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, 2021

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	**Trading Symbol**	**Name of Each Exchange on Which Registered**
Common Stock, $0.0001 par value	NKTR	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 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 has filed a report on and attestation to its management's assessment of the effectiveness of its internal control over financial reporting under Section 404(b) of the Sarbanes-Oxley Act (15 U.S.C. 7262(b)) by the registered public accounting firm that prepared or issued its audit report. ☒

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 30, 2021, as reported on The NASDAQ Global Select Market, was approximately $3.1 billion.

As of February 23, 2022, the number of outstanding shares of the registrant's common stock was 186,274,156.

DOCUMENTS INCORPORATED BY REFERENCE

Portions of registrant's definitive Proxy Statement to be filed for its 2022 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

2021 ANNUAL REPORT ON FORM 10-K

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Forward-Looking Statements

This report includes “forward-looking statements” within the meaning of Section 27A of the Securities Act of 1933, as amended, and Section 21E of the Securities Exchange Act of 1934, as amended. All statements other than statements of historical fact are “forward-looking statements” for purposes of this annual report on Form 10-K, including any projections of 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 “believe,” “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.

Summary of Risks

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. Investors in Nektar Therapeutics should carefully consider the risks described below before making an investment decision. 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 to our business are more fully described below in Item IA in this Form 10-K, which risks include, among others:

- **Risks Related to our Research and Development Efforts:**
  - we are highly dependent on the success of bempegaldesleukin, our lead immuno-oncology (I-O) candidate, and our business will be significantly harmed if we are not successful in developing this drug candidate;
  - 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 pipeline;
  - significant competition for our polymer conjugate chemistry technology platforms and our products and drug candidates could make our technologies, drug products or drug candidates obsolete or uncompetitive;
  - preliminary and interim data from our clinical studies 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; and
  - clinical trials for any of our drug candidates could be delayed for a variety of reasons.
- **Risks Related to our Collaboration Partners:**
  - we are highly dependent on our collaboration partners to initiate, properly conduct and prioritize clinical trials for bempegaldesleukin and NKTR-358, our lead drug candidates, and to perform important additional development and commercialization activities, and our business will be significantly harmed if their actions deprioritize or otherwise harm the prospects of our drug candidates; and
  - the operations of our collaboration partners have been affected by the COVID-19 pandemic in the past, and it is possible that the COVID-19 pandemic will affect the operations of our collaboration partners in the future, which would cause delays in initiating or completing one or more clinical trials involving our drug candidates.
- **Risks Related to our Financial Condition and Capital Requirements:**
  - 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 the market size for a new drug that receives approval is significantly smaller than we anticipate, it could negatively impact our revenue, results of operations and financial condition;
  - if third-party payers (including government programs) do not provide payment or reimbursement for our products, those products will not be widely accepted, which would negatively impact our business, results of operations and financial condition; and
  - our revenue is exclusively derived from our collaboration agreements. If we are unable to establish and maintain collaboration partnerships on attractive commercial terms, our business, results of operations and financial condition could suffer.
- **Risks Related to the COVID-19 Pandemic:**
  - our business could be adversely affected by the effects of health epidemics, including the ongoing COVID-19 pandemic. While the COVID-19 pandemic has not had a material adverse effect on our current operations, the ongoing challenges associated with the pandemic, including the emergence of new variants of the coronavirus, such as the Delta and Omicron variants, and resurgences in number and rates of infections, and shortages in raw materials and equipment and other supply chain disruptions, could have a material negative impact on our business and our clinical trial timelines.

- **Risks Related to Supply and Manufacturing:**
  - if we or our contract manufacturers are not able to manufacture drugs or drug substances in sufficient quantities that meet applicable quality standards, our business, financial condition and results of operations could be harmed; and
  - 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 delays, loss of revenue and contract liability.
- **Risks Related to Business Operations:**
  - 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 drug candidates successfully.
- **Risks Related to Intellectual Property, Litigation and Regulatory Concerns:**
  - we may not elect or be able to take advantage of any expedited development or regulatory review and approval processes available to drug candidates granted Breakthrough Therapy designation by the United States Food and Drug Administration (FDA);
  - we or our partners may not obtain regulatory approval for our drug candidates on a timely basis, or at all;
  - patents may not issue from our patent applications for our drug candidates, patents that have issued may not be enforceable, or additional intellectual property licenses from third parties may be required, which may not be available to us on commercially reasonable terms; and
  - from time to time, we are involved in legal proceedings and may incur substantial litigation costs and liabilities that could adversely affect our business, financial condition and results of operations.

In addition to the above-mentioned risks, our business is subject to a number of additional risks faced by businesses generally.

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 oncology, immunology and virology. 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 drug candidates as we believe that this is the best strategy to build long-term stockholder value.

Our Drug Candidates and Technology Platform

We have a targeted portfolio of novel drug candidates aimed at selectively modulating pathways within the immune system that play critical roles in a wide range of serious diseases, including oncology, immunology and virology. In oncology, we are focused on activating the immune system's natural tumor-fighting mechanisms, and we are studying several immuno-oncology (I-O) drug candidates in the clinic for a variety of cancer indications. These proprietary I-O candidates include bempegaldesleukin, NKTR-255 and NKTR-262, each in combination with one or more other therapeutic agents.

In immunology, we are focused on addressing imbalances in the immune system to restore the body's self-tolerance mechanisms and achieve immune homeostasis. In autoimmune disorders, our proprietary IL-2 T-regulatory (Treg) cell stimulator NKTR-358 is currently being clinically studied in systemic lupus erythematosus, ulcerative colitis, psoriasis and atopic dermatitis.

In virology, we believe selective immuno-modulators can be useful in addressing viral infections in people. Our programs in this area include studying bempegaldesleukin in treating individuals affected with COVID-19, and a preclinical research collaboration with Gilead Sciences Inc. (Gilead) to test the combination of NKTR-255 with therapies in Gilead's antiviral portfolio.

Our drug candidates are generated from our advanced and proven polymer conjugation technology platform. 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 first generation 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.

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 first generation techniques to allow for the application of technology to 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 technologies.

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 technologies that we may use when designing our own drug candidates, some of which are further described below.

Large Molecule Releasable Polymer Conjugates (Cytokines)

Our customized technologies with large molecule polymer conjugates can be applied to biologics, in particular cytokines, which utilize 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 bempegaldesleukin, which is a CD122-preferential IL-2 pathway agonist designed to stimulate the patient's own immune system to fight cancer, 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 technologies with large molecule polymer conjugates have enabled numerous successful PEGylated biologics on the market today. Through rational drug design, a protein's 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.

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: bempegaldesleukin, 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 Releasable Polymer Conjugates

Our proprietary releasable polymer conjugation technology 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 for NKTR-262. For NKTR-262 and other oncolytics, we believe this platform can improve sub-optimal half-lives that limit therapeutic efficacy. With our releasable polymer conjugate technology platform, we believe that oncolytic 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.

Small Molecule Polymer Conjugates

Our customized technology 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 technology can enable oral administration of subcutaneously or intravenously delivered small molecule drugs that have low

bioavailability when delivered orally. The benefits of this technology 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, the EU and other countries.

Antibody Fragment Polymer Conjugates

This technology 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 technology can be used to reduce antigenicity, reduce glomerular filtration rate, enhance uptake by inflamed tissues, and retain antigen-binding affinity and recognition. One approved product on the market that utilizes our technology with an antibody fragment is 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 Clinical Pipeline of Drug Candidates that Leverages Our Deep Understanding of Immunology and 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 leverage the expertise and experience within our internal research, preclinical, clinical development and regulatory departments. A key component of our development strategy is aimed at reducing 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. For some 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 the improved characteristics of our drug candidates will provide meaningful benefit to patients compared to 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 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.

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 bempegaldesleukin 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 bempegaldesleukin including global co-promotion rights for all combinations of bempegaldesleukin with any BMS proprietary therapy, and we lead global commercialization for all other bempegaldesleukin combination regimens. We also have the contractual right under our BMS Collaboration Agreement to record all worldwide sales and revenue for bempegaldesleukin and we have final decision-making authority regarding the pricing of bempegaldesleukin.

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 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.

Continue to Build a Leading Intellectual Property Estate across Therapeutic Modalities

We are committed to continuing to build on our intellectual property position to protect our scientific and therapeutic advances, whether in the I-O therapeutic area, the field of polymer conjugate chemistry or otherwise. 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, compositions of matter (such as our drug candidates, formulations, conjugates, and polymeric materials), methods of treatment, and methods of manufacture.

Our Research and Development Programs

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

Drug Candidate	Therapeutic Area	Status(1)
Bempegaldesleukin (CD122-preferential IL-2 pathway agonist)	Immuno-oncology	Phase 1, Phase 2, and Phase 3 studies ongoing in multiple indications
	Virology	Phase 1
NKTR-358 (cytokine Treg stimulant)	Autoimmune Disease	Phase 1 and Phase 2 studies ongoing in multiple indications
NKTR-255 (IL-15 receptor agonist)	Immuno-oncology	Phase 1 and Phase 1/2 studies ongoing in multiple indications
	Virology	Research/Preclinical
NKTR-262 (toll-like receptor agonist)	Oncology	Phase 1/2

(1) Status definitions are:
Phase 3 — 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 Our Pipeline

Immuno-oncology (I-O)

In the area of oncology, we have a particular focus on developing medicines in the area of I-O, which is a therapeutic approach based on targeting biological pathways that 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 to improve their function to recognize and attack cancer cells.

Bempegaldesleukin (previously known as NKTR-214, cytokine immunostimulatory therapy)

Bempegaldesleukin is a CD122-preferential IL-2 pathway agonist designed to stimulate the patient's own immune system to fight cancer without over-activating the immune system. Bempegaldesleukin is designed to grow specific cancer-killing T cells and natural (NK) cell populations in the body, which are known as endogenous tumor-infiltrating lymphocytes (TILs). Bempegaldesleukin stimulates these cancer-killing immune cells in the body by targeting CD122-specific receptors found on the surface of these immune cells, known as CD8+ effector T cells and NK cells. CD122, which is also known as the

IL-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. Our strategic objective is to establish bempegaldesleukin as a key component of many I-O combination regimens with the potential to improve the standard of care in multiple oncology settings. To this end, we are executing a comprehensive clinical development program for bempegaldesleukin, including a broad clinical collaboration with the Bristol-Myers Squibb Company (BMS), several clinical collaborations with other third parties with pharmacological agents that have potential complementary mechanisms to bempegaldesleukin, as well as pursuing our own independent clinical studies.

The development program for bempegaldesleukin 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 bempegaldesleukin and BMS' human monoclonal antibody that binds to PD-1, known as Opdivo®, 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 bempegaldesleukin 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 bempegaldesleukin 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 bempegaldesleukin with Opdivo®. On August 1, 2019, we and BMS announced that the FDA granted Breakthrough Therapy designation for bempegaldesleukin in combination with Opdivo® for the treatment of patients with previously untreated unresectable or metastatic melanoma. Breakthrough Therapy designation is intended to expedite the development and review of medicines aimed at treating serious or life-threatening disease where there is preliminary evidence that the investigational therapy may offer substantial improvement over existing therapies on at least one clinically significant endpoint.

On February 13, 2018, we entered into a Strategic Collaboration Agreement with BMS (as amended to date, the BMS Collaboration Agreement) that outlined a collaboration for the co-development and co-commercialization of bempegaldesleukin in combination regimens with BMS medicines including Opdivo®. 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 up to a total of approximately $1.455 billion (including the milestones which we have already received under the BMS Collaboration Agreement) upon achievement of certain development and regulatory milestones, and up to a total of $350.0 million upon achievement of certain sales milestones.

The collaboration development plan (the Collaboration Development Plan) under the BMS Collaboration Agreement is evaluating bempegaldesleukin in combination with Opdivo® in ongoing registrational trials in first-line metastatic melanoma, adjuvant melanoma, first-line cisplatin ineligible, PD-L1 low, locally advanced or metastatic urothelial cancer, first-line metastatic renal cell carcinoma (RCC), and muscle-invasive bladder cancer, as well as a Phase 1/2 dose escalation and expansion study to evaluate bempegaldesleukin plus Opdivo® in combination with either axitinib or cabozantinib in first line RCC in order to support a future Phase 3 registrational trial. We and BMS share development costs based on each party's relative ownership interest in the compounds included in the regimen. For example, we share clinical development costs for bempegaldesleukin in combination with Opdivo®, BMS 67.5% and Nektar 32.5%. For costs of manufacturing bempegaldesleukin, however, BMS is responsible for 35% and Nektar is responsible for 65% of costs. For indications not included in the Collaboration Development Plan, the parties are free to develop their own medicines in other indications subject to certain cost sharing, premium reimbursement, and timing terms and conditions.

