617
2021	13,649
2022	14,117
2023	14,599
2024 and thereafter	98,315
Total future minimum lease payments	$159,211

Note 7 — Liability Related to the Sale of Future Royalties

On February 24, 2012, we entered into a Purchase and Sale Agreement (the Purchase and Sale Agreement) with RPI Finance Trust (RPI), an affiliate of Royalty Pharma, pursuant to which we sold, and RPI purchased, our right to receive royalty payments (the Royalty Entitlement) arising from the worldwide net sales, from and after January 1, 2012, of (a) CIMZIA®, under our license, manufacturing and supply agreement with UCB Pharma (UCB), and (b) MIRCERA®, under our license, manufacturing and supply agreement with F. Hoffmann-La Roche Ltd and Hoffmann-La Roche Inc. (together referred to as Roche). We received aggregate cash proceeds of $124.0 million for the Royalty Entitlement. As part of this sale, we incurred approximately $4.4 million in transaction costs, which will be amortized to interest expense over the estimated life of the Purchase and Sale Agreement. Although we sold all of our rights to receive royalties from the CIMZIA® and MIRCERA® products, as a result of our ongoing manufacturing

and supply obligations related to the generation of these royalties, we will continue to account for these royalties as revenue, and we recorded the $124.0 million in proceeds from this transaction as a liability (Royalty Obligation) that will be amortized using the interest method over the estimated life of the Purchase and Sale Agreement.

The following table shows the activity within the liability account during the year ended December 31, 2018 and for the period from the inception of the royalty transaction on February 24, 2012 (inception) to December 31, 2018 (in thousands):

	Year ended December 31, 2018	Period from inception to December 31, 2018
Liability related to the sale of future royalties—beginning balance	$96,922	$—
Proceeds from sale of future royalties	—	124,000
Payments from Nektar to RPI	—	(10,000)
Non-cash CIMZIA® and MIRCERA® royalty revenue	(33,308)	(170,839)
Non-cash interest expense recognized	21,196	141,649
Liability related to the sale of future royalties – ending balance	84,810	84,810
Less: unamortized transaction costs	(1,899)	(1,899)
Liability related to the sale of future royalties, net	$82,911	$82,911

Pursuant to the Purchase and Sale Agreement, in March 2014 and March 2013, we were required to pay RPI $7.0 million and $3.0 million, respectively, as a result of worldwide net sales of MIRCERA® for the 12 month periods ended December 31, 2013 and 2012 not reaching certain minimum thresholds. The Purchase and Sale Agreement does not include any other potential payments related to minimum net sales thresholds and, therefore, we do not expect to make any further payments to RPI related to this agreement.

During the years ended December 31, 2018, 2017 and 2016, we recognized $33.3 million, $30.5 million, and $30.2 million, respectively, in non-cash royalties from net sales of CIMZIA® and MIRCERA®, and we recorded $21.2 million, $18.9 million and $19.7 million, respectively, of related non-cash interest expense.

As royalties are remitted to RPI from Roche and UCB, the balance of the Royalty Obligation will be effectively repaid over the life of the agreement. In order to determine the amortization of the Royalty Obligation, we are required to estimate the total amount of future royalty payments to be received by RPI. The sum of these amounts less the $124.0 million proceeds we received will be recorded as interest expense over the life of the Royalty Obligation. From inception until 2017, our estimate of this total interest expense resulted in an effective annual interest rate of approximately 17%. We periodically assess the estimated royalty payments to RPI from UCB and Roche and to the extent the amount or timing of such payments is materially different than our original estimates, we will prospectively adjust the amortization of the Royalty Obligation. During the three month period ended December 31, 2017, as a result of increases in the forecasted sales of CIMZIA®, our estimate of the effective annual interest rate over the life of the agreement increased to 17.6%, which resulted in a prospective interest rate of 21%. During the three month period ended December 31, 2018, primarily as a result of increases in the forecasted sales of MIRCERA®, our estimate of the effective annual interest rate over the life of the agreement increased to 18.7%, which results in a prospective interest rate of 29%.

There are a number of factors that could materially affect the amount and timing of royalty payments from CIMZIA® and MIRCERA®, most of which are not within our control. Such factors include, but are not limited to, changing standards of care, the introduction of competing products, manufacturing or other delays, biosimilar competition, intellectual property matters, adverse events that result in governmental health authority imposed restrictions on the use of the drug products, significant changes in foreign exchange rates as the royalties remitted to RPI are made in U.S. dollars (USD) while significant portions of the underlying sales of CIMZIA® and MIRCERA® are made in currencies other than USD, and other events or circumstances that could result in reduced royalty payments from CIMZIA® and MIRCERA®, all of which would result in a reduction of non-cash royalty revenues and the non-cash interest expense over the life of the Royalty Obligation. Conversely, if sales of CIMZIA® and MIRCERA® are more than expected, the non-cash royalty revenues and the non-cash interest expense recorded by us would be greater over the term of the Royalty Obligation.

In addition, the Purchase and Sale Agreement grants RPI the right to receive certain reports and other information relating to the Royalty Entitlement and contains other representations and warranties, covenants and indemnification obligations that are customary for a transaction of this nature. To our knowledge, we are currently in compliance with these provisions of the Purchase and Sale Agreement; however, if we were to breach our obligations, we could be required to pay damages to RPI that are not limited to the purchase price we received in the sale transaction.

Note 8 — Commitments and Contingencies

Purchase Commitments

In the normal course of business, we enter into various firm purchase commitments related to contract manufacturing, clinical development and certain other items. As of December 31, 2018, these commitments were approximately $63.3 million, all of which we expect to pay in 2019.

Legal Matters

From time to time, we are involved in lawsuits, arbitrations, claims, investigations and proceedings, consisting of intellectual property, commercial, employment and other matters, which arise in the ordinary course of business. We make provisions for liabilities when it is both probable that a liability has been incurred and the amount of the loss can be reasonably estimated. Such provisions are reviewed at least quarterly and adjusted to reflect the impact of settlement negotiations, judicial and administrative rulings, advice of legal counsel, and other information and events pertaining to a particular case. Litigation is inherently unpredictable. If any unfavorable ruling were to occur in any specific period, there exists the possibility of a material adverse impact on the results of our operations of that period and on our cash flows and liquidity.

On October 30, 2018, we and our CEO and CFO were named in a putative securities class action entitled, Mulquin v. Nektar Therapeutics et. al., N.D. Cal. Also, on February 13, 2019, and February 18, 2019, shareholder derivative complaints were filed in the U.S. District Court for the District of Delaware naming the CEO, CFO and certain members of Nektar’s board. Both the class action and shareholder derivative actions assert, among other things, that for a period beginning at least from November 11, 2017 through October 2, 2018, our stock was inflated due to alleged misrepresentations about the efficacy and safety of NKTR-214. These cases are in the early stages. Accordingly, we cannot reasonably estimate any range of potential future charges. However, an unfavorable resolution could potentially have a material adverse effect on our business, financial condition, and results of operations or prospects, potentially delay or limit our ability to use some of our research and development programs, and potentially result in paying monetary damages. We have recorded no liability for these matters on our Consolidated Balance Sheets as of December 31, 2018.

Foreign Operations

We operate in a number of foreign countries. As a result, we are subject to numerous local laws and regulations that can result in claims made by foreign government agencies or other third parties that are often difficult to predict even after the application of good faith compliance efforts.

Indemnification Obligations

During the course of our normal operating activities, we have agreed to certain contingent indemnification obligations as further described below. The term of our indemnification obligations is generally perpetual. There is generally no limitation on the potential amount of future payments we could be required to make under these indemnification obligations. To date, we have not incurred significant costs to defend lawsuits or settle claims based on our indemnification obligations. If any of our indemnification obligations is triggered, we may incur substantial liabilities. Because the aggregate amount of any potential indemnification obligation is not a stated amount, we cannot reasonably estimate the overall maximum amount of any such obligations. We have recorded no liabilities for these obligations on our Consolidated Balance Sheets as of December 31, 2018 or 2017.

Indemnifications in Connection with Commercial Agreements

As part of our collaboration agreements with our partners related to the license, development, manufacture and supply of drugs based on our proprietary technologies and drug candidates, we generally agree to defend, indemnify and hold harmless our partners from and against third party liabilities arising out of the agreement, including product liability (with respect to our activities) and infringement of intellectual property to the extent the intellectual property is developed by us and licensed to our partners. For example, as part of the sale of our royalty interest in the CIMZIA®

and MIRCERA® products, we and RPI made representations and warranties and entered into certain covenants and ancillary agreements which are supported by indemnity obligations. If it is determined that we breached certain of the representations and warranties or covenants and agreements made by us in any such agreements, we could incur substantial indemnification liabilities depending on the timing, nature, and amount of any such claims.

Indemnification of Underwriters and Initial Purchasers of our Securities

In connection with our sale of equity and senior secured debt securities, we have agreed to defend, indemnify and hold harmless our underwriters or initial purchasers, as applicable, as well as certain related parties from and against certain liabilities, including liabilities under the Securities Act of 1933, as amended.