Under the co-commercialization portion of the BMS Collaboration Agreement, we will book all worldwide sales and revenue for bempegaldesleukin. We and BMS will share global commercialization profits and losses for bempegaldesleukin, with Nektar sharing 65% and BMS sharing 35% of the net profits and losses. Each party bears their own non-product specific core commercialization infrastructure costs. We retain the final decision-making authority regarding the pricing for bempegaldesleukin. Bempegaldesleukin 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. On January 12, 2022, we and BMS entered into an Amendment No. 2 to the BMS Collaboration Agreement pursuant to which we and BMS allocated certain responsibilities related to price negotiations and promotion, market access, patient support and related activities to each party. The commercial economics under the BMS Collaboration Agreement remain unchanged under this amendment.

Outside of the Collaboration Development Plan with BMS, we are also conducting a broad array of development activities evaluating bempegaldesleukin in combination with other agents that have potential complementary mechanisms of action. For example, as specifically allowed under the BMS Collaboration Agreement, we are independently studying

bempegaldesleukin in combination with Keytruda®, a PD-1 inhibitor. We are also working with Vaccibody AS to evaluate bempegaldesleukin with Vaccibody's personalized cancer neoantigen vaccine in a Phase 1 proof-of-concept study.

On February 12, 2021, we entered into a financing and co-development collaboration (the SFJ Agreement) with SFJ Pharmaceuticals XII, L.P., a SFJ Pharmaceuticals Group company (SFJ), pursuant to which SFJ will pay up to $150.0 million in committed funding to support a Phase 2/3 study of bempegaldesleukin in combination with Keytruda® (pembrolizumab) for first-line treatment of patients with metastatic or unresectable recurrent squamous cell carcinoma of the head and neck (the SCCHN Clinical Trial) whose tumors express PD-L1 (the SCCHN Indication). SFJ Pharmaceuticals is a global drug development company backed by Blackstone Life Sciences and Abingworth. On February 11, 2021, we entered into a collaboration agreement with MSD International GmbH (MSD), an affiliate of Merck, Sharp & Dohme, pursuant to which MSD will provide Keytruda® at no cost for use in the SCCHN Clinical Trial but will not bear any other costs of the trial.

SFJ will have primary responsibility for the clinical trial management of the SCCHN Clinical Trial, and we will be the sponsor of the SCCHN Clinical Trial and will also have sole responsibility for regulatory interactions and filings for bempegaldesleukin. The SCCHN Clinical Trial provides for an interim futility analysis, and unless the futility criteria are met, SFJ is required to complete the SCCHN Trial, but if the futility criteria are met, SFJ has the responsibility to wind down the SCCHN Clinical Trial at its sole cost. We and BMS, pursuant to the BMS Collaboration Agreement, remain solely responsible for conducting the Phase 3 clinical trials of bempegaldesleukin in combination with Opdivo®, including the treatment of previously untreated unresectable or metastatic melanoma (the “Melanoma Indication” and the “Melanoma Clinical Trial”).

Other than the opportunity to receive Success Payments as outlined below, SFJ has no right to reimbursement of costs incurred by SFJ for the SCCHN Clinical Trial in the event that the Melanoma Clinical Trial and the SCCHN Clinical Trial do not achieve FDA approval. We will pay SFJ a series of success-based annual payments (collectively, the Success Payments) in the event of FDA approval of bempegaldesleukin for the Melanoma Indication, the SCCHN Indication, or both, and in the event of FDA approval of one additional bempegaldesleukin indication. The Success Payments do not begin until the substantial completion of the SCCHN Clinical Trial. The total success-based annual payments for the first indication approved by FDA, whether for the Melanoma Indication or the SCCHN Indication, is an aggregate of $450.0 million, paid in annual contractual payments over five years, with the first payment being $30.0 million, with the earliest possible payment expected to occur in late 2024 or early 2025, subject to the substantial completion of the SCCHN Clinical Trial. The total success-based payments for the second indication approved by FDA, whether for the Melanoma Indication or the SCCHN Indication, is an aggregate of $150.0 million, paid in annual contractual payments over seven years. Finally, in the event of FDA approval for bempegaldesleukin for any indication other than the Melanoma Indication or the SCCHN Indication, we will make a one-time payment of $37.5 million to SFJ. If the success criterion for the interim futility analysis is not met and SFJ winds down the SCCHN Clinical Trial, then the Success Payments, if any, for the Melanoma Indication and/or the additional bempegaldesleukin indication are reduced pro rata based on the costs incurred by SFJ for the SCCHN Clinical Trial over the aggregate commitment of $150.0 million.

The SFJ Agreement provides for certain positive and negative covenants, including restrictions on our ability to incur liens on our intellectual property related to bempegaldesleukin (the bempegaldesleukin IP), or assign or convey any right to receive income with respect to the bempegaldesleukin IP (other than royalty and other license fee obligations to licensors), except for the issuance of senior secured debt secured by all or substantially all of our assets, including the bempegaldesleukin IP.

The SFJ Agreement expires upon the payment of all Success Payments to SFJ, unless earlier terminated as provided under the SFJ Agreement. The SFJ Agreement may be terminated by either party for a safety or health concern for the patients, whether by the independent data monitoring company or by mutual agreement of both parties. The SFJ Agreement may also be terminated by either party for material breach or insolvency of the counterparty.

With our non-BMS clinical collaborations for bempegaldesleukin, generally each party supports the collaboration based on its expertise and resources. For example, in February 2021, we entered into a clinical trial collaboration and supply agreement with Merck wherein we will receive supplies of Keytruda® at no cost to us. We expect to continue to make significant and increasing investments exploring the potential of bempegaldesleukin with mechanisms of action that we believe are synergistic with bempegaldesleukin based on emerging scientific findings in cancer biology and preclinical development work.

In addition to these non-BMS clinical collaborations for bempegaldesleukin, we intend to initiate further clinical development programs, on our own or in collaboration with other potential partners, to explore the potential of combining bempegaldesleukin 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-255

NKTR-255 is a biologic that targets the IL-15 pathway in order to activate the body's innate and adaptive immunity. Activation of the IL-15 pathway enhances the survival and function of NK cells and induces survival of both effector and CD8 memory T cells. Recombindant human IL-15 is rapidly cleared from the body and must be administered frequently and in high doses limiting its utility due to toxicity. Through optimal engagement of the IL-15 receptor complex, NKTR-255 is designed to enhance functional NK cell populations and the formation of long-term immunological memory, which may lead to sustained anti-tumor immune response. We have initiated a Phase 1 clinical study of NKTR-255 in adults with relapsed or refractory non-Hodgkin lymphoma or multiple myeloma, as well as a Phase 1/2 clinical study of NKTR-255 in patients with relapsed or refractory head and neck squamous cell carcinoma or colorectal cancer. Additionally, we have entered into a separate preclinical research collaboration with Janssen to test the combination of NKTR-255 with therapies in Janssen's oncology portfolio.

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 (APCs), 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 bempegaldesleukin in order to induce an abscopal response and achieve the goal of tumor regression in cancer patients treated with both therapies. We have completed the dose-escalation portion of a Phase 1/2 clinical study, which we call the REVEAL study, and the dose-expansion portion of the study is ongoing.

Immunology

NKTR-358, Agreement with Eli Lilly and Company

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 IL-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 a worldwide license agreement with Eli Lilly and Company (Lilly), pursuant to which we and Lilly will co-develop NKTR-358 (Lilly Agreement). 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 drug supply responsibilities assigned to us under the Lilly Agreement. We will share Phase 2 development costs with Lilly, with Lilly responsible for 75% and Nektar responsible for 25% of these costs. We will also 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 costs and the level of global product annual sales. Lilly will be responsible for all costs of global commercialization and we have an option to co-promote in the U.S. under certain conditions.

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. We also completed treatment of a Phase 1 multiple-ascending dose trial to evaluate NKTR-358 in patients with systemic lupus erythematosus (SLE). Lilly is conducting two Phase 1b studies in patients with psoriasis and atopic dermatitis, and initiated a Phase 2 study in SLE in October 2020 and a Phase 2 study in ulcerative colitis in March 2021. In addition, Lilly is planning to initiate a Phase 2 study in atopic dermatitis based on positive interim Phase 1b results in that indication and also plans to initiate another Phase 2 study in another immune-mediated disease.

Virology

Our drug candidates, bempegaldesleukin and NKTR-255, also have potential applications in the area of virology. With regard to bempegaldesleukin, we believe this drug candidate's ability to directly increase the numbers of anti-viral CD4+, CD8+ and NK lymphocytes, which are known to be critical for the resolution of many viral infections in people, and specifically infections with respiratory coronaviruses in a variety of animal models, could be useful as a therapeutic in treating individuals affected with COVID-19. We completed a Phase 1b clinical trial of bempegaldesleukin plus standard of care for treatment of adults with mild COVID-19.

With regard to NKTR-255, we believe this drug candidate's ability to activate and proliferate NK cells and memory CD8+ T cells to target activated CD4+ T cells can result in killing virus-infected cells. We have entered into a preclinical research collaboration with Gilead to test the combination of NKTR-255 with therapies in Gilead's antiviral portfolio.

Collaboration Partner Programs

We have a number of other drug 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. 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.

Drug	Primary or Target Indications	Drug Marketer/Partner	Status(1)
ADYNOVATE® and ADYNOVI® (brand name for ADYNOVATE® in Europe)	Hemophilia A	Takeda Pharmaceutical Company Limited	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); Opioid-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 International, Inc.)	Approved 2004
Somavert® (pegvisomant)	Acromegaly	Pfizer Inc.	Approved 2003
Dapirolizumab Pegol	Systemic Lupus Erythematosus	UCB Pharma (Biogen)	Phase 3

(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 — 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 December 2020, pursuant to a purchase and sale agreement (the "2020 Purchase and Sale Agreement") we sold our rights to receive royalties on future worldwide new sales of ADYNOVATE®/ADYNOVI® and MOVANTIK®/MOVANTIG® (as well as REBINYN® and specified licensed products under a Right to Sublicense Agreement, dated October 27, 2017) from and after October 1, 2020 until the purchaser of these rights has received payments equal to $210.0 million (the "2025 Threshold"), if the 2025 Threshold is achieved on or prior to December 31, 2025, or $240.0 million, if the 2025 Threshold is not achieved on or prior to December 31, 2025 (or, if earlier, the date on which the last royalty payment under the relevant license agreements is made). All rights to receive royalties will return to Nektar once the 2020 Purchase and Sale Agreement expires.

** 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" and "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."

Overview of Ongoing Collaboration Partner Programs

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), to develop products with an extended half-life for the treatment and prophylaxis of Hemophilia A patients using our proprietary PEGylation technology. 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. 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 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.

In December 2020, pursuant to the 2020 Purchase and Sale Agreement we sold our rights to receive royalties on future worldwide new sales of ADYNOVATE®/ADYNOVI® and from the third party products under a right to sublicense agreement from and after October 1, 2020 until the purchaser of these rights has received payments equal to $210.0 million (the "2025 Threshold"), if the 2025 Threshold is achieved on or prior to December 31, 2025, or $240.0 million, if the 2025 Threshold is not achieved on or prior to December 31, 2025 (or, if earlier, the date on which the last royalty payment under the relevant license agreements is made). All rights to receive royalties will return to Nektar once the 2020 Purchase and Sale Agreement expires. This 2020 Purchase and Sale Agreement is further discussed in Note 8 of our Consolidated Financial Statements.

MOVANTIK® and MOVENTIG® (brand name for MOVANTIK® in Europe), 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.

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 (EC), granted Marketing Authorisation to MOVENTIG® (the naloxegol brand name in the European Union (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 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.

In December 2020, pursuant to the 2020 Purchase and Sale Agreement, we sold our rights to receive royalties on future worldwide new sales of MOVANTIK®/MOVANTIG® from and after October 1, 2020 until the purchaser of these rights has received payments equal to $210.0 million (the "2025 Threshold"), if the 2025 Threshold is achieved on or prior to December 31, 2025, or $240.0 million, if the 2025 Threshold is not achieved on or prior to December 31, 2025 (or, if earlier, the date on which the last royalty payment under the relevant license agreements is made). All rights to receive royalties will return to Nektar once the 2020 Purchase and Sale Agreement expires. This 2020 Purchase and Sale Agreement is further discussed in Note 7 of our Consolidated Financial Statements. 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.

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 all 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 8 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®. As of December 31, 2016, we no longer had any continuing manufacturing or supply obligations under this MIRCERA® agreement. 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 8 of our Consolidated Financial Statements.

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 (LMS Agreement) with Sensus Drug Development Corporation (subsequently acquired by Pharmacia Corp. in 2001 and then acquired by Pfizer in 2003), for the PEGylation of Somavert® (pegvisomant), a human growth hormone receptor antagonist for the treatment of acromegaly. In January 2017, we entered into a master material supply agreement (Supply Agreement) with Pfizer, in which the LMS Agreement was terminated. We currently manufacture our proprietary PEGylation reagent for Pfizer on a price per gram basis under the Supply Agreement. Our obligation under the Supply Agreement to supply our proprietary PEGylation reagent to Pfizer continues until December 31, 2023.

Dapirolizumab Pegol, Agreement with UCB Pharma S.A.

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). Most recently, in July 2019, Biogen announced a plan to initiate with UCB a Phase 3 study of dapriolizumab pegol in patients with active SLE, which clinical study is currently ongoing.

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 Investigational New Drug (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 a New Drug Application (NDA) for approval of a drug or a Biological License Application (BLA) for approval of a biological product.

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 trial.

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 typically 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 commercialization. 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 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 product. For those products for which we have development responsibility, we prepare and submit an IND and are responsible for additional clinical and regulatory procedures for drug 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., the FDA may grant Fast Track or Breakthrough Therapy designation to a drug 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. On August 1, 2019, we and BMS announced that the FDA granted Breakthrough Therapy designation for bempegaldesleukin in combination with Opdivo® for the treatment of patients with previously untreated unresectable or metastatic melanoma.

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.

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 payers. Third-party payers include government programs such as Medicare, Medicaid, TRICARE and the Veterans Administration, as well as managed care providers, private health insurers and other organizations. Other countries and jurisdictions will also have their own unique mechanisms for approval and reimbursement.

The process for determining whether a payer will provide coverage for a product is typically separate from the process for setting the reimbursement rate that the payer will pay for the product. Third-party payers 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 payers 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 payers 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 payers 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 payers 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 approved. If third-party payers 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 payers 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 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, or 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 (currently defined to include doctors, dentists, optometrists, podiatrists and chiropractors) 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. Effective January 1, 2022, these reporting obligations will extend to include transfers of value made to certain non-physician providers such as physician assistants and nurse practitioners;
- 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.

If our drug candidates become commercialized, it is possible that governmental authorities will conclude that our business practices may not comply with current or future statutes, regulations, agency guidance or case law involving applicable fraud and abuse or other healthcare laws and regulations. If our operations are found to be in violation of any of these laws or any other governmental regulations that may apply to us, we may be subject to significant civil, criminal, and administrative penalties, damages, fines, disgorgement, exclusion from government-funded healthcare programs, such as Medicare and Medicaid, integrity and oversight agreements to resolve allegations of non-compliance, contractual damages, reputational harm, diminished profits and future earnings, and the curtailment or restructuring of our operations, any of which could adversely affect our ability to operate our business and our results of operations. Defending against any such actions can be costly, time-consuming and may require significant financial and personnel resources. Therefore, even if we are successful in defending against any such actions that may be brought against us, our business may be impaired.

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 payers, 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 $11,463 and $23,331 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.

In each country or jurisdiction outside of the U.S. in which we seek and receive regulatory approval to commercialize our products, we will be subject to additional laws and regulations specific to those locations. These regulations and laws will also impact, among other things, our proposed sales and marketing programs in those jurisdictions.

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. 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 private 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 310 U.S. and 1,200 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 drug 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 *inter partes* review, opposition, reexamination or other proceedings that can result in the revocation of the patent or maintenance of the patent but in an 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 post-grant proceedings before 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, clinical research reimbursement or co-funding, milestone payments based on clinical progress, regulatory progress or net sales achievements, royalties and/or product sales revenue. Our revenues are concentrated among a limited number of collaboration partners under long-term arrangements. We derive the substantial majority of our product sales from UCB and Pfizer. Following the 2020 Purchase and Sale Agreement (wherein under a capped return sale arrangement we sold our rights to receive royalties on future worldwide new sales of MOVANTIK®/MOVANTIG® and ADYNOVATE®/ADYNOVI®, as well as REBINYN® and specified licensed products), other than our product sales, substantially all of our revenues are non-cash royalty revenues. However, our collaborations with BMS and Lilly for the development of bempegaldesleukin and NKTR-358, respectively, provide for the most significant portion of our potential future development and regulatory milestone payments, as well as royalties from net sales of NKTR-358, if approved. Additionally, these collaboration partners provide significant financial support for the development and commercialization of these programs. BMS bears 67.5% of the costs of developing bempegaldesleukin in combination with Opdivo®, 35% of the costs of manufacturing bempegaldesleukin and 35% of the costs of joint commercialization. Lilly bears

75% of the costs of Phase 2 development of NKTR-358, will bear 100% of the costs of Phase 3 development, subject to our right to contribute up to 25% of Phase 3 development costs on an indication-by-indication basis in exchange for higher royalties, if approved, and will be responsible for all costs of global commercialization, subject to our option to co-promote in the U.S. under certain conditions.

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 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 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., Horizon 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

Bempegaldesleukin

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 in the cytokine-based therapies space with potential competitors including Alkermes PLC, Asher Biotherapeutics, Aulos Bioscience, Bright Peak Therapeutics, Cue Biopharma, Neoleukin, Sanofi SA (through its acquisition of Synthorx, Inc.), Synthekine, Inc., Werewolf Therapeutics, and Xilio Therapeutics. We may also face competition from other therapeutic approaches including tumor infiltrating lymphocytes, or TILs, and chimeric antigen receptor-expressing T cells, or CAR-Ts. Potential competitors in the TIL and CAR-T space include Gilead (through its acquisition of Kite Pharma)/NCI, Apeiron Biologics, Philogen S.p.A., Brooklyn ImmunoTherapeutics LLC, Anaveon AG, Adaptimmune LLC, and Iovance Biotherapeutics, Inc.

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, Jassen Pharmaceuticals, AstraZeneca and Tizona Therapeutics), regulatory T cell therapies (Targazyme, Inc., Caladrius BioSciences, Inc., and Tract Therapeutics, Inc.), or IL-2 based therapies (Amgen, Inc., BMS (through its acquisition of Delnia, Inc.), GentiBio, Inc., ILTOO Pharma, Kyverna Therapeutics, Merck & Co, through its acquisition of Pandion Therapeutics, and Sanofi SA, through its acquisition of Synthorx, Inc.).

NKTR-255

There are numerous companies engaged in developing immunotherapies with different approaches to enhancing NK cell populations which are a key component of the innate immune system. The approaches include engineered biologics

targeting the IL-15 pathway as well as autologous and allogenic cell therapy approaches. For NKTR-255, we believe companies that are currently researching and developing engineered IL-15 biologics and cell therapies that could compete with this drug candidate include Artiva Biotherapeutics, Fate Therapeutics, ImmunityBio, Inc., nkarta therapeutics, NKMax America, and Roche/Genentech (through its partnership with Xencor, Inc.).

Research and Development

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

	Year Ended December 31,	
	2021	2020
Third party and direct materials costs	$ 176.9	$ 195.1
Personnel, overhead and other costs	158.7	147.2
Stock-based compensation and depreciation	64.7	66.4
Research and development expense	$ 400.3	$ 408.7

Manufacturing and Supply

We have a manufacturing facility located in Huntsville, Alabama that manufactures our proprietary PEG reagents for subsequent conjugation to active pharmaceutical ingredients (APIs). The facility is also used to produce APIs themselves, as well as PEG conjugates of those APIs, to support the early phases of clinical development of our 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. Our contract manufacturers have contractual obligations to comply with 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 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 could 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 the U.S. Environmental Protection Agency 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. To our knowledge, we comply with all material governmental regulations applicable to our business. We would be subject to significant penalties for failure to comply with these laws and regulations.

Human Capital

As of December 31, 2021, we had 740 employees, of which 577 employees were engaged in research and development, manufacturing, and quality activities and 163 employees in general administrative and commercial operations function. Of the 740 employees, 661 were located in the U.S. We have a number of employees who hold advanced degrees, such as a Ph.D. None of our employees are covered by a collective bargaining agreement, and we have experienced no work stoppages. We are committed to attracting, developing, advancing and retaining a diverse and talented workforce. As part of our measures to attract and retain personnel, we offer a total rewards package to our full-time employees consisting of base salary, cash bonuses based on individual and company performance, equity compensation and comprehensive benefits, including health insurance, life insurance, retirement plans, and paid holiday and vacation time. We support our employee’s further development by providing professional development opportunities. We believe that we maintain good relations with our employees.

To complement our own expert professional staff, we utilize specialists in clinical development, regulatory affairs, pharmacovigilance, process engineering, manufacturing and quality assurance. 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 SEC maintains an Internet site that contains reports, proxy and information statements and other information regarding our filings at *www.sec.gov.*

INFORMATION ABOUT OUR EXECUTIVE OFFICERS

The following table sets forth the names, ages and positions of our executive officers as of February 28, 2022:

Name	Age	Position
Howard W. Robin	69	Director, President and Chief Executive Officer
Gil M. Labrucherie, J.D.	50	Chief Operating Officer and Chief Financial Officer
John Northcott	44	Senior Vice President and Chief Commercial Officer
Jillian B. Thomsen	56	Senior Vice President, Finance and Chief Accounting Officer
Mark A. Wilson, J.D.	50	Senior Vice President and General Counsel
Jonathan Zalevsky, Ph.D.	47	Chief Research and Development 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.

Gil M. Labrucherie has served as our Senior Vice President, Chief Financial Officer since June 2016, and added the role of Chief Operating Officer in October 2019. 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, a platform enterprise software as a service company. While at E2open, Mr. Labrucherie was responsible for global corporate alliances and merger 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 his B.A. from the University of California Davis.

John Northcott has served as our Senior Vice President and Chief Commercial Officer since December 2019. From 2015 to 2019, Mr. Northcott served as the Chief Commercial Officer of Pharmacyclics. From 2013 to 2015, Mr. Northcott was Chief Commercial Officer at Lexicon Pharmaceuticals. He has held commercial roles from 2007 to 2013 in both U.S. and Global marketing with Genentech and the Roche Group, including the role of International Business Leader. Prior to Roche/Genentech, Mr. Northcott held management positions in sales and marketing in a variety of therapeutic areas at other pharmaceutical companies including Merck and Pfizer. Mr. Northcott received a bachelor's degree in Business Administration from St. Francis Xavier University.

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.

Mark A. Wilson has served as our Senior Vice President and General Counsel since June 2016. Mr. Wilson joined Nektar in May 2002 and initially served as Patent Counsel and then as Senior Patent Counsel to the company prior to 2008 when he was promoted to Vice President, Intellectual Property. Before joining Nektar in 2002, Mr. Wilson was an associate at Reed & Associates, a patent law firm in Menlo Park, California, where he represented both start-up and Fortune 500 companies. Mr. Wilson received his J.D. from Seton Hall University, School of Law, and his B.S. in Pharmacy from Rutgers University, College of Pharmacy. He is registered to practice before the U.S. Patent and Trademark Office and is a member of the California Bar.

Jonathan Zalevsky has served as our Chief Research & Development Officer since October 2019. Dr. Zalevsky served as our Senior Vice President, Biology and Preclinical Development from April 2017 through November 2017 and served as our Senior Vice President, Research and Chief Science Officer from November 2017 to October 2019. From July 2015 through April 2017, Dr. Zalevsky served as our Vice President, Biology and Preclinical Development. Prior to joining Nektar, Dr. Zalevsky was Global Vice President and Head of the Inflammation Drug Discovery Unit at Takeda Pharmaceuticals. Prior to working at Takeda, Dr. Zalevsky held a number of research and development positions at Xencor, Inc. Dr. Zalevsky received his Ph.D. in Biochemistry from the Tetrad Program at the University of California, San Francisco. He received dual bachelor degrees in Biochemistry and Molecular, Cellular and Developmental Biology from the University of Colorado at Boulder.

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. Investors in Nektar Therapeutics should carefully consider the risks described below before making an investment decision. 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 bempegaldesleukin, our lead I-O candidate. We are executing a clinical development program for bempegaldesleukin and clinical and regulatory outcomes for bempegaldesleukin, 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 bempegaldesleukin. In general, most investigational drugs, including I-O drug candidates such as bempegaldesleukin, do not become approved drugs. Accordingly, there is a very meaningful risk that bempegaldesleukin will not succeed in one or more clinical trials sufficient to support one or more regulatory approvals. To date, reported clinical outcomes from bempegaldesleukin have had a significant impact on our market valuation, and business prospects and we expect this to continue in future periods. If one or more clinical studies of bempegaldesleukin are delayed (as a result of, for example, our collaboration partner causing a delay of the initiation or completion of one or more clinical trials for reasons outside of our control) 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 approximately $1.455 billion in development milestone payments (of which we have received $50.0 million) that are based upon clinical and regulatory successes from the bempegaldesleukin development program. One or more failures in bempegaldesleukin studies could jeopardize such milestone payments, and any product sales or royalty revenue or commercial milestone payments that we would otherwise be entitled to receive could be reduced, delayed or eliminated.