Director and Officer Indemnifications

As permitted under Delaware law, and as set forth in our Certificate of Incorporation and our Bylaws, we indemnify our directors, executive officers, other officers, employees, and other agents for certain events or occurrences that may arise while in such capacity. The maximum potential amount of future payments we could be required to make under this indemnification is unlimited; however, we have insurance policies that may limit our exposure and may enable us to recover a portion of any future amounts paid. Assuming the applicability of coverage, the willingness of the insurer to assume coverage, and subject to certain retention, loss limits and other policy provisions, we believe any obligations under this indemnification would not be material, other than up to $2.5 million per incident for merger and acquisition related claims, $2.5 million per incident for securities related claims and $1.25 million per incident for non-securities related claims retention deductible per our insurance policy. However, no assurances can be given that the covering insurers will not attempt to dispute the validity, applicability, or amount of coverage without expensive litigation against these insurers, in which case we may incur substantial liabilities as a result of these indemnification obligations.

Note 9 — Stockholders' Equity

Common Stock

As discussed in Note 10, on April 3, 2018, we completed the issuance and sale of 8,284,600 shares of our common stock under a Share Purchase Agreement with BMS. These shares are unregistered and subject to certain lock-up and stand-still provisions for a five-year period.

On October 24, 2016, we completed the issuance and sale of 14,950,000 shares of our common stock in an underwritten public offering with total proceeds of approximately $189.7 million after deducting the underwriting commissions and discounts of approximately $12.1 million. In addition, we incurred approximately $0.4 million in legal and accounting fees, filing fees, and other costs in connection with this offering.

Equity Compensation Plans

At December 31, 2018, we had 31,940,416 reserved shares of common stock, all of which are reserved for issuance under our equity compensation plans, of which approximately 19,250,000 shares may be issued upon the exercise of outstanding options or the vesting of restricted stock units (RSUs) and 12,690,000 shares are available for issuance under equity compensation plans.

2017 Performance Incentive Plan

Our 2017 Performance Incentive Plan (2017 Plan) was adopted by our board of directors (Board of Directors) on March 28, 2017 and was approved by our stockholders on June 14, 2017. On the date of approval, any shares of our common stock that were available for issuance under our 2012 Performance Incentive Plan (2012 Plan) ceased to be available for future grants.

Subject to the terms of the 2017 Plan, 8,300,000 shares of our common stock, reduced by the number of shares of common stock subject to awards granted under the 2012 Plan on or after March 31, 2017 and prior to the adoption of the 2017 Plan, were initially available for awards under the 2017 Plan. On June 26, 2018, our stockholders approved an amendment to the 2017 Plan whereby 10,900,000 additional shares were made available for award grants under the 2017 Plan. Shares issued in respect of any "full-value award" granted under the 2017 Plan will be counted against the share limit described in the preceding sentences as 1.5 shares for every one share actually issued in connection with the award. Shares that are subject to or underlie awards which expire or for any reason are cancelled or terminated, are

forfeited, fail to vest, or for any other reason are not paid or delivered under the 2017 Plan or any Prior Plan (as defined below) will again be available for subsequent awards under the 2017 Plan (with any such shares subject to full-value awards increasing the 2017 Plan's share limit based on the full-value award ratio described above or, in the case of an award granted under a Prior Plan, the full-value award ratio set forth in such Prior Plan). Notwithstanding the foregoing, shares that are exchanged by a participant or withheld by us to pay the exercise price of an award granted under the 2017 Plan, as well as any shares exchanged or withheld to satisfy the tax withholding obligations related to any award, will not be available for subsequent awards under the 2017 Plan.

The purpose of the 2017 Plan and our other incentive plans is to promote our success by providing an additional means for us to attract, motivate, retain and reward directors, officers, employees, and other eligible persons through the grant of awards. Equity-based awards are also intended to further align the interests of award recipients and our stockholders. The 2017 Plan authorizes stock options, stock appreciation rights, stock bonuses, restricted stock, performance stock, stock units, phantom stock or similar rights to purchase or acquire shares, and other forms of awards granted or denominated in our common stock or units of our common stock, as well as cash bonus awards. Members of the Board of Directors, officers or employees, certain consultants and advisors and our subsidiaries are eligible to receive awards under the 2017 Plan. Pursuant to the 2017 Plan, we granted or issued non-qualified stock options and RSUs to employees, officers, and non-employee directors during 2017 and 2018. The requisite service period for stock options granted to our employees under the 2017 Plan as well as our Prior Plans is generally four years; the requisite service period for

stock options granted to our directors is generally one year. The requisite service period for RSUs granted under the 2017 Plan and our Prior Plans is generally three years for employees and one year for directors.

The 2017 Plan will terminate on March 27, 2027, unless earlier terminated by the Board of Directors. The maximum term of a stock option or stock appreciation right under the 2017 Plan and our Prior Plans is eight years from the date of grant. The per share exercise price of an option generally may not be less than the fair market value of a share of our common stock on The NASDAQ Stock Market on the date of grant.

Other Equity Incentive Plans

In addition to the 2017 Plan, we have other equity incentive plans under which options and restricted stock units granted remain outstanding but no new options or restricted stock units may be granted either as a result of the effectiveness of the 2017 Plan or the expiration of such other plan. These other equity incentive plans include: (i) the 2012 Plan which was adopted by the Board of Directors on April 4, 2012 and approved by our stockholders on June 28, 2012, and replaced by the 2017 Plan; (ii) the 2008 Equity Incentive Plan (2008 Plan) which was adopted by the Board of Directors on March 20, 2008 and approved by our stockholders on June 6, 2008; and (iii) the 1998 Non-Officer Equity Incentive Plan which was adopted by our Board of Directors on August 18, 1998, and amended and restated in its entirety and renamed the 2000 Non-Officer Equity Incentive Plan on June 6, 2000 (2000 Non-Officer Plan and collectively with the 2012 Plan and the 2008 Plan, the Prior Plans).

Pursuant to the Prior Plans, we previously granted or issued incentive stock options to employees and officers and non-qualified stock options, rights to acquire restricted stock, restricted stock units, and stock bonuses to employees, officers, non-employee directors, and consultants.

Employee Stock Purchase Plan

In February 1994, our Board of Directors adopted the Employee Stock Purchase Plan (ESPP) pursuant to section 423(b) of the Internal Revenue Code of 1986. Under the ESPP, 2,500,000 shares of our common stock have been authorized for issuance. The terms of the ESPP provide eligible employees with the opportunity to acquire an ownership interest in Nektar through participation in a program of periodic payroll deductions for the purchase of our common stock. Employees may elect to enroll or re-enroll in the ESPP on a semi-annual basis. Stock is purchased at 85% of the lower of the closing price on the first day of the enrollment period or the last day of the enrollment period.

401(k) Retirement Plan

We sponsor a 401(k) retirement plan whereby eligible employees may elect to contribute up to the lesser of 60% of their annual compensation or the statutorily prescribed annual limit allowable under Internal Revenue Service regulations. The 401(k) plan permits us to make matching contributions on behalf of all participants, up to a maximum of $6,000 per participant. For the years ended December 31, 2018, 2017, and 2016, we recognized $2.8 million, $1.6 million, and $1.1 million, respectively, of compensation expense in connection with our 401(k) retirement plan.

Change in Control Severance Plan

On December 6, 2006, our Board of Directors approved a Change of Control Severance Benefit Plan (CIC Plan). This CIC Plan has subsequently been amended a number of times by our Board of Directors with the most recent amendment occurring on April 5, 2011. The CIC Plan is designed to make certain benefits available to our eligible employees in the event of a change of control of Nektar and, following such change of control, an employee’s employment with us or a successor company is terminated in certain specified circumstances. We adopted the CIC Plan to support the continuity of the business in the context of a change of control transaction. The CIC Plan was not adopted in contemplation of any specific change of control transaction.

86

Under the CIC Plan, in the event of a change of control of Nektar and a subsequent termination of employment initiated by us or a successor company other than for Cause (as defined in the CIC Plan) or initiated by the employee for a Good Reason Resignation (as defined in the CIC Plan) in each case within twelve months following a change of control transaction, (i) the Chief Executive Officer would be entitled to receive cash severance pay equal to 24 months base salary plus annual target incentive pay, the extension of employee benefits over this severance period and the full acceleration of unvested outstanding equity awards, and (ii) our Senior Vice Presidents and Vice Presidents (including Principal Fellows) would each be entitled to receive cash severance pay equal to twelve months base salary plus annual target incentive pay, the extension of employee benefits over this severance period and the full acceleration of unvested outstanding equity awards. In the event of a change of control of Nektar and a subsequent termination of employment initiated by the Company or a successor company other than for Cause within twelve months following a change of control transaction, all other employees would each be entitled to receive cash severance pay equal to six months base salary plus a pro-rata portion of annual target incentive pay, the extension of employee benefits over this severance period and the full acceleration of each such employee's unvested outstanding equity awards. Under the CIC Plan, as amended, non-employee directors would also be entitled to full acceleration of vesting of all outstanding stock awards in the event of a change of control transaction.