Additionally, promising results from earlier trials may not predict similarly favorable outcomes in subsequent trials. For example, several of our past, planned and ongoing clinical trials utilize an “open-label” trial design. An “open-label” clinical trial is one where both the patient and investigator know whether the patient is receiving the investigational drug candidate or either an existing approved drug or placebo. Most typically, open-label clinical trials test only the investigational drug candidate and sometimes may do so at different dose levels. Open-label clinical trials are subject to various limitations that may exaggerate any therapeutic effect as patients in open-label clinical trials are aware when they are receiving treatment. Open-label clinical trials may be subject to a “patient bias” where patients perceive their symptoms to have improved merely due to their awareness of receiving an experimental treatment. In addition, open-label clinical trials may be subject to an “investigator bias” where those assessing and reviewing the physiological outcomes of the clinical trials are aware of which patients have received treatment and may interpret the information of the treated group more favorably given this knowledge. The results from an open-label trial may not be predictive of future clinical trial results with any of our drug candidates for which we include an open-label clinical trial when studied in a controlled environment with a placebo or active control.

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 bempegaldesleukin, including trials evaluating bempegaldesleukin as a potential combination treatment with BMS’s Opdivo® as well as other ongoing and planned combination trials. Our partner Lilly is conducting two Phase 2 studies of NKTR-358 in patients with SLE and ulcerative colitis as well as two Phase 1b studies in patients with psoriasis and atopic dermatitis. We also continue to conduct a Phase 1/2 study evaluating bempegaldesleukin in combination with NKTR-262 in patients with solid tumors. In addition, we have initiated a Phase 1 clinical study of NKTR-255 in adults with relapsed or refractory non-Hodgkin lymphoma or multiple myeloma, as well as a Phase 1/2 clinical study of NKTR-255 in patients with relapsed or refractory head and neck squamous cell carcinoma or colorectal cancer. 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 drug 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;
- for drug candidates (such as bempegaldesleukin and NKTR-358) partnered with other companies, delays caused by our partner;
- delays caused by the COVID-19 pandemic (see also the risk factor in this Item 1A titled "*Our business could be adversely affected by the effects of health epidemics, including the recent COVID-19 pandemic*").
- 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 due to the detriment of enrollment rates;
- delays in manufacturing and delivery of sufficient supply of clinical trial materials;
- changes in regulatory authorities policies or guidance applicable to our drug candidates; and
- delays caused by changing standards of care or new treatment options.

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, results for the studies would be delayed, and consequently the regulatory approval process would be delayed which would also delay our ability to commercialize these drug candidates, 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 drug 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 tens of billions of dollars of investment each year. Our clinical trial plans for bempegaldesleukin, 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. As I-O combination therapies are relatively new approaches in cancer treatment and few have successfully completed late stage development, I-O drug development entails substantial risks and uncertainties that include rapidly changing standards of care, identifying contribution of component therapies, 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.

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 drug candidate may not predict the results that will be obtained in later phase clinical trials of the drug candidate. We, the FDA, an independent Institutional Review Board (IRB), an independent ethics committee (IEC), or other applicable regulatory authorities may suspend clinical trials of a drug 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 IEC 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.

Significant competition for our polymer conjugate chemistry technology platforms and our partnered and proprietary drugs and drug candidates could make our technologies, drugs or drug 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 drug candidates compete with various pharmaceutical and biotechnology companies. Competitors of our polymer conjugate chemistry technologies include Biogen Inc., Horizon Pharma, Dr. Reddy's Laboratories Ltd., SunBio Corporation, Laysan Bio, Inc., 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 drug candidates currently in development. For bempegaldesleukin, 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., Brooklyn ImmunoTherapeutics LLC, Anaveon AG, Adaptimmune LLC, and Novartis AG; potential competitors in the cytokine-based therapies space include Alkermes PLC, Asher Biotherapeutics, Aulos Bioscience, Bright Peak Therapeutics, Cue Biopharma, ImmunityBio, Inc., Neoleukin Therapeutics, Inc., Philogen S.p.A., Roche, Sanofi SA (through its acquisition of Synthorx, Inc.), Synthekine, Inc., Werewolf Therapeutics, and Xilio Therapeutics, and Eli Lilly & Co. (through its acquisition of Armo BioSciences); and potential competitors in the checkpoint inhibitor space include GlaxoSmithKline plc (through its acquisition of Tesaro, Inc.), Macrogenics, Inc., Merck, Bristol-Myers Squibb Company, and Roche. 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, Janssen, AstraZeneca, and Tizona Therapeutics), regulatory T cell therapies (Targazyme, Inc., Caladrius BioSciences, Inc., and Tract Therapeutics, Inc.), or IL-2-based-therapies (Amgen Inc., Celgene Corporation, GentiBio, Inc., ILTOO Pharma, Kyverna Therapeutics, Merck & Co, through its acquisition of Pandion Therapeutics, and Roche). For NKTR-255, we believe companies that are currently researching and developing engineered IL-15 biologics and cell therapies that could compete with this drug candidate include Artiva Biotherapeutics, Fate Therapeutics, ImmunityBio, Inc., nkarta therapeutics, NKMax America, and Roche/Genentech (through its partnership with Xencor, Inc.). 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.

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.

Risks Related to our Collaboration Partners

We are highly dependent on our collaboration partners to initiate, properly conduct and prioritize clinical trials for bempegaldesleukin and NKTR-358 and to perform important additional development and commercialization activities, and our business will be significantly harmed if their actions deprioritize or otherwise harm the prospects of our drug candidates.

We rely on BMS (through the BMS Collaboration Agreement) and Lilly (through the Lilly Agreement) to initiate, properly conduct, and prioritize clinical trials and other development-related activities for bempegaldesleukin and NKTR-358, respectively. Furthermore, we will rely on BMS and Lilly to perform specified commercialization activities for bempegaldesleukin and NKTR-358, respectively, pursuant to the applicable agreement. In the event BMS or Lilly fails to initiate, properly conduct and prioritize their obligations under their applicable agreement with us, our business will be significantly harmed. Even if the applicable agreement provides us with enforcement or other curative rights to address the harm caused by BMS's or Lilly's action (or failure to act), our efforts in pursuing a remedy would be costly and there is no guarantee that efforts would succeed or be sufficient to fully address the harm.

In addition, for reasons outside of our control, the operations of our collaboration partners may be affected by the COVID-19 pandemic, or they may adopt more restrictive procedures for addressing the COVID-19 pandemic, either of which would delay initiating or completing one or more clinical trials involving our drug candidates.

Risks Related to our Financial Condition and Capital Requirement

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 Nektar-run trials under 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 drug 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;
- 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; and
- partners may respond to natural disasters or health epidemics, such as the COVID-19 pandemic, by ceasing all or some of their development responsibilities (including the responsibility to clinical develop our drug candidates).

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 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 that 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, 2021, we had cash and investments in marketable securities valued at approximately $798.8 million. 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 drug candidates, particularly bempegaldesleukin and NKTR-358;
- 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 could 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 to advance our drug candidates to later stage research and development, 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 drug candidates due to important factors such as safety and efficacy compared to other available treatments, including changing standards of care, third party payer reimbursement standards, patient and physician preferences, the availability of competitive alternatives that may emerge either during the long drug development process or after commercial introduction, and the availability of generic and biosimilar versions of our drug 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 drug 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 drug or proprietary drugs, those drugs will not be widely accepted, which would have a negative impact on our business, results of operations and financial condition.

In the United States and markets in other countries, patients generally rely on third-party payers to reimburse all or part of the costs associated with their treatment. In both domestic and foreign markets, sales of our partnered and proprietary products that receive 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 in the U.S., managed care providers, private health insurers and other organizations. However, eligibility for coverage does not necessarily signify that a biologic 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. Further, due to the COVID-19 pandemic, millions of individuals have lost or will be losing employer-based insurance coverage, which may adversely affect our ability to commercialize our biologic candidates even if there is adequate coverage and reimbursement from third-party payers. It is unclear what effect, if any, the American Rescue Plan Act will have on the number of covered individuals.

There is also significant uncertainty related to the insurance coverage and reimbursement of newly approved products and coverage may be more limited than the purposes for which the medicine is approved by the FDA or comparable foreign regulatory authorities. In the United States, the principal decisions about reimbursement for new medicines are typically made by the Centers for Medicare & Medicaid Services, or CMS, an agency within the U.S. Department of Health and Human Services. CMS decides whether and to what extent a new medicine will be covered and reimbursed under Medicare and private payers tend to follow CMS to a substantial degree.

Factors payers consider in determining reimbursement are based on whether the product is (i) a covered benefit under its health plan; (ii) safe, effective and medically necessary; (iii) appropriate for the specific patient; (iv) cost-effective; and (v) neither experimental nor investigational. In addition, net prices for drugs may be reduced by mandatory discounts or rebates required by government healthcare programs or private payers and by any future relaxation of laws that presently restrict imports of drugs from countries where they may be sold at lower prices than in the United States. Increasingly, third-party payers are requiring that drug companies provide them with predetermined discounts from list prices and are challenging the prices charged for medical products. We cannot be sure that reimbursement will be available for any product candidate that we commercialize and, if reimbursement is available, the level of reimbursement. In addition, many pharmaceutical manufacturers must calculate and report certain price reporting metrics to the government, such as average sales price, or ASP, and best price. Penalties may apply in some cases when such metrics are not submitted accurately and timely. Further, these prices for drugs may be reduced by mandatory discounts or rebates required by government healthcare programs.

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. 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.

In addition, in some foreign countries, the proposed pricing for a drug must be approved before it may be lawfully marketed. The requirements governing drug pricing vary widely from country to country. For example, the European Union provides options for its Member States to restrict the range of medicinal products for which their national health insurance systems provide reimbursement and to control the prices of medicinal products for human use. To obtain reimbursement or pricing approval, some of these countries may require the completion of clinical trials that compare the cost effectiveness of a particular product candidate to currently available therapies. A Member State may approve a specific price for the medicinal product or it may instead adopt a system of direct or indirect controls on the profitability of the company placing the medicinal product on the market. There can be no assurance that any country that has price controls or reimbursement limitations for pharmaceutical products will allow favorable reimbursement and pricing arrangements for any of our product candidates. Historically, products launched in the European Union do not follow price structures of the U.S. and generally prices tend to be significantly lower.

Recent federal legislation and actions by federal, state and local governments may permit reimportation of drugs from foreign countries into the United States, including foreign countries where the drugs are sold at lower prices than in the United States, which could materially adversely affect our operating results.

We may face competition in the United States for our development candidates and investigational medicines, if approved, from therapies sourced from foreign countries that have placed price controls on pharmaceutical products. In the United States, the Medicare Modernization Act (MMA) contains provisions that call for the promulgation of regulations that expand pharmacists' and wholesalers' ability to import cheaper versions of an approved drug and competing products from Canada, where there are government price controls. Further, the MMA provides that these changes to U.S. importation laws will not take effect, unless and until the U.S. Secretary of Health and Human Services (HHS) certifies that the changes will pose no additional risk to the public's health and safety and will result in a significant reduction in the cost of products to consumers. On September 23, 2020, the U.S. Secretary of HHS made such certification to Congress, and on October 1, 2020, FDA published a final rule that allows for the importation of certain prescription drugs from Canada. Under the final rule, States and Indian Tribes, and in certain future circumstances pharmacists and wholesalers, may submit importation program proposals to the FDA for review and authorization. Since the issuance of the final rule, several industry groups have filed federal lawsuits challenging multiple aspects of the final rule, and authorities in Canada have passed rules designed to safeguard the Canadian drug supply from shortages. On September 25, 2020, CMS stated drugs imported by States under this rule will not be eligible for federal rebates under Section 1927 of the Social Security Act and manufacturers would not report these drugs for "best price" or Average Manufacturer Price purposes. Since these drugs are not considered covered outpatient drugs, CMS further stated it will not publish a National Average Drug Acquisition Cost for these drugs. Separately, the FDA also issued a final guidance document outlining a pathway for manufacturers to obtain an additional National Drug Code, or NDC, for an FDA-approved drug that was originally intended to be marketed in a foreign country and that was authorized for sale in that foreign country. The market implications of the final rule and guidance are unknown at this time. Proponents of drug reimportation may attempt to pass legislation that would directly allow reimportation under certain circumstances. Legislation or regulations allowing the reimportation of drugs, if enacted, could decrease the price we receive for any products that we may develop and adversely affect our future revenues and prospects for profitability.

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 biologic 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, research and development reimbursement and funding, 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 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 biologic candidate under our collaboration agreement, our business, financial condition, and results of operations could be materially and adversely affected.