Note 10 — License and Collaboration Agreements

We have entered into various collaboration agreements including license agreements and collaborative research, development and commercialization agreements with various pharmaceutical and biotechnology companies. Under these collaboration arrangements, we are entitled to receive license fees, upfront payments, milestone and other contingent payments, royalties, sales milestone payments, and payments for the manufacture and supply of our proprietary PEGylation materials and/or reimbursement for research and development activities. All of our collaboration agreements are generally cancelable by our partners without significant financial penalty. Our costs of performing these services are generally included in research and development expense, except that costs for product sales to our collaboration partners are included in cost of goods sold. We analyze our agreements to determine whether we should account for the agreements within the scope of ASC 808, Collaborative Arrangements, and, if so, we analyze whether we should account for any elements under the relevant revenue recognition guidance or whether we should record the reimbursements from our partner as contra research and development expense. As described in Note 1, on January 1, 2018, we adopted ASC 606, Revenue Recognition - Revenue from Contracts with Customers, which supersedes the guidance in ASC 605, Revenue Recognition. We recognized revenue under ASC 606 for the year ended December 31, 2018 and under ASC 605 for the years ended December 31, 2017 and 2016. In the year ended December 31, 2018, we recognized $95.3 million of revenue for performance obligations that we had satisfied in prior periods. This amount includes all of our royalty revenue, non-cash royalty revenue and the $10.0 million ADYNOVATE® sales milestone because these revenues substantially relate to the licenses that we had previously granted. This amount also includes the $10.0 million development milestone payment earned from Baxalta described below.

In accordance with our collaboration agreements, we recognized license, collaboration and other revenue as follows (in thousands):

		Year Ended December 31,		
Partner	Agreement	2018	2017	2016
Bristol-Myers Squibb	NKTR-214	$1,059,768	$—	—
Baxalta Incorporated / Takeda	Hemophilia, including ADYNOVATE® and ADYNOVI™	20,328	11,443	650
Eli Lilly and Company	NKTR-358	11,634	130,087	—
Amgen, Inc.	Neulasta®	5,000	5,000	5,000
Ophthotech Corporation(1)	Fovista®	—	19,123	1,408

Bayer Healthcare LLC[1]	BAY41-6551 (Amikacin Inhale)	—	17,931	1,429
AstraZeneca AB	MOVANTIK® and MOVENTIG®	—	4,600	33,000
Other		535	22,781	18,895
License, collaboration and other revenue		$1,097,265	$210,965	$60,382

(1) These collaboration agreements were completed as of December 31, 2017.

The following table presents the changes in our deferred revenue balance from our collaboration agreements during the year ended December 31, 2018 (in thousands):

	For the year ended December 31, 2018
Deferred revenue—December 31, 2017	$ 37,970
Transition adjustment related to adoption of ASC 606	(1,953)
Additions to deferred revenue	5,950
Recognition of previously unearned revenue	(17,331)
Deferred revenue—December 31, 2018	$ 24,636

Our balance of deferred revenue contains the transaction price from our collaboration agreements allocated to performance obligations which are partially unsatisfied. We expect to recognize approximately $13.9 million of our deferred revenue over the next twelve months and recognize approximately half of the remaining $10.7 million over the following twelve months.

As of December 31, 2018, our collaboration agreements with partners included potential future payments for development milestones totaling approximately $1.7 billion, including amounts from our agreements with BMS and Lilly described below. In addition, under our collaboration agreements we are entitled to receive other contingent payments, including contingent sales milestones and royalty payments, as described below.

Bristol-Myers Squibb (BMS): NKTR-214

On February 13, 2018, we entered into a Strategic Collaboration Agreement with BMS (BMS Collaboration Agreement) and Share Purchase Agreement, both of which became effective on April 3, 2018. Pursuant to these agreements, we and BMS will jointly develop NKTR-214, including, without limitation, in combination with BMS's Opdivo® (nivolumab) and Opdivo® plus Yervoy® (ipilimumab), and other compounds of BMS, us or any third party. The parties have agreed to jointly commercialize NKTR-214 on a worldwide basis. We retained the right to record all worldwide sales for NKTR-214. We will share global commercialization profits and losses with BMS for NKTR-214, with Nektar sharing 65% and BMS sharing 35% of the net profits and losses. The parties will share the internal and external development costs for NKTR-214 in combination regimens based on each party's relative ownership interest in the compounds included in the regimens. In accordance with the agreement, the parties will share development costs for NKTR-214 in combination with Opdivo®, 67.5% of costs to BMS and 32.5% to Nektar, and for NKTR-214 in a triplet combination with Opdivo® and Yervoy®, 78% of costs to BMS and 22% to Nektar. The parties will share costs for the production of NKTR-214, 35% of costs to BMS and 65% to Nektar.

The BMS Collaboration Agreement superseded and replaced the Clinical Trial Agreement we entered into with BMS in September 2016 to develop NKTR-214 in combination with Opdivo®. Under the Clinical Trial Agreement, we acted as the sponsor of each Combination Therapy Trial and BMS was responsible for 50% of all out-of-pocket costs reasonably incurred in connection with third party contract research organizations, laboratories, clinical sites and institutional review boards. We recorded cost reimbursement payments to us from BMS as a reduction to research and development expense. Each party was otherwise responsible for its own internal costs, including internal personnel costs, incurred in connection with each Combination Therapy Trial.

Upon the effective date in April 2018, BMS paid us a non-refundable upfront cash payment of $1.0 billion. We are eligible to receive additional cash payments up to a total of approximately $1.4 billion upon the achievement of certain development and regulatory milestones and up to a total of $350.0 million upon the achievement of certain sales milestones. In April 2018, BMS also purchased 8,284,600 shares of our common stock for total additional cash

consideration of $850.0 million.

We determined that the BMS Collaboration Agreement falls within the scope of ASC 808. As mentioned above, BMS shares certain percentages of development costs incurred by us and we share certain percentages of development costs incurred by BMS. We consider these activities to represent collaborative activities under ASC 808 and we recognize such cost sharing proportionately with the performance of the underlying services. We recognize BMS' reimbursement of our expenses as a reduction of research and development expense and our reimbursement of BMS' expenses as research and development expense. For the year ended December 31, 2018 and 2017, we recorded $62.5 million and $7.8 million, respectively, as a reduction of research and development expenses for BMS' share of our expenses, net of our share of BMS' expenses. As of December 31, 2018, we have recorded a receivable of $19.0 million from BMS in accounts receivable in our Consolidated Balance Sheet.

We analogized to ASC 606 for the accounting for our two performance obligations, consisting of the delivery of the licenses to develop and commercialize NKTR-214 and our participation on joint steering and other collaboration committees. We determined that our committee participation is not material.

We aggregated the total consideration of $1.85 billion received under the agreements and allocated it between the stock purchase and the revenue generating elements, because we and BMS negotiated the agreements together and the effective date of the BMS Collaboration Agreement was dependent upon the effective date of the Share Purchase Agreement. We recorded the estimated fair value of the shares of $790.2 million in stockholders' equity based on the closing date price of our common stock of $99.36 per share, adjusted for a discount for lack of marketability reflecting the unregistered nature of the shares. We allocated the remaining $1,059.8 million to the transaction price of the collaboration agreement. We consider the future potential development, regulatory and sales milestones of up to approximately $1.8 billion to be variable consideration. We excluded these milestones from the transaction price as of December 31, 2018 because we determined such payments to be fully constrained under ASC 606 as the achievement of such milestone payments are uncertain and highly susceptible to factors outside of our control. We will re-evaluate the transaction price at each reporting period and as uncertain events are resolved or other changes in circumstances occur.

Accordingly, we allocated the entire transaction price of $1,059.8 million to the granting of the licenses and therefore recognized $1,059.8 million for the year ended December 31, 2018 as license, collaboration and other revenue.

Baxalta Incorporated/Takeda: Hemophilia

We are a party to an exclusive research, development, license and manufacturing and supply agreement with Baxalta Incorporated (Baxalta), a subsidiary of Takeda Pharmaceutical Company Ltd. (Takeda), entered into in September 2005 to develop products designed to improve therapies for Hemophilia A patients using our PEGylation technology. Under the terms of the agreement, we are entitled to research and development funding for our active programs, which are now complete for Factor VIII, and are responsible for supplying Takeda with its requirements of our proprietary materials. Takeda is responsible for all clinical development, regulatory, and commercialization expenses. The agreement is terminable by the parties under customary conditions.

This Hemophilia A program includes ADYNOVATE®, which was approved by the Food and Drug Administration (FDA) in November 2015 for use in adults and adolescents, aged 12 years and older, who have Hemophilia A, and is now marketed in the U.S., the European Union, and many other countries. As a result of the marketing authorization in the EU in January 2018, we earned a $10.0 million development milestone, which was received in March 2018. In the three months ended December 31, 2018, we recognized an additional $10.0 million milestone for annual sales of ADYNOVATE®/ADYNOVI™ reaching a certain specified amount. We are entitled to an additional sales milestone upon achievement of an annual sales target and royalties based on annual worldwide net sales of products resulting from this agreement.

In October 2017, we entered into a right to sublicense agreement with Baxalta, under which we granted to Baxalta the right to grant a nonexclusive sublicense to certain patents that were previously exclusively licensed to Baxalta under our 2005 agreement. Under the right to sublicense agreement, Baxalta paid us $12.0 million in November 2017 and agreed to pay us single digit royalty payments based upon net sales of the products covered under the sublicense throughout the term of the agreement.