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

For the year ended December 31, 2021, we reported a net loss of $523.8 million. If and when we achieve profitability depends upon a number of factors, including the timing and recognition of milestones and other contingent payments and royalties received, the timing of revenue under our collaboration agreements, the amount of investments we make in our biologic candidates and the regulatory approval and market success of our biologic 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 bempegaldesleukin, NKTR-358, NKTR-262, and NKTR-255;
- receive necessary regulatory and marketing approvals;
- maintain or expand manufacturing at necessary levels;
- achieve market acceptance of our partnered products;
- receive revenue or royalties on products that have been approved, marketed or submitted for marketing approval with regulatory authorities; and
- maintain sufficient funds to finance our activities.

Risks Related to the COVID-19 Pandemic

Our business could be adversely affected by the effects of health epidemics, including the recent COVID-19 pandemic.

Our business could be adversely affected, directly or indirectly, by health epidemics in regions where we have concentrations of clinical trial sites or other business operations, including both our own manufacturing operations as well as the manufacturing operations of third parties upon whom we rely. With respect to the ongoing COVID-19 pandemic, national, state and local governments in regions affected by the COVID-19 pandemic have implemented, and may continue to implement or reinstate safety precautions, including quarantines, border closures, increased border controls, travel restrictions, shelter-in-place orders and shutdowns, business closures and other measures. These measures may disrupt normal business operations both in and outside areas affected by COVID-19, and may have significant negative impacts on our business. Even as these safety precautions are eased or reduced over time, there may be long lasting effects of these precautions on our business that may only be fully realized in the future.

We continue to monitor our operations and applicable government recommendations, and we have made modifications to our normal operations because of the COVID-19 pandemic. Throughout the pandemic we have modified our office policies to maintain productivity and safety of our employees. Although we believe these and the other safety measures we have taken in response to the COVID-19 pandemic have not substantially impacted our productivity, it is not certain that this will continue to be the case. Operating requirements may continually change due to the COVID-19 pandemic and we may experience unpredictability in our expenses, employee productivity and availability and employee work culture.

Certain of our clinical trials have been and may continue to be affected by the COVID-19 pandemic. Investigator recruitment, clinical site initiation, patient screening and patient enrollment may be delayed due to, for example, prioritization of hospital resources toward the COVID-19 pandemic. Some patients who are successfully enrolled in clinical trials involving our biologic candidates may not be able to comply with clinical trial protocols due to, for example, shelter-in-place orders impeding movement, disrupted healthcare services, or health issues for suspected or confirmed COVID-19 status. Similarly, our ability to recruit and retain patients and principal investigators and site staff, all of whom may have heightened risk for COVID-19, could adversely impact our clinical trial operations.

Delays and disruptions experienced by our collaborators or other third parties due to the COVID-19 pandemic could adversely impact the ability of such parties to fulfill their obligations, which could affect clinical development or regulatory approvals of our biologic candidates. For example, due to recent supply chain disruptions, we have been monitoring our supply chains for any disruptions or constraints caused by the COVID-19 pandemic. To date, we have not experienced any supply impact. However, if we, our collaborators or any third parties which we rely on are adversely effected by any supply disruptions or shortages in raw materials and equipment caused by the COVID-19 pandemic, our ability to manufacture our products and to supply drug candidates for our clinical trials could be negatively impacted, which could harm our business prospects, results of operations and financial condition.

Although we are implementing measures to maintain the integrity of our clinical trials, there is no guarantee that we will prevent all study protocol violations, missed study treatment visits, and other influences that jeopardize reliability and

validity of our clinical trial data. If a regulatory authority determines our clinical trial data lacks integrity, there is no guarantee that we will have a remedy to correct or otherwise address the deficiency. Even if such a remedy is identified, the cost for implementing the remedy could be prohibitively expensive, time consuming, or both. As a consequence, a clinical study of our biologic candidate in which the integrity of the clinical study is questioned or doubted may require lengthy and costly remediation measures (such as, for example, over-enrolling patients into the study or repeating the study), thereby causing substantial harm to our business.

Also, the COVID-19 pandemic could postpone necessary interactions with regulators regarding our drug candidates in development and could delay review or approval of our regulatory submissions.

The spread of COVID-19, which has caused a broad impact globally, may materially affect us economically. While the potential economic impact brought by, and the duration of, the COVID-19 pandemic is difficult to assess or predict, the pandemic could result in significant disruption of global financial markets, reducing our ability to access capital, which could in the future negatively affect our liquidity. In addition, a recession or market correction resulting from the spread of COVID-19 could materially affect our business and the value of our common stock.

The rapid development and fluidity of the COVID-19 pandemic results in a substantial number of individual variables that could cause a significant negative impact on our operations and our business, thereby precluding useful predictions as to how this pandemic will ultimately affect us. In particular, it is unclear how our business may be affected by the emergence of new variants of the coronavirus, such as the Delta and Omicron variants, and recent resurgences in number and rates of COVID-19 infections. Thus, any current assessment of the effects of the COVID-19 pandemic, including the impact of this disease on our clinical trial timelines, is subject to change. We do not yet know the full extent of potential impacts on our business, our clinical trials, healthcare systems or the global economy as a whole. However, these effects could have a material negative impact on our operations and our business. Furthermore, to the extent the ongoing COVID-19 pandemic adversely affects our operations and business, it may also heighten the other risks described in this “Risk Factors” section.

Risks Related to Supply and Manufacturing

If we or our contract manufacturers are not able to manufacture biologic substance or 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 manufacturing organizations (CMOs) 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 CMOs to manufacture and supply drug product for our clinical studies and those of our collaboration partners. The manufacturing of biologics 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. These risks and uncertainties are compounded by the COVID-19 pandemic wherein the facilities and employees responsible for manufacturing biologics for use in clinical trials may be negatively impacted such that there is an insufficient supply of study biologic drugs. We have faced and may in the future face significant difficulties, delays and unexpected expenses as we validate third party CMOs required for drug supply to support our clinical studies and the clinical studies and products of our collaboration partners. Failure by us or our CMOs 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.

On March 27, 2020, the President of the United States signed into law the Coronavirus Aid, Relief, and Economic Security Act (CARES Act) in response to the COVID-19 pandemic. Throughout the COVID-19 outbreak, there has been public concern over the availability and accessibility of critical medical products, and the CARES Act enhances FDA’s existing authority with respect to drug shortage measures. Under the CARES Act, we must have in place a risk management plan that identifies and evaluates the risks to the supply of approved drugs for certain serious diseases or conditions for each establishment where the drug or API is manufactured. The risk management plan will be subject to FDA review during an inspection. If we experience shortages in the supply of our marketed products, our results could be materially impacted.

If any CMO with whom we contract fails to perform its obligations, we may be forced to manufacture the materials ourselves, for which we may not have the capabilities or resources, or enter into an agreement with a different CMO, which we

may not be able to do on reasonable terms, if at all. In either scenario, our clinical trials or commercial distribution could be delayed significantly as we establish alternative supply sources. In some cases, the technical skills required to manufacture our products or biologic candidates may be unique or proprietary to the original CMO and we may have difficulty, or there may be contractual restrictions prohibiting us from, transferring such skills to a back-up or alternate supplier, or we may be unable to transfer such skills at all. In addition, if we are required to change CMOs for any reason, we will be required to verify that the new CMO maintains facilities and procedures that comply with quality standards and with all applicable regulations. We will also need to verify, such as through a manufacturing comparability study, that any new manufacturing process will produce our product according to the specifications previously submitted to or approved by the FDA or another regulatory authority. The delays associated with the verification of a new CMO could negatively affect our ability to develop biologic candidates or commercialize our products in a timely manner or within budget. Furthermore, a CMO may possess technology related to the manufacture of our biologic candidate that such CMO owns independently. This would increase our reliance on such a CMO or require us to obtain a license from such CMO in order to have another CMO manufacture our products or biologic candidates. In addition, in the case of the CMOs that supply our biologic candidates, changes in manufacturers often involve changes in manufacturing procedures and processes, which could require that we conduct bridging studies between our prior clinical supply used in our clinical trials and that of any new manufacturer. We may be unsuccessful in demonstrating the comparability of clinical supplies which could require the conduct of additional clinical trials.

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 biologics and biologic 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, diminution in quality of raw materials supplied to us 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 CMOs 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, 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 CMOs for compliance with applicable regulatory requirements. Any failure to follow and document our or our CMOs' 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 CMOs, pending resolution of regulatory deficiencies or suspensions could have a material adverse effect on our business, results of operations and financial condition.

Risks Related to Business Operations

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 biologic candidates successfully.

We are in the very early stages of building commercialization and distribution capabilities for bempegaldesleukin in the United States and Europe. To commercialize any of our biologic candidates 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 is both expensive and time consuming, or enter into arrangements with third parties to perform these services. For example, we have committed to co-commercialize bempegaldesleukin with BMS and establish global distribution and infrastructure for us to be able to book global revenue for bempegaldesleukin if it achieves regulatory approval. Establishing this commercialization capability requires a significant commitment of 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 management talent to lead key marketing and distribution roles;
- our inability to recruit and retain adequate numbers of effective sales and marketing personnel;
- the inability of sales personnel and medical science liaisons 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 biologic 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 biologic 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 biologic candidates 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 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 and execution. 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 biologic candidates. Our strategy also calls for us to undertake increased research and development activities and establish a commercial organization in collaboration with our partners, 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 dilutive financing arrangements on unfavorable terms.

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. 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. We would also incur substantial costs in building such capabilities before receiving regulatory approval of our products, which would have an adverse effect on our financial condition if our products are not ultimately approved.

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 research, development (including clinical testing), manufacturing, 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 awards 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.

Risks Related to Intellectual Property, Litigation and Regulatory Concerns

We may not elect or be able to take advantage of any expedited development or regulatory review and approval processes available to biologic candidates granted Breakthrough Therapy designation by the FDA.

We intend to evaluate and continue ongoing discussions with the FDA on regulatory strategies that could enable us to take advantage of expedited development pathways for certain of our biologic candidates, although we cannot be certain that our biologic candidates will qualify for any expedited development pathways or that regulatory authorities will grant, or allow us to maintain, the relevant qualifying designations.

Breakthrough Therapy designation is intended to expedite the development and review of biologic candidates that are designed to treat serious or life-threatening diseases when preliminary clinical evidence indicates that the biologic may demonstrate substantial improvement over existing therapies on one or more clinically significant endpoints, such as substantial treatment effects observed early in clinical development. The designation of a biologic candidate as a Breakthrough Therapy provides potential benefits that include more frequent meetings with FDA to discuss the development plan for the biologic candidate and ensure collection of appropriate data needed to support approval; more frequent written correspondence from FDA about such things as the design of the proposed clinical trials and use of biomarkers; intensive guidance on an efficient drug development program, beginning as early as Phase 1; organizational commitment involving senior managers; and eligibility for rolling review and priority review.

Although bempegaldesleukin in combination with Opdivo® received Breakthrough Therapy designation for the treatment of patients with previously untreated unresectable or metastatic melanoma, we may elect not to pursue Breakthrough Therapy designation for our other biologic candidates, and the FDA has broad discretion whether or not to grant these designations.

Accordingly, even if we believe a particular biologic candidate is eligible for Breakthrough Therapy, we cannot be assured that the FDA would decide to grant it. Breakthrough Therapy designation does not change the standards for biologic approval, and there is no assurance that such designation will result in expedited review or approval or that the approved indication will not be narrower than the indication covered by the Breakthrough Therapy designation. Thus, even though we have received Breakthrough Therapy designation for bempegaldesleukin in combination with Opdivo®, we may not experience a faster development process or review, and, upon any filing seeking regulatory approval, we may not obtain an approval from the FDA for bempegaldesleukin or any of our other biologic candidates.

If we or our partners do not obtain regulatory approval for our biologic 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 biologic 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. Biologic 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. For example, although the FDA granted a Breakthrough Therapy designation to bempegaldesleukin in combination with Opdivo® for the treatment of patients with previously untreated unresectable or metastatic melanoma, there is no guarantee regulatory approval will follow, if at all, for this or any indication of bempegaldesleukin on a timely basis. 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. 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 biologic candidate. In addition, undesirable side effects caused by our biologic 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 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®, which could reduce our future royalties from sales 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 drug candidates, any product marketing limitations or a product withdrawal would negatively impact our business, results of operations and financial condition.

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

- 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 biologic 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, we could be subject to substantial liabilities, which would 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.

We may not be able to obtain intellectual property licenses related to the development of our biologic 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 rights will be considered relevant to our or our collaboration partners' technology or biologic 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 sufficiency of the scope and adequacy of these licenses is very uncertain in view of the 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 to avoid a need to secure a license. 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 biologic, 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 310 U.S. and 1,200 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, re-examinations 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 prior to the commercialization of the biologic. Moreover, even if a patent encompassing a biologic has not expired prior to the biologic's commercialization, the patent may only provide a short period of protection following the commercialization of products. In addition, our patents may be subject to post grant proceedings, such as or *inter partes* review and re-examinations, before the U.S. Patent and Trademark Office (or equivalent proceedings in other jurisdictions), 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 biologic candidates. There can be no assurance that the patent applications for which we apply will 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 and other unpatented proprietary rights 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 (or if we cannot secure product liability insurance), 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 biologic candidates, if approved, 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 biologic 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. A person or entity does not need to have actual knowledge of the federal Anti-Kickback Statute or specific intent to violate it to have committed a violation. On December 2, 2020, the Office of Inspector General, or

OIG, published further modifications to the federal Anti-Kickback Statute. Under the final rules, OIG added safe harbor protections under the Anti-Kickback Statute for certain coordinated care and value-based arrangements among clinicians, providers, and others. This rule (with exceptions) became effective January 19, 2021. Implementation of this change and new safe harbors for point-of-sale reductions in price for prescription pharmaceutical products and pharmacy benefit manager service fees are currently under review by the Biden administration and may be amended or repealed. We continue to evaluate what effect, if any, the rule will have on our business;

- federal civil and criminal false claims laws and civil monetary penalty laws, such as the U.S. federal False Claims Act (FCA), 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. In addition, the government may assert that a claim including items and services resulting from a violation of the federal Anti-Kickback Statute constitutes a false or fraudulent claim for purposes of the FCA. Manufacturers can be held liable under the federal False Claims Act even when they do not submit claims directly to government payers if they are deemed to "cause" the submission of false or fraudulent claims. The federal False Claims Act also permits a private individual acting as a "whistleblower" to bring actions on behalf of the federal government alleging violations of the federal False Claims Act and to share in any monetary recovery;
- 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;
- the 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 (currently defined to include doctors, dentists, optometrists, podiatrists and chiropractors) 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, effective January 1, 2022, these reporting obligations will extend to include transfers of value made to certain non-physician assistants and nurse practitioners;
- 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 also includes the Final Omnibus Rule published in January 2013, which impose requirements on certain covered healthcare providers, health plans, and healthcare clearinghouses as well as their respective business associates, independent contractors or agents of covered entities, that perform services for them that involve the creation, maintenance, receipt, use, or disclosure of, individually identifiable health information relating to the privacy, security and transmission of individually identifiable health information. HITECH also created new tiers of civil monetary penalties, amended HIPAA to make civil and criminal penalties directly applicable to business associates, and gave state attorneys general new authority to file civil actions for damages or injunctions in federal courts to enforce the federal HIPAA laws and seek attorneys' fees and costs associated with pursuing federal civil actions. In addition, there may be additional federal, state and non-U.S. laws which govern the privacy and security of health and other personal information in certain circumstances, many of which differ from each other in significant ways and may not have the same effect, thus complicating compliance efforts;
- federal government price reporting laws, which require us to calculate and report complex pricing metrics in an accurate and timely manner to government programs;
- federal consumer protection and unfair competition laws, which broadly regulate marketplace activities and activities that potentially harm consumers; and
- additionally, 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. These state-equivalent laws may also apply to our business practices, including, but not limited to, research, distribution, and sales or marketing arrangements. In addition, some states have passed laws that require pharmaceutical companies to comply with the April 2003 Office of Inspector General Compliance Program Guidance for Pharmaceutical Manufacturers and/or the Pharmaceutical Research and Manufacturers of America's Code on Interactions with Healthcare Professionals. Several states also impose other marketing restrictions or require pharmaceutical companies to make marketing or price disclosures to the state and require the registration of pharmaceutical sales.

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 administrative, civil or criminal penalties, imprisonment, 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.

Disruptions to the normal functioning of the FDA and other government agencies could hinder their ability to perform and carry out important roles and activities on which the operation of our business relies, which could negatively impact our business.

The ability of the FDA to review and approve new products can be affected by a variety of factors, including government budget and funding levels, ability to hire and retain key personnel and accept the payment of user fees, and statutory, regulatory, and policy changes. Average review times at the agency have fluctuated in recent years as a result. In addition, government funding of other agencies on which our operations may rely is subject to the political process, which is inherently fluid and unpredictable. Since March 2020 when foreign and domestic inspections of facilities were largely placed on hold due to the COVID-19 pandemic, the FDA has been working to resume routine surveillance, bioresearch monitoring and pre-approval inspections on a prioritized basis. The FDA has developed a rating system to assist in determining when and where it is safest to conduct prioritized domestic inspections. In April 2021, the FDA issued guidance for industry formally announcing plans to employ remote interactive evaluations, suing risk management methods, to meet user fee commitments and goal dates. Should FDA determine that an inspection is necessary for approval and an inspection cannot be completed during the review cycle due to restrictions on travel, and the FDA does not determine a remote interactive evaluation to be appropriate, FDA has stated that it generally intends to issue a complete response letter. Further, if there is inadequate information to make a determination on the acceptability of a facility, FDA may defer action on the application until an inspection can be completed. Regulatory authorities outside the U.S. may adopt similar restrictions or other policy measures in response to the COVID-19 pandemic and may experience delays in their regulatory activities.

Disruptions at the FDA and other agencies may also slow the time necessary for new drugs to be reviewed and/or approved by necessary government agencies, which would adversely affect our business. For example, over the last several years the U.S. government has shut down several times and certain regulatory agencies, such as the FDA, have had to furlough critical FDA and other government employees and stop critical activities. Additionally, as of June 23, 2020, the FDA noted it is continuing to ensure timely reviews of applications for medical products during the COVID-19 pandemic in line with its user fee performance goals. On July 16, 2020, the FDA noted that it is continuing to expedite oncology product development with its staff teleworking full-time. However, the FDA may not be able to continue its current pace and review timelines could be extended, including where a pre-approval inspection or an inspection of clinical sites is required and due to the COVID-19 pandemic and travel restrictions the FDA is unable to complete such required inspections during the review period. If a prolonged government shutdown occurs, it could significantly impact the ability of the FDA to timely review and process our regulatory submissions, which could have a material adverse effect on our business. Further, future shutdowns of other government agencies, such as the SEC, may also impact our business through review of our public filings and our ability to access the public markets.

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, 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. 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 biologic 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. For example, we are involved in ongoing litigation with Aether Therapeutics Inc., who in March 2020 filed a complaint against AstraZeneca, Nektar and Daiichi-Sanko, Inc. alleging that MOVANTIK® infringes U.S. Patent Nos. 6,713,488, 8,748,448, 8,883,817 and 9,061,024. 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. We are also regularly involved in opposition proceedings at the European Patent Office and in *inter partes* review and re-examination proceedings at the U.S. Patent and Trademark Office where third parties

seek to invalidate or limit the scope of our allowed patent applications or issued patents covering (among other things) our biologic candidates and platform technologies. 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 biologics or biologic 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.

From time to time, we are involved in legal proceedings other than those related to intellectual property. In October 2018, we and certain of our executives were named in a putative securities class action complaint filed in the U.S. District Court for the Northern District of California (Case No. 18-cv-06607, which we refer to as the Mulquin action). The Mulquin plaintiffs have challenged public statements Nektar made, between January 2017 and June 2018, about clinical trials of bempegaldesleukin. In December 2020, the court dismissed the action with prejudice. The plaintiffs filed a notice of appeal in January 2021 and appellate briefing in the U.S. Court of Appeals for the Ninth Circuit was completed in September 2021. Oral argument was held on December 10, 2021.

In February 2021, a derivative action was filed against certain of the Company's current and former officers and directors in the Court of Chancery of the State of Delaware (C.A. No. 2021-0118-PAF) alleging that the Company's officers and directors breached their fiduciary duties by exposing the Company to securities actions. The parties agreed to stay further proceedings in this action until thirty days after the U.S. Court of Appeal for the Ninth Circuit's final resolution of the appeal in the Mulquin action.

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. There is no guarantee that our insurance coverage for damages resulting from a litigation or the settlement thereof (including the Mulquin action and related shareholder derivative lawsuit) is sufficient, thereby resulting in substantial financial risk to the Company.

Given the nature of lawsuits and complaints, we cannot reasonably estimate a potential future loss or a range of potential future losses for any of the legal proceedings we are currently involved in. However, an unfavorable resolution could potentially have a material adverse effect on our business, financial condition, and results of operations or prospects, and potentially result in paying monetary damages. We have recorded no liability for these matters in our Consolidated Balance Sheets at December 31, 2021.

If we are found in violation of privacy and data protection laws, we may be required to pay penalties, be subjected to scrutiny by regulators or governmental entities, or be suspended from participation in government healthcare programs, which may adversely affect our business, financial condition and results of operations.

Our business is subject to many laws and regulations intended to protect the privacy and data of individuals participating in our clinical trials and our employees, among others. For example, with regard to individuals participating in our clinical trials, these laws and regulations govern the safeguarding the privacy, integrity, availability, security and transmission of individually identifiable health information. In addition to federal laws and regulations in the United States, such as the HIPAA requirements relating to the privacy, security and transmission of individually identifiable health information, many state and foreign laws also govern the privacy and security of health information. These laws often differ from each other in significant ways, thus complicating compliance efforts. The global data protection landscape is rapidly evolving, and implementation standards and enforcement practices are likely to remain uncertain for the foreseeable future.

In the United States, California recently enacted the California Consumer Privacy Act (CCPA), which took effect on January 1, 2020. The CCPA gives California residents expanded rights to access and delete their personal information, opt out of certain personal information sharing, and receive detailed information about how their personal information is used. The CCPA provides for civil penalties for violations, as well as a private right of action for data breaches that is expected to increase data breach litigation. The CCPA has increased our compliance costs and may increase our potential liability. The CCPA has prompted a number of proposals for new federal and state privacy legislation. If passed, these proposals could increase our potential liability, increase our compliance costs and adversely affect our business.

The European Regulation 2016/679, known as the General Data Protection Regulation (GDPR), and the implementing legislation of EU Member States, which became effective on May 25, 2018, apply to the collection and processing of personal data, including health-related information, by companies located in the EU, or in certain circumstances, by companies located outside of the EU and processing personal information of individuals located in the EU. The GDPR is wide-ranging in scope and imposes strict obligations on the ability to process personal data, including health-related information, in particular in relation to their collection, use, disclosure and transfer. These include several requirements relating to, for example, (i)

obtaining, in some situations, the consent of the individuals to whom the personal data relates, (ii) the information provided to the individuals about how their personal information is used, and (iii) ensuring the security and confidentiality of the personal data. The GDPR prohibits the transfer of personal data to countries outside of the European Economic Area (EEA), such as the United States, which are not considered by the European Commission to provide an adequate level of data protection. Potential pecuniary fines for noncompliant companies may be up to the greater of €20 million or 4% of annual global revenue.

To the extent that we are found liable for the inappropriate collection, storage, use or disclosure of protected information of individuals (such as employees and or clinical patients protected by any privacy or data protection law), we could be subject to reputational harm, monetary fines (such as those imposed by the GDPR and CCPA), civil suits, civil penalties or criminal sanctions and requirements to disclose the breach, and the development of our biologic candidates could be delayed. In addition, we continue to be subject to new and evolving data protection laws and regulations from a variety of jurisdictions, and there is a risk that our systems and processes for managing and protecting data may be found to be inadequate, which could materially adversely affect our business, financial condition and results of operations.

Our operations may involve hazardous materials and are subject to environmental, health, and safety laws and regulations. Compliance with these laws and regulations is costly, and we may incur substantial liability arising from our activities involving the use of hazardous materials.

As a research-based biopharmaceutical company with significant research and development and manufacturing operations, we are subject to extensive environmental, health, and safety laws and regulations, including those governing the use of hazardous materials. Our research and development and manufacturing activities involve the controlled use of chemicals, radioactive compounds, and other hazardous materials. The cost of compliance with environmental, health, and safety regulations (including, but not limited to, the handling and disposal of both our hazardous and non-hazardous waste) is substantial. If an accident involving these materials or an environmental discharge were to occur, we could be held liable for any resulting damages, or face regulatory actions, which could exceed our resources or insurance coverage.

Risks Related to Investment and Securities

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 and shareholder derivative litigation.

Our stock price is volatile. During the year ended December 31, 2021, based on closing prices on the NASDAQ Global Select Market, the closing price of our common stock ranged from $10.83 to $25.46 per share. In response to volatility in the price of our common stock in the past, plaintiffs' securities litigation firms have sought information from us and/or shareholders as part of their investigation into alleged securities violations and breaches of duties (among other corporate misconduct allegations). Following their investigations, plaintiffs' securities litigation firms have often initiated legal action, including the filing of class action lawsuits, derivative lawsuits, and other forms of redress. We expect our stock price to remain volatile and we continue to expect the initiation of legal actions by plaintiffs' securities litigation firms following share price fluctuations. 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 bempegaldesleukin has had a significant impact on our stock price;
- the timing of outcomes from our clinical trials which can be difficult to predict particularly for clinical studies that have event-driven end points such as progression-free survival and overall survival;
- announcements by collaboration partners as to their plans or expectations related to biologic candidates and approved biologics 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 partnered 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.