Under our adoption of ASC 606 as of January 1, 2018, we determined that our satisfied performance obligations consist of granting the license, granting the right to sublicense and performing research and development services. We determined that we have an unsatisfied performance obligation related to our ongoing supply of PEGylation materials at a price less than their standalone selling prices. We updated the arrangement transaction price for the $10.0 million EU approval milestone upon achievement in January 2018 since we had previously excluded it due to the significant uncertainty from regulatory approval. Based on the terms of this milestone, we allocated the entire milestone to the license grant and research and development services, and therefore recognized the entire $10.0 million in year ended December 31, 2018 as we had previously satisfied those performance obligations. As of December 31, 2018, we have accounts receivable of $15.4 million and deferred revenue of $0.8 million related to this agreement.

Eli Lilly and Company (Lilly): NKTR-358

Effective August 23, 2017, we entered into a worldwide license agreement with Eli Lilly and Company (Lilly) to co-develop NKTR-358, a novel immunological drug candidate that we invented. Under the terms of the agreement, we (i) received an initial payment of $150.0 million in September 2017 and are eligible for up to $250.0 million in additional development milestones, (ii) will co-develop NKTR-358 with Lilly with Nektar responsible for completing Phase 1 clinical development and certain drug product development and supply activities, (iii) will share with Lilly Phase 2 development costs with 75% of those costs borne by Lilly and 25% of the costs borne by Nektar, (iv) will have the option to contribute funding to Phase 3 development on an indication-by-indication basis ranging from zero to 25% of development costs, and (v) will have the opportunity to receive up to double-digit sales royalty rates that escalate based upon our Phase 3 development cost contribution and the level of annual global product sales. Lilly will be responsible for all costs of global commercialization, and we will have an option to co-promote in the U.S. under certain conditions. A portion of the development milestones may be reduced by 50% under certain conditions, related to the final formulation of the approved product and the timing of prior approval (if any) of competitive products with a similar mechanism of action, which could reduce these milestone payments by 75% if both conditions occur.

The agreement will continue until Lilly no longer has any royalty payment obligations to us or, if earlier, the termination of the agreement in accordance with its terms. The agreement may be terminated by Lilly for convenience, and may also be terminated under certain other circumstances, including material breach.

We identified our license grant to Lilly, our ongoing Phase 1 clinical development obligation, our drug product development obligation and our obligation to supply clinical trial materials as the significant performance obligations under the agreement and concluded that each of these deliverables represents a separate unit of accounting. The valuation of each performance obligation involves significant estimates and assumptions, including but not limited to, expected market opportunity and pricing, assumed royalty rates, clinical trial costs, timelines and likelihood of success; in each case these estimates and assumptions covering long time periods. We determined the selling price for the license based on a discounted cash flow analysis of projected revenues from NKTR-358 and development and commercial costs using a discount rate based on a market participant's weighted average cost of capital adjusted for forecasting risk. We determined the selling prices for Phase 1 clinical development, and drug product development deliverables based on the nature of the services to be performed and estimates of the associated efforts and third-party rates for similar services.

Although we are entitled to significant development milestones under this arrangement, we did not include any of such milestones in the transaction price due to the significant uncertainties involved with clinical development. We have therefore determined the transaction price to consist of the upfront payment of $150.0 million in September 2017. Based on our estimates of the standalone selling prices of the performance obligations, we allocated the $150.0 million upfront payment as $125.9 million to the license, $17.6 million to the Phase 1 clinical development and $6.5 million to the drug product development.

Under our adoption of ASC 606 as of January 1, 2018, we made no changes to our deferred revenue balance. We concluded that it was appropriate to have recognized the $125.9 million of revenue allocated to the license upon the effective date of the license agreement in August 2017, since we determined that the license was a right to use our intellectual property, for which, as of the effective date, we had provided all necessary information to Lilly to benefit from the license and the license term had begun. We recognize revenue for the Phase 1 clinical development and drug product development using an input method, using costs incurred, as this method depicts our progress towards providing Lilly with the results of clinical trials and drug production processes. As of December 31, 2018, we have deferred revenue of approximately $8.3 million related to this agreement, which we expect to recognize through December 2019, the estimated end of our performance obligations under this agreement.

Amgen, Inc.: Neulasta®

In October 2010, we amended and restated an existing supply and license agreement by entering into a supply, dedicated suite and manufacturing guarantee agreement (the amended and restated agreement) and a license agreement with Amgen Inc. and Amgen Manufacturing, Limited (together referred to as Amgen). Under the terms of the amended and restated 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 (the Manufacturing Suite) in our manufacturing facility in Huntsville, Alabama (the Facility). 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 amended and restated agreement, we received a $50.0 million payment in the fourth quarter of 2010 in return for our guaranteeing the supply of certain quantities of Polymer Materials to Amgen including without limitation the Additional Rights described below and manufacturing fees that are 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, significant additional payments become payable to us in return for our guaranteeing the supply of additional quantities of the Polymer Materials.

90

The term of the amended and restated agreement ends on October 29, 2020. In the event we become subject to a bankruptcy or insolvency proceeding, we cease to own or control the Facility, we fail to manufacture and supply or certain other events, 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 Facility to operate the Manufacturing Suite solely for the purpose of manufacturing the Polymer Materials. Amgen may terminate the amended and restated agreement for convenience or due to an uncured material default by us.

Under our adoption ASC 606 as of January 1, 2018, we determined that our obligation to manufacture and supply of our PEGylation materials and to maintain the dedicated manufacturing suite solely for the production of such materials for Amgen represented an obligation to stand ready to manufacture such materials. We concluded that we should recognize revenue based on the passage of time as this method depicts the satisfaction of Amgen's right to require production of PEGylation materials at any time. As of December 31, 2018, we have deferred revenue of approximately $9.2 million related to this agreement, which we expect to recognize through October 2020, the estimated end of our obligations under this agreement.

Ophthotech Corporation: Fovista®

On October 27, 2017, we terminated our license and supply agreement with Ophthotech Corporation (Ophthotech) dated September 2006, pursuant to which Ophthotech received a worldwide, exclusive license to certain of our proprietary PEGylation technology to develop, manufacture and sell Fovista®. Under the terms of our agreement, we were the exclusive supplier of all of Ophthotech's clinical and commercial requirements for our proprietary PEGylation reagent used in Fovista®. The termination of our agreement with Ophthotech followed Opthotech's previous announcements, in December 2016 and August 2017, that their three pivotal Phase 3 studies investigating the superiority of Fovista® therapy in combination with Lucentis® therapy compared to Lucentis® monotherapy and evaluating Fovista® in combination with Eylea® or Avastin® compared to Eylea® or Avastin® monotherapy for the treatment of wet age-related macular degeneration (AMD) did not achieve the pre-specified primary endpoints.

Under our agreement with Ophthotech, in June 2014, we received a $19.8 million payment from Ophthotech in connection with its licensing agreement with Novartis. In addition, in January 2017, we received a $12.7 million advance payment from Ophthotech, which included $10.4 million for reagent shipments recognized in the second quarter of 2017 as well as approximately $2.3 million for 2017 minimum purchase requirements. As a result of the termination of this agreement, we recognized the remaining $18.0 million of deferred revenue from this arrangement in the three months ended December 31, 2017.

Bayer Healthcare LLC: BAY41-6551 (Amikacin Inhale)

In December 2017, Bayer Healthcare LLC (Bayer) terminated our co-development, license and co-promotion agreement entered into in August 2007 to develop a specially-formulated inhaled Amikacin. Under this agreement, we were responsible for development, manufacturing and supply of our proprietary nebulizer device included in the Amikacin product. Bayer was responsible for most clinical development and commercialization activities and costs, all activities and costs to support worldwide regulatory filings, approvals and related activities, further development of Amikacin Inhale and final product packaging and distribution. The termination of this agreement followed Bayer's announcement in November 2017 that the Phase 3 Amikacin Inhale clinical program for the treatment of intubated and mechanically ventilated patients with Gram-negative pneumonia did not meet its primary endpoint or key secondary endpoints.

Under this collaboration, we received an upfront payment of $40.0 million (which was paid to us in 2007) and milestone payments totaling $30.0 million (the last of which was paid to us in 2013). As a result of the termination of the agreement, we recognized the remaining $16.8 million of deferred revenue related to this arrangement in the three months ended December 31, 2017.

AstraZeneca AB: MOVANTIK® (naloxegol oxalate), previously referred to as naloxegol and NKTR-118,

In September 2009, we entered into an agreement with AstraZeneca AB (AstraZeneca) under which we granted AstraZeneca a worldwide, exclusive license under our patents and other intellectual property to develop, market, and sell MOVANTIK®. AstraZeneca is responsible for all research, development and commercialization and is responsible for all drug development and commercialization decisions for MOVANTIK®. In September 2014 and December 2014, MOVANTIK® /MOVENTIG® was approved in the US and EU, respectively. As of December 31, 2018, we have received a total of $385.0 million of upfront and contingent milestone payments from this agreement, all of which was received in or before 2015. We are entitled to significant and escalating double-digit royalty payments and sales milestone payments based on annual worldwide net sales of MOVANTIK® / MOVENTIG ®.

In March 2016, AstraZeneca announced that it had entered into an agreement with ProStrakan Group plc, a subsidiary of Kyowa Hakko Kirin Co. Ltd. (Kirin), granting Kirin exclusive marketing rights to MOVENTIG® in the EU, Iceland, Liechtenstein, Norway and Switzerland. Under our license agreement with AstraZeneca, we and AstraZeneca will share the upfront payment, market access milestone payments, royalties and sales milestone payments made by Kirin to AstraZeneca with AstraZeneca receiving 60% and Nektar receiving 40%. In the years ended December 31, 2017 and 2016, we recognized a total of $4.6 million and $33.0 million,

respectively, related to our share of license-related payments made from Kirin to AstraZeneca. As of December 31, 2018, we do not have deferred revenue related to our agreement with AstraZeneca.

Other

In addition, as of December 31, 2018, we have a number of other collaboration agreements, including with our collaboration partners UCB and Halozyme Therapeutics, Inc., under which we are entitled to up to a total of $45.5 million of development milestones upon achievement of certain development objectives, as well as sales milestones upon achievement of annual sales targets and royalties based on net sales of commercialized products, if any. However, given the current phase of development of the potential products under these collaboration agreements, we cannot estimate the probability or timing of achieving these milestones. As of December 31, 2018, we have deferred revenue of approximately $6.4 million related to these other collaboration agreements.

Note 11 — Stock-Based Compensation

We issue stock-based awards from our equity incentive plans, which are more fully described in Note 9. Stock-based compensation expense was recognized as follows (in thousands):

	Year Ended December 31,		
	2018	2017	2016
Cost of goods sold	$4,629	$2,333	$1,620
Research and development	56,193	21,252	13,093
General and administrative	27,279	13,030	11,137
Total stock-based compensation	$88,101	$36,615	$25,850

As of December 31, 2018, total unrecognized compensation costs of $258.4 million related to unvested stock-based compensation arrangements are expected to be recognized as expense over a weighted-average period of 1.9 years.

Stock-based compensation expense resulting from our ESPP was not significant in the years ended December 31, 2018, 2017, and 2016.

Black-Scholes Assumptions

The following table lists the Black-Scholes option-pricing model assumptions used to calculate the fair value of employee and director stock options:

	Year Ended December 31,		
	2018	2017	2016
Average risk-free interest rate	2.8%	2.0%	1.4%
Dividend yield	0.0%	0.0%	0.0%
Average volatility factor	61.0%	54.2%	51.7%
Average weighted average expected life	5.1 years	5.3 years	5.3 years

The average risk-free interest rate is based on the U.S. treasury yield curve in effect at the time of grant for periods commensurate with the expected life of the stock-based award. We have never paid dividends, nor do we expect to

pay dividends in the foreseeable future; therefore, we used a dividend yield of zero. Our estimate of expected volatility is based on the daily historical trading data of our common stock at the time of grant over a historical period commensurate with the expected life of the stock-based award. We estimated the weighted-average expected life based on the contractual and vesting terms of the stock options, as well as historical cancellation and exercise data.

Summary of Stock Option Activity

The table below presents a summary of stock option activity under our equity incentive plans (in thousands, except for price per share and contractual life information):

	Number of Shares	Weighted-Average Exercise Price per Share	Weighted-Average Remaining Contractual Life (in Years)	Aggregate Intrinsic Value(1)
Outstanding at December 31, 2017	18,826	$ 20.35		
Options granted	1,846	55.35		
Options exercised	(4,374)	13.24		
Options forfeited & canceled	(368)	27.75		
Outstanding at December 31, 2018	15,930	$ 26.18	4.96	$214,525
Exercisable at December 31, 2018	9,393	16.16	3.69	$173,436

(1) Aggregate intrinsic value represents the difference between the exercise price of the option and the closing market price of our common stock on December 31, 2018.

The weighted-average grant-date fair value per share of options granted during the years ended December 31, 2018, 2017, and 2016 was $29.86, $20.08, and $6.54, respectively. The total intrinsic value of options exercised during the years ended December 31, 2018, 2017, and 2016 was $303.4 million, $84.0 million, and $17.9 million, respectively. The estimated fair value of options vested during the years ended December 31, 2018, 2017, and 2016 was $39.0 million, $19.3 million, and $16.7 million, respectively.

Summary of RSU Activity

A summary of RSU award activity is as follows (in thousands except for per share amounts):

	Units Issued	Weighted-Average Grant Date Fair Value	Aggregate Intrinsic Value(1)
Balance at December 31, 2017	2,578	$ 35.52	

Granted	2,125	41.67	
Vested and released	(1,255)	29.44	
Forfeited and canceled	(128)	40.39	
Balance at December 31, 2018	3,320	$ 41.57	$ 109,125

(1) Aggregate intrinsic value represents the difference between the grant price of the award, which is zero, and the closing market price of our common stock on December 31, 2018.

The fair value of restricted stock that vested in the years ended December 31, 2018, 2017 and 2016 totaled $80.4 million, $22.3 million and $7.7 million, respectively.

Note 12 — Income Taxes

Income (loss) before provision for income taxes includes the following components (in thousands):

	Year Ended December 31,		
	2018	2017	2016
Domestic	$680,423	$(97,938)	$(155,375)
Foreign	2,302	1,862	2,727
Income (loss) before provision for income taxes	$682,725	$(96,076)	$(152,648)

Provision for Income Taxes

The provision for income taxes consists of the following (in thousands):

	Year Ended December 31,		
	2018	2017	2016
Current:			
Federal	$—	$—	$—
State	699	1	(1)
Foreign	620	580	992
Total Current	1,319	581	991
Deferred:			
Federal	—	—	—
State	—	—	—
Foreign	93	35	(115)
Total Deferred	93	35	(115)
Provision for income taxes	$1,412	$616	$876

Income tax provision related to continuing operations differs from the amount computed by applying the statutory income tax rate of 21% for 2018 and 35% for 2017 and 2016 to pretax income (loss) as follows (in thousands):

	Year Ended December 31,		
	2018	2017	2016
Income tax expense (benefit) at federal statutory rate	$143,372	$(33,627)	$(53,427)
Non-cash interest expense on liability related to sale of future royalties	4,451	6,604	6,899
Non-deductible officers' compensation	3,182	2,547	220
Tax law changes	45	248,155	—
Stock-based compensation	(66,716)	(20,665)	528
Change in valuation allowance	(46,885)	(186,124)	51,981
Research credits	(17,295)	(8,038)	(4,543)
Premium on equity issuance	(12,551)	—	—
Sale of future royalties	(6,995)	(8,236)	—
Other	804	—	(782)
Provision for income taxes	$1,412	$616	$876

Tax Law Changes

The U.S. Tax Cuts and Jobs Act (the Tax Act) was enacted on December 22, 2017. The Tax Act reduces the U.S. federal corporate tax rate from 35% in 2017 to 21% in 2018, requires companies to pay a one-time transition tax on earnings of certain foreign subsidiaries that were previously tax deferred and creates new taxes on certain foreign sourced earnings. At December 31, 2018, we have completed our accounting for the tax effects of enactment of the Tax Act, which, other than the $248.2 million decrease in the valuation of our federal deferred tax assets shown above, did not have a material effect on our Consolidated Financial Statements.

Deferred Tax Assets and Liabilities

Deferred income taxes reflect the net tax effects of loss and credit carryforwards and temporary differences between the carrying amount of assets and liabilities for financial reporting purposes and the amounts used for income tax purposes. We remeasured certain deferred tax assets and liabilities based on the rates at which they are expected to reverse in the future, which includes the change in the federal rate to 21% as of December 31, 2017. Significant components of our deferred tax assets for federal and state income taxes are as follows (in thousands):

	December 31,	
	2018	2017
Deferred tax assets:		
Net operating loss carryforwards	$300,693	$364,864
Research and other credits	116,955	94,103
Stock-based compensation	21,518	14,552
Capitalized research expenses	8,072	5,497
Reserves and accruals	8,066	5,659
Deferred revenue	4,467	3,796
Property, plant and equipment	2,124	6,848
Other	(1,270)	1,156
Deferred tax assets before valuation allowance	460,625	496,475
Valuation allowance for deferred tax assets	(460,455)	(496,191)
Total deferred tax assets	170	284
Total deferred tax liabilities	—	—
Net deferred tax assets	$170	$284

Realization of our deferred tax assets is dependent upon future earnings, if any, the timing and amount of which are uncertain. Because of our lack of U.S. earnings history, other than income resulting from revenue recognized from the BMS collaboration agreement, and projected future losses, the net U.S. deferred tax assets have been fully offset by a valuation allowance. The valuation allowance decreased by $35.7 million and $169.3 million during the years ended December 31, 2018 and 2017, respectively, and increased by $52.5 million during the year ended December 31, 2016. The decrease in the valuation allowance for the year ended December 31, 2018 reflects the utilization of net operating loss carryforwards to offset federal and state taxable income, and the decrease in the valuation allowance for the year ended December 31, 2017 is primarily due to the change in the federal rate. The valuation allowance includes approximately $35.6 million of income tax benefit at both December 31, 2018 and December 31, 2017 related to stock-based compensation that will be included in income tax expense in our Consolidated Statement of Operations when realized.