General Risk Factors

We significantly rely on information technology systems, and any failure, inadequacy, interruption, breach, or security lapse of that technology within our internal computer systems, or those of our partners, vendors, CROs, CMOs or other contractors or consultants, may result in a material disruption of our development programs and our operations.

As part of our business, we collect, store and transmit large amounts of confidential information, proprietary data, intellectual property and personal data. Despite the implementation of security measures, our internal computer systems and those of our partners, vendors, contract research organizations (CROs), contract manufacturing organizations (CMOs) and other contractors and consultants are vulnerable to loss, damage, denial-of-service, unauthorized access, or misappropriation. Such cybersecurity breaches may be the result of unauthorized activity by our employees and contractors, as well as by third parties who use cyberattack techniques involving malware, hacking and phishing, among others. Additionally, the risk of cyber-attacks or other privacy or data security incidents may be heightened as a result of an increase in the number of employees adopting a remote working environment during the COVID-19 pandemic, which may be less secure and more susceptible to hacking attacks. Our information technology systems, and those of our partners, vendors, CROs, CMOs or other contractors or consultants are also vulnerable to natural disasters, terrorism, war and telecommunication and electrical failures. Any such compromise or disruption, no matter the origin, may cause an interruption of our operations. For instance, the loss of preclinical data or data from any clinical trial involving our biologic candidates could result in delays in our development and regulatory filing efforts and significantly increase our costs. In addition, the loss, corruption or unauthorized disclosure of our trade secrets, personal data or other proprietary or sensitive information could compromise the commercial viability of one or more of our programs, which would negatively affect our business. Also, the costs to us to investigate and mitigate cybersecurity incidents could be significant.

Changes in tax law could adversely affect our business and financial condition.

Our business is subject to numerous international, federal, state, and other governmental laws, rules, and regulations that may adversely affect our operating results, including, taxation and tax policy changes, tax rate changes, new tax laws, or revised tax law interpretations, which individually or in combination may cause our effective tax rate to increase. In the U.S., the rules dealing with federal, state, and local income taxation are constantly under review by persons involved in the legislative process and by the Internal Revenue Service and the U.S. Treasury Department. Changes to tax laws (which changes may have

retroactive application) could adversely affect us or holders of our common stock. In recent years, such changes have been made and changes are likely to continue to occur in the future. For example, on March 27, 2020, the CARES Act was signed into law and included certain changes in tax law intended to stimulate the U.S. economy in light of the COVID-19 pandemic, including temporary changes to the treatment of net operating losses, interest deductibility limitations and payroll tax matters. Future changes in tax laws could have a material adverse effect on our business, cash flow, financial condition or results of operations.

The United Kingdom's withdrawal from the EU may have a negative effect on global economic conditions, access to patient markets, and regulatory certainty, which could adversely affect our operations.

Effective January 31, 2020, the U.K. ceased to be a member state of the EU, a process known as Brexit, and began a transition period, which expired on December 31, 2020.

In December 2020, the U.K. and the EU agreed on a trade and cooperation agreement, under which the EU and the U.K. will now form two separate markets governed by two distinct regulatory and legal regimes. The trade and cooperation agreement covers the general objectives and framework of the relationship between the U.K. and the EU, including as it relates to trade, transport and visas. Under the trade and cooperation agreement, U.K. service suppliers no longer benefit from automatic access to the entire EU single market, U.K. goods no longer benefit from the free movement of goods and there is no longer the free movement of people between the U.K. and the EU. Depending on the application of the terms of the trade and cooperation agreement, we, our collaboration partners and others could face new regulatory costs and challenges.

Global economic and political 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, including, for example, adverse global economic conditions resulting from the COVID-19 pandemic. See also the risk factor in this Item 1A titled "*Our business could be adversely affected by the effects of health epidemics, including the recent COVID-19 pandemic.*" In addition, our operations and performance may be affected by political or civil unrest or military action, including the current conflict between Russia and Ukraine, terrorist activity, unstable governments and legal systems. 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. Our ability to conduct clinical trials in regions experiencing political or civil unrest could negatively affect clinical trial enrollment or the timely completion of a clinical trial. We believe the aforementioned economic 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, with rising international trade tensions or sanctions, our business may be adversely affected following new or increased tariffs that result in increased global clinical trial costs as a result of international transportation of clinical drug supplies, as well as the costs of materials and products imported into the U.S. 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.

Our business could be negatively impacted by corporate citizenship and sustainability matters.

There is an increased focus from certain investors, employees, and other stakeholders concerning corporate citizenship and sustainability matters, which include environmental concerns and social investments. We could fail to meet, or be perceived to fail to meet, the expectations of these certain investors, employees and other stakeholders concerning corporate citizenship and sustainability matters, thereby resulting in a negative impact to our business.

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 biologic 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 collaboration partners and important vendors and suppliers to us or our collaboration partners may also be subject to catastrophic events, such as earthquakes, floods, hurricanes, tornadoes and pandemics any of which could harm our business (including, for example, by disrupting supply chains important to the success of 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 155,215 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.

We also lease 135,936 square feet of office space in San Francisco (the Third Street Facility), under an operating lease which expires in 2030. The Third Street Facility provides additional space to support our research and development activities.

Alabama

We currently own a facility consisting of approximately 124,000 square feet in Huntsville, Alabama, which houses 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.

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 2024.

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. With respect to ongoing securities class action and shareholder derivative litigation, please refer to Note 9 to our Consolidated Financial Statements and Item 1A. Risk Factors, including without limitation, “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.”

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."

Holders of Record

As of February 23, 2022, there were approximately 153 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, 2021.

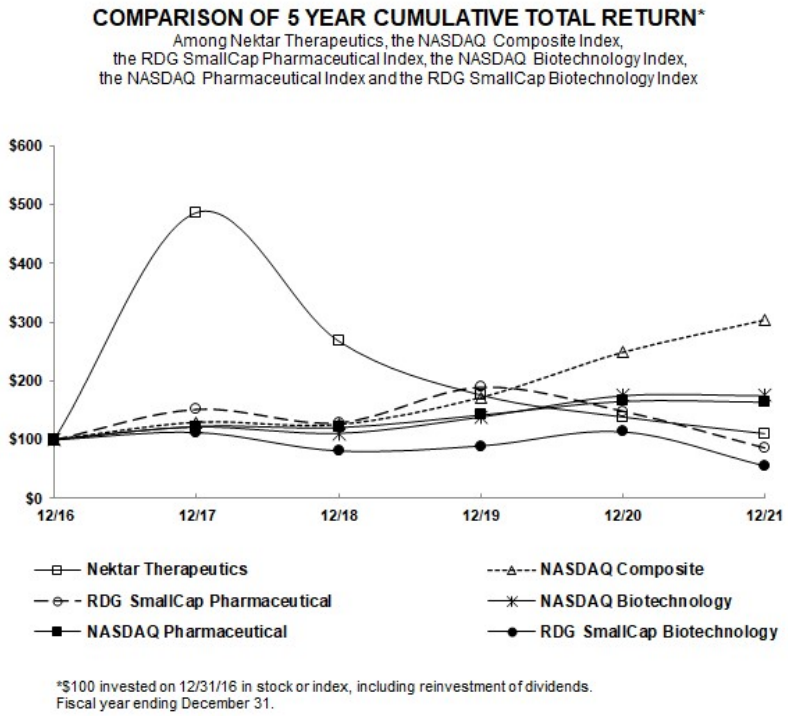
Securities Authorized for Issuance Under Equity Compensation Plans

Information regarding our equity compensation plans as of December 31, 2021 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 2022 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, 2021, 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, 2017, December 31, 2018, December 31, 2019, December 31, 2020 and December 31, 2021. The graph assumes that $100 was invested on December 31, 2016 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. Reserved

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

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."

Overview

Strategic Direction of Our Business

Nektar Therapeutics is a research-based biopharmaceutical company that discovers and develops innovative new medicines in areas of high unmet medical need. Our research and development pipeline of new investigational drugs includes potential therapies for oncology, immunology and virology. 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 new drug discovery and advancing our pipeline of drug candidates as we believe that this is the best strategy to build long-term stockholder value.

In oncology, we focus on developing medicines in immuno-oncology (I-O), which is a therapeutic approach based on targeting biological pathways that stimulate and sustain the body's immune response in order to fight cancer. In the I-O area, we are executing a broad clinical development program evaluating bempegaldesleukin (previously referred to as NKTR-214).

We are developing bempegaldesleukin in combination with Opdivo®, in collaboration with Bristol-Myers Squibb Company (BMS) as well as other independent development work evaluating bempegaldesleukin in combination with other checkpoint inhibitors and agents with potential complementary mechanisms of action. In August of 2019, the FDA granted a Breakthrough Therapy designation for bempegaldesleukin in combination with Opdivo® for the treatment of patients with untreated unresectable or metastatic melanoma. We expect to continue to make substantial research and development investments as we execute our broad clinical development program for bempegaldesleukin.

On February 13, 2018, we entered into a Strategic Collaboration Agreement with BMS (as amended to date, the BMS Collaboration Agreement) that outlined a collaboration for the development and co-commercialization of bempegaldesleukin in combination regimens with BMS medicines including Opdivo®. Under the joint development portion of the arrangement, we and BMS share development costs based on each party's relative ownership interest in the compounds included in the regimen. For example, we share clinical development costs for bempegaldesleukin in combination with Opdivo®, with 67.5% to BMS and 32.5% to Nektar. For costs of manufacturing bempegaldesleukin, however, BMS is responsible for 35% and Nektar is responsible for 65% of costs. BMS supplies Opdivo® free of charge.

The Collaboration Development Plan is evaluating bempegaldesleukin in combination with Opdivo® in ongoing registrational trials in first-line metastatic melanoma, adjuvant melanoma, first-line cisplatin ineligible, PD-L1 low, locally advanced or metastatic urothelial cancer, first-line metastatic renal cell carcinoma (RCC), and muscle-invasive bladder cancer, as well as a Phase 1/2 dose escalation and expansion study to evaluate bempegaldesleukin plus Opdivo® in combination with either axitinib or cabozantinib in first line RCC in order to support a future Phase 3 registrational trial. Several other registrational-supporting pediatric and safety studies for the combination of bempegaldesleukin and Opdivo® are currently ongoing. For indications not included in the Collaboration Development Plan, the parties are free to develop their own medicines in other indications subject to certain cost sharing, premium reimbursement, and timing terms and conditions.

Under our collaboration, we have received $1.9 billion from BMS, including a $1.0 billion upfront payment and an $850.0 million equity investment upon the effective date of the arrangement in 2018 and $50.0 million in milestones for the initiation of two registrational trials in 2020. The BMS Collaboration Agreement entitles Nektar to receive up to $1.4 billion of potential future milestones for the acceptance of our regulatory submissions and commercial launch of bempegaldesleukin in the US, EU and Japan in up to four indications.

If the results of one or more of our registrational trials in bempegaldesleukin in combination with Opdivo® meet their primary endpoints, we are entitled to milestones of $35.0 million and $25.0 million for the acceptance of our Biologics License Application (BLA) with the US Food and Drug Administration (FDA) and Marketing Authorisation Application (MAA) with the European Medicines Agency (EMA), respectively, for bempegaldesleukin in the first indication and $30.0 million in aggregate per indication for the acceptance of our BLA and MAA in up to three additional indications. If approved, we are entitled to milestones of $250.0 million in the US and $250.0 million in the European Union (EU) for the first commercial sale of bempegaldesleukin in the first indication and $100.0 million in each of the US and EU for the first commercial sale of bempegaldesleukin in up to three additional indications. As a result, whether and when bempegaldesleukin is approved in any indication will have a significant impact on our future results of operations and financial condition.

On January 12, 2022, we and BMS entered into an Amendment No. 2 to the BMS Collaboration Agreement pursuant to which we and BMS allocated certain responsibilities related to price negotiations and promotion, market access, patient support and related activities to each party. We retain the final decision-making authority regarding the pricing for bempegaldesleukin. Bempegaldesleukin 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. We and BMS will share global commercialization profits and losses for bempegaldesleukin, with Nektar sharing 65% and BMS sharing 35% of the net profits and losses. Each party bears their own non-product specific core commercialization infrastructure costs.