For 2017, the one-time transition tax under the Tax Act was based on our total post-1986 earnings and profits (E&P) that we previously deferred from U.S. income taxes. We concluded that there was negative E&P on an aggregate basis and we have not recorded any amount for any one-time transition tax triggered by the Tax Act. No additional income taxes have been provided for any remaining undistributed foreign earnings not subject to the transition tax, or any

additional outside basis difference inherent in these entities, as these amounts continue to be indefinitely reinvested in foreign operations.

Net Operating Loss and Tax Credit Carryforwards

As of December 31, 2018, we had a net operating loss carryforward for federal income tax purposes of approximately $1,304.1 million, portions of which will begin to expire in 2022. As of December 31, 2018, we had a total state net operating loss carryforward of approximately $471.1 million, portions of which will begin to expire in 2024. Utilization of some of the federal and state net operating loss and credit carryforwards are subject to annual limitations due to the “change in ownership” provisions of the Internal Revenue Code of 1986 and similar state provisions.

We have federal research credits of approximately $101.0 million, which will begin to expire in 2020 and state research credits of approximately $40.0 million which have no expiration date. We have federal orphan drug credits of $17.7 million which will begin to expire in 2026. These tax credits are subject to the same limitations discussed above.

Unrecognized tax benefits

With the exception of net income recognized in 2018, we have incurred net operating losses since inception. Our policy is to include interest and penalties related to unrecognized tax benefits, if any, within the provision for income taxes in the consolidated statements of operations. If we are eventually able to recognize our uncertain positions, our effective tax rate may be reduced. We currently have a full valuation allowance against our U.S. net deferred tax asset which would impact the timing of the effective tax rate benefit should any of these uncertain tax positions be favorably settled in the future. Adjustments to the substantial majority of our uncertain tax positions would result in an adjustment of our net operating loss or tax credit carry forwards rather than resulting in a cash outlay.

We file income tax returns in the U.S., California, Alabama, certain other states and India. Because of net operating losses and research credit carryovers, substantially all of our domestic tax years remain open and subject to examination. We are currently under examination in India for the fiscal years ending 2009, 2016 and 2017.

We have the following activity relating to unrecognized tax benefits (in thousands):

	December 31,		
	2018	2017	2016
Beginning balance	$20,483	$18,413	$17,384
Tax positions related to current year			
Additions:			
Federal	2,019	1,206	530
State	3,645	1,666	499
Reductions	—	—	—
Tax positions related to prior year			
Additions:			
Federal	669	—	—
State	603	—	—
Foreign	—	—	—
Reductions		(802)	—
Settlements	—	—	—
Lapses in statute of limitations	—	—	—
Ending balance	$27,419	$20,483	$18,413

Although it is reasonably possible that certain unrecognized tax benefits may increase or decrease within the next twelve months, we do not anticipate any significant changes to unrecognized tax benefits over the next twelve months. During the years ended December 31, 2018, 2017 and 2016, no significant interest or penalties were recognized relating to unrecognized tax benefits.

Note 13 — Segment Reporting

We operate in one business segment which focuses on applying our technology platforms to develop novel drug candidates. Our business offerings have similar economics and other characteristics, including the nature of products and manufacturing processes, types of customers, distribution methods and regulatory environment. We are comprehensively managed as one business segment by our Chief Executive Officer.

Our revenue is derived primarily from customers in the pharmaceutical and biotechnology industries. Revenue from BMS represented 89% of our revenue for the year ended December 31, 2018. Revenue from Lilly and UCB represented 42% and 12% of our revenue, respectively, for the year ended December 31, 2017. Revenue from AstraZeneca, UCB, Ophthotech and Roche represented 29%, 21%, 19% and 11% of our revenue, respectively, for the year ended December 31, 2016.

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

	Year Ended December 31,		
	2018	2017	2016
United States	$1,090,794	$190,810	$39,147
Europe	102,529	116,901	126,289
Total revenue	$1,193,323	$307,711	$165,436

At December 31, 2018, $42.9 million, or approximately 88%, of the net book value of our property, plant and equipment was located in the United States and $5.9 million, or approximately 12%, was located in India. At December 31, 2017, $41.7 million, or approximately 88%, of the net book value of our property, plant and equipment was located in the United States and $5.8 million, or approximately 12%, was located in India.

Note 14 — Selected Quarterly Financial Data (Unaudited)

The following table sets forth certain unaudited quarterly financial data. In our opinion, the unaudited information set forth below has been prepared on the same basis as our audited information and includes all adjustments necessary to present fairly the information set forth herein. We have experienced fluctuations in our quarterly results and expect these fluctuations to continue in the future. Due to these and other factors, we believe that quarter-to-quarter comparisons of our operating results will not be meaningful, and the results for any one quarter may not be indicative of our future performance. We have reclassified certain items previously reported in specific financial statement captions to conform to the current period presentation. Such reclassifications have not materially impacted previously reported total revenues, operating income (loss) or net income (loss). All data is in thousands except per share information.

	Year Ended December 31, 2018				Year Ended December 31, 2017			
	Q1	Q2	Q3	Q4	Q1	Q2	Q3	Q4
Product sales	$6,295	$5,863	$4,256	$4,360	$4,756	$15,693	$4,448	$7,791
Total revenue	$38,018	$1,087,717	$27,762	$39,826	$24,728	$34,589	$152,928	$95,466
Cost of goods sold	$6,646	$5,522	$4,783	$7,461	$6,131	$8,989	$5,674	$9,753
Research and development expenses	$99,424	$88,334	$102,895	$108,883	$61,058	$60,260	$65,714	$81,429
Operating income (loss)	$(86,739)	$973,600	$(98,634)	$(100,295)	$(54,437)	$(50,656)	$69,485	$(24,034)
Net income (loss)	$(95,792)	$971,460	$(96,143)	$(98,212)	$(63,866)	$(59,871)	$60,871	$(33,826)
Net income (loss) per share(1)								
Basic	$(0.60)	$5.67	$(0.56)	$(0.57)	$(0.42)	$(0.39)	$0.39	$(0.21)
Diluted	$(0.60)	$5.33	$(0.56)	$(0.57)	$(0.42)	$(0.39)	$0.37	$(0.21)

(1) Quarterly income (loss) per share amounts may not total to the year-to-date income (loss) per share due to rounding.

Item 9. Changes in and Disagreements with Accountants on Accounting and Financial Disclosure

None.

Item 9A. Controls and Procedures

Disclosure Controls and Procedures

We maintain disclosure controls and procedures that are designed to ensure that information required to be disclosed in our Securities Exchange Act of 1934 (Exchange Act) reports is recorded, processed, summarized and reported within the time periods specified in the SEC's rules and forms, and that such information is accumulated and communicated to management, including our Chief Executive Officer and Chief Financial Officer, as appropriate, to allow timely decisions regarding required financial disclosure.

As of the end of the period covered by this report, we carried out an evaluation, under the supervision and with the participation of our management, including the Chief Executive Officer and the Chief Financial Officer, of the effectiveness of the design and operation of our disclosure controls and procedures pursuant to Exchange Act Rule 13a-15. Based upon, and as of the date of, this evaluation, the Chief Executive Officer and the Chief Financial Officer concluded that our disclosure controls and procedures were effective. Accordingly, management believes that the financial statements included in this report fairly present in all material respects our financial condition, results of operations and cash flows for the periods presented.

Management's Annual Report on Internal Control over Financial Reporting

Our management is responsible for establishing and maintaining adequate internal control over financial reporting, as such term is defined in Exchange Act Rule 13a-15(f). Our internal control over financial reporting is a process designed to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with GAAP.

Our management has assessed the effectiveness of our internal control over financial reporting as of December 31, 2018. In making its assessment of internal control over financial reporting, management used the criteria described in Internal Control — Integrated Framework issued by the Committee of Sponsoring Organizations of the Treadway Commission (2013 Framework).

Based on our evaluation under the framework described in Internal Control — Integrated Framework, our management concluded that our internal control over financial reporting was effective as of December 31, 2018.

The effectiveness of our internal control over financial reporting as of December 31, 2018 has been audited by Ernst & Young LLP, an independent registered public accounting firm, as stated in their report, which is included herein.

Changes in Internal Control Over Financial Reporting

We continuously seek to improve the efficiency and effectiveness of our internal controls. This results in refinements to processes throughout the Company. There was no change in our internal control over financial reporting during the quarter ended December 31, 2018, which was identified in connection with our management's evaluation required by Exchange Act Rules 13a-15(f) and 15d-15(f) that has materially affected, or is reasonably likely to materially affect, our internal control over financial reporting.

Inherent Limitations on the Effectiveness of Controls

Our management, including the Chief Executive Officer and Chief Financial Officer, does not expect that our disclosure controls and procedures or our internal control over financial reporting will prevent all error and all fraud. A control system, no matter how well conceived and operated, can provide only reasonable, not absolute, assurance that the objectives of the control system are met. Because of the inherent limitations in all control systems, no evaluation of controls can provide absolute assurance that all control issues and instances of fraud, if any, within the company have been detected. These inherent limitations include the realities that judgments in decision making can be faulty and that breakdowns can occur because of simple error or mistake. Additionally, controls can be circumvented by the individual acts of some persons, by collusion of two or more people or by management override of the control. The design of any system of controls also is based in part upon certain assumptions about the likelihood of future events, and there can be no assurance that any design will succeed in achieving its stated goals under all potential future conditions. Over time, controls may become inadequate because of changes in conditions, or the degree of compliance with the policies or procedures may deteriorate. Because of the inherent limitations in a cost-effective control system, misstatements due to error or fraud may occur and not be detected.

Item 9B. Other Information

None.

PART III

Item 10. Directors, Executive Officers and Corporate Governance

Information relating to our executive officers required by this item is set forth in Part I — Item 1 of this report under the caption “Executive Officers of the Registrant” and is incorporated herein by reference. The other information required by this Item is incorporated by reference from the definitive proxy statement for our 2019 Annual Meeting of Stockholders to be filed with the SEC pursuant to Regulation 14A (Proxy Statement) not later than 120 days after the end of the fiscal year covered by this Form 10-K under the captions “Corporate Governance and Board of Directors,” “Proposal 1 — Election of Directors” and “Section 16(a) Beneficial Ownership Reporting Compliance.”

Information regarding our audit committee financial expert will be set forth in the Proxy Statement under the caption “Audit Committee,” which information is incorporated herein by reference.

We have a Code of Business Conduct and Ethics applicable to all employees, including the principal executive officer, principal financial officer and principal accounting officer or controller, or persons performing similar functions. The Code of Business Conduct and Ethics is posted on our website at www.nektar.com. Amendments to, and waivers from, the Code of Business Conduct and Ethics that apply to any of these officers, or persons performing similar functions, and that relate to any element of the code of ethics definition enumerated in Item 406(b) of Regulation S-K will be disclosed at the website address provided above and, to the extent required by applicable regulations, on a current report on Form 8-K.

As permitted by SEC Rule 10b5-1, certain of our executive officers, directors and other employees have or may set up a predefined, structured stock trading program with their broker to sell our stock. The stock trading program allows a broker acting on behalf of the executive officer, director or other employee to trade our stock during blackout periods or while such executive officer, director or other employee may be aware of material, nonpublic information, if the trade is performed according to a pre-existing contract, instruction or plan that was established with the broker when such executive officer, director or employee was not aware of any material, nonpublic information. Our executive officers, directors and other employees may also trade our stock outside of the stock trading programs set up under Rule 10b5-1 subject to our securities trading policy.

Item 11. Executive Compensation

The information required by this Item is included in the Proxy Statement and incorporated herein by reference.

Item 12. Security Ownership of Certain Beneficial Owners and Management and Related Stockholder Matters

The information required by this Item is included in the Proxy Statement and incorporated herein by reference.

Item 13. Certain Relationships and Related Transactions and Director Independence

The information required by this Item is included in the Proxy Statement and incorporated herein by reference.

Item 14. Principal Accountant Fees and Services

The information required by this Item is included in the Proxy Statement and incorporated herein by reference.

PART IV

Item 15. Exhibits and Financial Statement Schedules

(a) The following documents are filed as part of this report:

(1) Consolidated Financial Statements:

The following financial statements are filed as part of this Annual Report on Form 10-K under Item 8 “Financial Statements and Supplementary Data.”

	Page
Reports of Independent Registered Public Accounting Firm	66
Consolidated Balance Sheets at December 31, 2018 and 2017	68
Consolidated Statements of Operations for each of the three years in the period ended December 31, 2018	69
Consolidated Statements of Comprehensive Income (Loss) for each of the three years in the period ended December 31, 2018	70
Consolidated Statements of Stockholders’ Equity for each of the three years in the period ended December 31, 2018	71
Consolidated Statements of Cash Flows for each of the three years in the period ended December 31, 2018	72
Notes to Consolidated Financial Statements	73

(2) Financial Statement Schedules:

All financial statement schedules have been omitted because they are not applicable, or the information required is presented in our consolidated financial statements and notes thereto under Item 8 of this Annual Report on Form 10-K.

(3) Exhibits.

Except as so indicated in Exhibit 32.1, the following exhibits are filed as part of, or incorporated by reference into, this Annual Report on Form 10-K.

Exhibit Number	Description of Documents
2.1(1)	Asset Purchase Agreement, dated October 20, 2008, by and between Nektar Therapeutics, a Delaware corporation, AeroGen, Inc., a Delaware corporation and wholly-owned subsidiary of Nektar Therapeutics,

	Novartis Pharmaceuticals Corporation, a Delaware corporation, and Novartis Pharma AG, a Swiss corporation.+
3.1(2)	Certificate of Incorporation of Inhale Therapeutic Systems (Delaware), Inc.
3.2(3)	Certificate of Amendment of the Amended Certificate of Incorporation of Inhale Therapeutic Systems, Inc.
3.3(4)	Certificate of Ownership and Merger of Nektar Therapeutics.
3.4(5)	Certificate of Ownership and Merger of Nektar Therapeutics AL, Corporation with and into Nektar Therapeutics.
3.5(6)	Amended and Restated Bylaws of Nektar Therapeutics.
4.1	Reference is made to Exhibits 3.1, 3.2, 3.3, 3.4, and 3.5.
4.2(4)	Specimen Common Stock certificate.
4.3(7)	Indenture dated October 5, 2015 by and between Nektar Therapeutics and Wilmington Trust, National Association, and TC Lending, LLC including the form of 7.75% Senior Secured Note due 2020.
10.1(8)	2000 Equity Incentive Plan, as amended and restated.++
10.2(8)	2000 Non-Officer Equity Incentive Plan, as amended and restated.++
10.3(8)	2008 Equity Incentive Plan, as amended and restated.++
10.4(8)	Discretionary Incentive Compensation Policy++
101	

Exhibit Number	Description of Documents
10.5(8)	Amended and Restated Change of Control Severance Benefit Plan.++
10.6(9)	2012 Performance Incentive Plan.++
10.7(10)	Forms of Stock Option Agreement, Performance Stock Option Agreement, Restricted Stock Unit Agreement and Performance Restricted Stock Unit Agreement under the 2012 Performance Incentive Plan.++
10.8(11)	Nektar Therapeutics Amended and Restated 2017 Performance Incentive Plan.++
10.9(28)	Forms of Stock Option Agreement, Performance Stock Option Agreement, Non-Employee Director Stock Option Agreement, Restricted Stock Unit Agreement, Performance Restricted Stock Unit Agreement, and Non-Employee Director Restricted Stock Unit Agreement under the Amended and Restated 2017 Performance Incentive Plan.++
10.10(12)	Employee Stock Purchase Plan, as amended and restated.++
10.11(13)	Amended and Restated Compensation Plan for Non-Employee Directors.++
10.12(14)	401(k) Retirement Plan.++
10.13(15)	Form of Severance Letter for executive officers of the company.++
10.14(1)	Amended and Restated Letter Agreement, executed effective on December 1, 2008, with Howard W. Robin.++
10.15(1)	Amended and Restated Letter Agreement, executed effective on December 1, 2008, with John Nicholson.++
10.16(16)	Letter Agreement, executed effective on December 10, 2009, with Stephen K. Doberstein, Ph.D.++
10.17(17)	Letter Agreement dated as of May 14, 2014, by and between Nektar Therapeutics and Ivan Gergel, M.D.++
10.18(18)	Separation and General Release Agreement dated as of December 20, 2017, by and between Nektar Therapeutics and Ivan Gergel, M.D.++
10.19(15)	Amended and Restated Built-to-Suit Lease between Nektar Therapeutics and BMR-201 Industrial Road LLC, dated August 17, 2004, as amended on January 11, 2005 and July 19, 2007.
10.20(19)	Lease Agreement dated August 4, 2017, as amended by the First Amendment to Lease dated as of August 29, 2017, by and between ARE-San Francisco No. 19, LLC and Nektar Therapeutics.
10.21(20)	Settlement Agreement and General Release, dated June 30, 2006, by and between The Board of Trustees of the University of Alabama, The University of Alabama in Huntsville, Nektar Therapeutics AL, Corporation (a wholly-owned subsidiary of Nektar Therapeutics), Nektar Therapeutics and J. Milton Harris.
10.22(1)	Exclusive Research, Development, License and Manufacturing and Supply Agreement, by and among Nektar AL Corporation, Baxter Healthcare SA, and Baxter Healthcare Corporation, dated September 26,

2005, as amended.+

10.23(1) Exclusive License Agreement, dated December 31, 2008, between Nektar Therapeutics, a Delaware corporation, and Novartis Pharma AG, a Swiss corporation.+

10.24(16) Supply, Dedicated Suite and Manufacturing Guarantee Agreement, dated October 29, 2010, by and among Nektar Therapeutics, Amgen Inc. and Amgen Manufacturing, Limited.+

10.25(21) License Agreement by and between AstraZeneca AB and Nektar Therapeutics, dated September 20, 2009.+

10.26(22) Collaboration and License Agreement dated as of May 30, 2016, by and between Daiichi Sankyo Europe GmbH and Nektar Therapeutics.

10.27(19) License Agreement effective as of August 23, 2017, by and between Eli Lilly and Company and Nektar Therapeutics.

10.28(7) Purchase Agreement dated September 30, 2015 by and among Nektar Therapeutics and TC Lending, LLC and TAO Fund, LLC.

10.29(7) Pledge and Security Agreement dated October 5, 2015 by and among Nektar Therapeutics and TC Lending, LLC.

10.30(23) Purchase and Sale Agreement, dated as of February 24, 2012, between Nektar Therapeutics and RPI Finance Trust.+

10.31(24) Amendment No. 1 to License Agreement dated effective as of August 8, 2013, by and between Nektar Therapeutics and AstraZeneca AB.+

Exhibit Number	Description of Documents
10.32(25)	Investor Agreement, dated as of February 13, 2018, by and between Bristol-Myers Squibb and Company and Nektar Therapeutics.+
10.33(25)	Strategic Collaboration Agreement, dated as of February 13, 2018, by and between Bristol-Myers Squibb and Company and Nektar Therapeutics.+
10.34(26)	Share Purchase Agreement, dated as of February 13, 2018, by and between Bristol-Myers Squibb and Company and Nektar Therapeutics.
10.35(27)	Office Lease, effective as of May 31, 2018, by and between Kilroy Realty Finance Partnership, L.P., and Nektar Therapeutics.
21.1(28)	Subsidiaries of Nektar Therapeutics.
23.1(28)	Consent of Independent Registered Public Accounting Firm.
24	Power of Attorney (reference is made to the signature page).
31.1(28)	Certification of Nektar Therapeutics' principal executive officer required by Rule 13a-14(a) or Rule 15d-14(a).
31.2(28)	Certification of Nektar Therapeutics' principal financial officer required by Rule 13a-14(a) or Rule 15d-14(a).
32.1*	Section 1350 Certifications.
101**	The following materials from Nektar Therapeutics' Annual Report on Form 10-K for the year ended December 31, 2018, formatted in XBRL (Extensible Business Reporting Language): (i) Consolidated Balance Sheets, (ii) Consolidated Statements of Operations, (iii) Consolidated Statements of Comprehensive Income (Loss), (iv) Consolidated Statements of Stockholders' Equity, (v) Consolidated Statements of Cash Flows, and (vi) Notes to Consolidated Financial Statements.

+ Confidential treatment with respect to specific portions of this Exhibit has been requested, and such portions are omitted and have been filed separately with the SEC.

++ Management contract or compensatory plan or arrangement.

* Exhibit 32.1 is being furnished and shall not be deemed to be "filed" for purposes of Section 18 of the Securities Exchange Act of 1934, as amended, or otherwise subject to the liability of that section, nor shall such exhibit be deemed to be incorporated by reference in any registration statement or other document filed under the Securities Act of 1933, as amended, or the Securities Exchange Act, except as otherwise stated in such filing.

** XBRL information is filed herewith.

(1) Incorporated by reference to the indicated exhibit in Nektar Therapeutics' Annual Report on Form 10-K for the year ended December 31, 2008.

(2) Incorporated by reference to the indicated exhibit in Nektar Therapeutics' Quarterly Report on Form 10-Q for the quarter ended June 30, 1998.

(3) Incorporated by reference to the indicated exhibit in Nektar Therapeutics' Quarterly Report on Form 10-Q for the quarter ended June 30, 2000.

(4) Incorporated by reference to the indicated exhibit in Nektar Therapeutics' Current Report on Form 8-K, filed on January 23, 2003.

(5) Incorporated by reference to the indicated exhibit in Nektar Therapeutics' Annual Report on Form 10-K for the year ended December 31, 2009.

(6) Incorporated by reference to the indicated exhibit in Nektar Therapeutics' Current Report on Form 8-K, filed on February 4, 2019.

(7) Incorporated by reference to the indicated exhibit in Nektar Therapeutics' Current Report on Form 8-K, filed on October 6, 2015.

(8) Incorporated by reference to the indicated exhibit in Nektar Therapeutics' Annual Report on Form 10-K for the year ended December 31, 2011.

(9) Incorporated by reference to the indicated exhibit in Nektar Therapeutics' Current Report on Form 8-K, filed on June 17, 2015.

(10) Incorporated by reference to the indicated exhibit in Nektar Therapeutics' Current Report on Form 8-K filed on December 17, 2015.

(11) Incorporated by reference to the indicated exhibit in Nektar Therapeutics' Current Report on Form 8-K, filed on June 27, 2018.

(12) Incorporated by reference to the indicated exhibit in Nektar Therapeutics' Current Report on Form 8-K, filed on June 27, 2014.

(13) Incorporated by reference to the indicated exhibit in Nektar Therapeutics' Annual Report on Form 10-K for the year ended December 31, 2012.

(14) Incorporated by reference to the indicated exhibit in Nektar Therapeutics Quarterly Report on Form 10-Q for the quarter ended June 30, 2004.

(15) Incorporated by reference to the indicated exhibit in Nektar Therapeutics' Quarterly Report on Form 10-Q for the quarter ended September 30, 2007.
(16) Incorporated by reference to the indicated exhibit in Nektar Therapeutics' Annual Report on Form 10-K for the year ended December 31, 2010.
(17) Incorporated by reference to the indicated exhibit in Nektar Therapeutics' Annual Report on Form 10-K for the year ended December 31, 2014.
(18) Incorporated by reference to the indicated exhibit in Nektar Therapeutics' Annual Report on Form 10-K for the year ended December 31, 2017.
(19) Incorporated by reference to the indicated exhibit in Nektar Therapeutics' Quarterly Report on Form 10-Q for the quarter ended September 30, 2017.
(20) Incorporated by reference to the indicated exhibit in Nektar Therapeutics' Quarterly Report on Form 10-Q for the quarter ended June 30, 2006.
(21) Incorporated by reference to the indicated exhibit in Nektar Therapeutics' Quarterly Report on Form 10-Q for the quarter ended September 30, 2009.
(22) Incorporated by reference to the indicated exhibit in Nektar Therapeutics' Quarterly Report on Form 10-Q for the quarter ended June 30, 2016.
(23) Incorporated by reference to the indicated exhibit in Nektar Therapeutics' Quarterly Report on Form 10-Q for the quarter ended March 31, 2012.
(24) Incorporated by reference to the indicated exhibit in Nektar Therapeutics' Quarterly Report on Form 10-Q for the quarter ended September 30, 2013.
(25) Incorporated by reference to the indicated exhibit in Nektar Therapeutics' Quarterly Report on Form 10-Q for the quarter ended March 31, 2018.
(26) Incorporated by reference to the indicated exhibit in Nektar Therapeutics' Current Report on Form 8-K filed on February 14, 2018.
(27) Incorporated by reference to the indicated exhibit in Nektar Therapeutics' Quarterly Report on Form 10-Q for the quarter ended June 30, 2018.
(28) Filed herewith.

Item 16. Form 10-K Summary

None.

SIGNATURES

Pursuant to the Securities Exchange Act of 1934, the Registrant has duly caused this report to be signed on its behalf by the undersigned, thereunto duly authorized, in the City and County of San Francisco, State of California on February 28, 2019.

By: /s/ Gil M. Labrucherie
Gil M. Labrucherie
Senior Vice President and Chief Financial Officer

By: /s/ JILLIAN B. THOMSEN
Jillian B. Thomsen
Senior Vice President, Finance and Chief Accounting Officer

POWER OF ATTORNEY

KNOW ALL PERSON BY THESE PRESENTS, that each person whose signature appears below constitutes and appoints Gil M. Labrucherie and Jillian B. Thomsen and each of them, as his or her true and lawful attorneys-in-fact and agents, with full power of substitution and resubstitution, for him or her and in his or her name, place and stead, in any and all capacities, to sign any and all amendments to this Annual Report on Form 10-K and to file the same, with all exhibits thereto and other documents in connection therewith, with the Securities and Exchange Commission, granting unto said attorneys-in-fact and agents and each of them, full power and authority to do and perform each and every act and thing requisite and necessary to be done in connection therewith, as fully to all intents and purposes as he or she might or could do in person, hereby ratify and confirming all that said attorneys-in-fact and agents, or any of them, or their or his or her substitute or substitutes, may lawfully do or cause to be done by virtue hereof.

Pursuant to the requirements of the Securities Exchange Act of 1934, as amended, this report has been signed by the following persons in the capacities and on the dates indicated:

Signature	Title	Date
/s/ Howard W. Robin Howard W. Robin	Chief Executive Officer, President and Director (Principal Executive Officer)	February 28, 2019
/s/ Gil M. Labrucherie Gil M. Labrucherie	Senior Vice President and Chief Financial Officer (Principal Financial Officer)	February 28, 2019
/s/ Jillian B. Thomsen Jillian B. Thomsen	Senior Vice President, Finance and Chief Accounting Officer (Principal Accounting Officer)	February 28, 2019
/s/ Robert B. Chess Robert B. Chess	Director, Chairman of the Board of Directors	February 28, 2019
/s/ Jeffrey R. Ajer Jeffrey R. Ajer	Director	February 28, 2019
/s/ Karin Eastham Karin Eastham	Director	February 28, 2019
/s/ R. Scott Greer R. Scott Greer	Director	February 28, 2019
/s/ Lutz Lingnau Lutz Lingnau	Director	February 28, 2019
/s/ Roy A. Whitfield Roy A. Whitfield	Director	February 28, 2019

106