Outside of the Collaboration Development Plan with BMS, we are conducting and pursuing additional I-O research and development activities evaluating bempegaldesleukin in combination with other agents that have potential complementary mechanisms of action. Our strategic objective is to establish bempegaldesleukin as a key component of many I-O combination regimens with the potential to enhance the standard of care in multiple oncology settings. For example, we are independently studying bempegaldesleukin in combination with Keytruda® in a non-small cell lung cancer (NSCLC) Phase 1/2 trial. In addition, on February 12, 2021, we entered into a financing and co-development collaboration with SFJ Pharmaceuticals to support a Phase 2/3 registrational clinical study of bempegaldesleukin plus Keytruda® in patients with head and neck cancer whose tumors express PD-L1. We expect to continue to make significant and increasing investments exploring the potential of bempegaldesleukin with mechanisms of action that we believe are synergistic with bempegaldesleukin based on emerging clinical development outcomes, scientific findings in cancer biology and preclinical development work.

With our non-BMS clinical collaborations for bempegaldesleukin, generally each party supports the collaboration based on its expertise and resources. For example, our co-development collaboration agreement with SFJ includes both

financial support from SFJ in the form of up to $150.0 million to fund the Phase 2/3 registrational clinical study of bempegaldesleukin plus Keytruda® in head and neck cancer, as well as operational support from SFJ in managing the clinical trial. In addition, we announced on February 17, 2021, that we had entered into a clinical trial collaboration and supply agreement with Merck wherein we will receive supplies of Keytruda® at no cost to us.

Our next most advanced I-O program is NKTR-255. NKTR-255 is a biologic that targets the IL-15 pathway in order to activate the body's innate and adaptive immunity. Activation 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. Recombinant human IL-15 is rapidly cleared from the body and must be administered frequently and in high doses limiting its utility due to toxicity. Through optimal engagement of the IL-15 receptor complex, NKTR-255 is designed to enhance functional NK cell populations and formation of long-term immunological memory, which may lead to sustained and durable anti-tumor immune response. Preclinical findings suggest NKTR-255 has the potential to synergistically combine with antibody-dependent cellular toxicity molecules as well as to enhance CAR-T therapies. We have initiated a Phase 1 dose escalation and expansion clinical study of NKTR-255 in adults with relapsed or refractory non-Hodgkin lymphoma or multiple myeloma, as well as a Phase 1/2 clinical study of NKTR-255 in patients with relapsed or refractory head and neck squamous cell carcinoma or colorectal cancer. In addition, we announced on September 21, 2021, that we had entered into a new oncology clinical collaboration with Merck KGaA Darmstadt, Germany and Pfizer Inc. to evaluate the maintenance regimen of NKTR-255 in combination with avelumab, a PD-L1 inhibitor, in patients with locally advanced or metastatic urothelial carcinoma in the Phase II JAVELIN Bladder Medley study.

We are also conducting studies of bempegaldesleukin in combination with NKTR-262. 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, 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 bempegaldesleukin to induce an abscopal response and achieve the goal of tumor regression in cancer patients treated with both therapies. The Phase 1/2 dose-escalation and expansion trial in patients with solid tumors is currently ongoing.

In immunology, NKTR-358 targets 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 develop and commercialize NKTR-358, pursuant to which we received an initial payment of $150.0 million and are eligible for up to an additional $250.0 million for development and regulatory milestones. We have completed our responsibilities for Phase 1 clinical development and certain drug product development and supply activities. We also share Phase 2 development costs with Lilly, with Lilly responsible for 75% and Nektar responsible for 25% of these costs. 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 and receive a royalty rate on global NKTR-358 sales up to the low twenties 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.

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. We also completed treatment of a Phase 1 multiple-ascending dose trial to evaluate NKTR-358 in patients with systemic lupus erythematosus (SLE). Lilly is conducting two Phase 1b studies in patients with psoriasis and atopic dermatitis, and initiated a Phase 2 study in SLE in October 2020 and a Phase 2 study in ulcerative colitis in March 2021. In addition, based on positive interim Phase 1b results in atopic dermatitis announced in December 2021, Lilly is planning to initiate a Phase 2 study in that indication and also plans to initiate another Phase 2 study in another immune-mediated disease.

In virology, we have studied bempegaldesleukin in a Phase 1b clinical study in adult patients who had been diagnosed with mild COVID-19 infection to evaluate whether bempegaldesleukin's adaptive immune-stimulating mechanism to promote priming and proliferation of T cells and NK cells could be useful in the emerging treatment options for COVID-19. We also have a preclinical research collaboration with Gilead to test the combination of NKTR-255 with therapies in Gilead's antiviral portfolio.

The level of our future research and development investment will depend on a number of trends and uncertainties including clinical study 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. Over the next several years, we plan to continue to make significant investments to advance our early drug candidate pipeline.

We have historically derived all of our revenue and substantial amounts of operating capital from our collaboration agreements. In addition to our collaborations with BMS and Lilly, we have received upfront and milestone payments under a

number of other previous collaboration agreements, several of which have resulted in approved drugs, for which we may continue to manufacture the polymer reagents used in the production of the drug products and may be entitled to royalties for net sales of these approved drugs. As of December 31, 2020, however, we have sold the majority of our rights to receive royalties under these arrangements, including:

- 2012 Purchase and Sale Agreement: In 2012, we sold all of our rights to receive royalties from CIMZIA® (for the treatment of Chron's disease and other autoimmune indications) and MIRCERA® (for the treatment of anemia associated with chronic kidney disease) under our collaborations with UCB Pharma and F. Hoffmann-La Roche Ltd, respectively, to RPI Finance Trust (RPI), an affiliate of Royalty Pharma for $124.0 million.
- 2020 Purchase and Sale Agreement: In December 2020, we sold our rights, subject to a cap, to receive royalties from MOVANTIK® / MOEVNTIG® (for the treatment of opioid-induced constipation), ADYNOVATE® / ADYNOVI® (a half-life extension product of Factor VIII) and other hemophilia products, under our arrangements with AstraZeneca AB, Baxalta, Inc. (a wholly owned-subsidiary of Takeda Pharmaceutical Company Ltd.), and Novo Nordisk A/S, respectively, for $150.0 million to entities managed by HealthCare Royalty Management (HCR) under a capped sale arrangement, such that all future royalties return to Nektar if HCR receives $210.0 million in royalties by December 31, 2025 (the 2025 Threshold) or $240.0 million if the 2025 Threshold is not met. See Note 8 to our Consolidated Financial Statements for a further description of the capped nature of this agreement.

While in the near-term we continue to expect to generate substantially all of our revenue from collaboration arrangements, including the potential remaining $1.4 billion in regulatory and commercial launch milestones under the BMS collaboration, our plan is to generate significant commercial revenue from proprietary products, the first of which being bempegaldesleukin, if approved. Since we do not have experience commercializing products or an established commercial organization, there will be substantial risks and uncertainties in future years as we build commercial, organizational, and operational capabilities.

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".

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 clinical trials in future years. We are also advancing several other drug candidates in preclinical development in the areas of I-O, 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 with a high risk of failure at every stage prior to approval. 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.

Effects of the COVID-19 Pandemic

In March 2020, COVID-19, the disease resulting from a novel strain of coronavirus infection, was declared a global pandemic. Many countries, including the United States and India, initially took steps such as restricting travel, closing schools, and issuing shelter-in-place orders to slow or moderate the spread of the virus. More recently, states and countries have adopted individualized approaches to respond to the COVID-19 pandemic. In particular, the emergence of new variants of the coronavirus, such as the Delta and Omicron variants, and local resurgences in number and rates of infections, and the further spread of the virus may result in the return of prior restrictions or the institution of restrictions in the affected areas, which could have an adverse effect on our business, including our clinical trial timelines. We have been monitoring our supply chains for any disruptions or constraints caused by the COVID-19 pandemic. To date, we have not experienced any significant impacts on our supply, but ongoing global shortages in labor, raw materials and equipment could limit our ability to manufacture our products or to supply drug candidates for our clinical trials, or delay our research and development efforts. It remains unclear how long the negative impacts caused by the coronavirus will continue into the future.

Currently, our operations in research, manufacturing and maintenance that occur within our facilities are continuing in accordance with applicable guidelines and orders. Across all our locations, we have instituted a temporary work from home policy for office personnel who do not need to work on site to maintain productivity and we allow employees to voluntarily return to work on site with appropriate health and safety measures. The safety and well-being of our employees, and the patients

and healthcare providers in our clinical trial programs, are of first and foremost importance to us. We believe that the safety measures we are taking and instructing our contractors to take in response to the COVID-19 pandemic meet or exceed the guidance and requirements issued from government and public health officials. We continue to monitor our operations and applicable government recommendations in light of new developments in the ongoing COVID-19 pandemic.

We and our partners are currently engaged in the clinical testing of our drug candidates and the COVID-19 pandemic introduces significant challenges to our clinical development programs which are central to our business. The evolving situation around the COVID-19 pandemic, along with the resulting public health guidance measures that have been put into place, have thus far had varying impacts on the clinical testing of our drug candidates depending on the therapeutic indication, geographic distribution of clinical trial sites, the clinical trial stage, and, in certain cases, our partners' general corporate approach to the COVID-19 pandemic. Any current assessments of the effects of the COVID-19 pandemic on our clinical programs, including the specific clinical programs discussed below, are difficult to predict and subject to change and, with regard to individual clinical trial sites within these studies, will likely vary by the geographic region in which they are located.

The COVID-19 pandemic has not had a significant impact on timelines for the ongoing registrational clinical trials studying the combination of bempegaldesleukin and Opdivo® in cancer indications being led by Nektar (such as adjuvant melanoma, RCC and first-line cisplatin ineligible, PD-L1 low, locally advanced or metastatic urothelial cancer). We currently expect to have topline data readouts for our RCC and urothelial cancer trials in the first half of 2022. For Nektar's Phase 1/2 trial studying the combination of bempegaldesleukin and Keytruda® in NSCLC, although the COVID-19 pandemic delayed the initiation of certain investigator sites in Europe earlier in the trial, we presented initial safety as well as preliminary overall response rate data for the dose-escalation and 0.006 mg/kg NSCLC expansion cohorts of this study in the second half of 2021. We are closely monitoring the impact of the COVID-19 pandemic on the European and other ex-U.S. sites for any impact on timelines for the ongoing study. With regard to Nektar's ongoing Phase 1/2 clinical study of NKTR-262 in patients with solid tumors, this study largely remains on schedule although we experienced some initial challenges with new investigator site initiations. Nektar's Phase 1 clinical study of NKTR-255 in patients with relapsed/refractory hematologic malignancies has enrolled slower than anticipated due to ongoing challenges caused by the COVID-19 pandemic, and the dose-escalation monotherapy portion of the study is currently expected to be completed in the first half of 2022.

For clinical studies of our drug candidates being run by our partners, BMS is enrolling patients in each of the BMS-led registration studies and re-started initiation of new investigator sites in the third quarter of 2020 following a pause in the initiation of new investigator sites it instituted for all of its studies as a result of the COVID-19 pandemic. In the summer of 2020, BMS extended its timeline estimates by approximately six months for the first data read-outs for the first-line melanoma trial, which we currently expect to occur in the first half of 2022. The overall supply chain impact stemming from the COVID-19 pandemic delayed the start of the Phase 2b study of NKTR-358 in ulcerative colitis (UC), which is run by our partner Lilly and which Lilly is currently enrolling along with a Phase 2 study in moderate to severe lupus patients. Resource constraints at contract research organizations also caused some delays in data availability. While BMS and Lilly are not currently projecting any delays related to the COVID-19 pandemic, the rapid development and fluidity of the COVID-19 pandemic preclude any firm estimates as to the ultimate effect this disease will have on our collaborators' clinical trials. As a result, there remains substantial uncertainty as to potential impacts on our collaboration partner studies.

In an effort to mitigate the negative effects of the COVID-19 pandemic on our clinical trials (both in terms of clinical trial timelines and integrity of clinical study data), we have taken steps to help our clinical trial investigators and their teams continue to provide care and uninterrupted access to their patients. Particularly, in the context of our clinical trials directed to investigational cancer treatments, for example, we are actively working with our study sites to implement measures to prevent study protocol violations, to minimize any disruption of treatment visits, to accommodate for patient visit delays caused by limited access to healthcare facilities, to leverage alternative methods for maintaining clinical trial integrity, and to properly record patient event data that may be influenced by the COVID-19 pandemic. In addition, to the extent that the integrity of individual patient data is negatively affected by the COVID-19 pandemic, we will consider measures to maintain the integrity of the clinical study overall (such as over-enrolling patients into the study and removing all patients originating from an affected study site when performing statistical analyses of study endpoints). Although these measures may have the benefit of preserving the overall integrity of a clinical study, implementing these measures could result in a delay in completing the study.

With respect to financing our near-term business needs, as set forth below in "Key Developments and Trends in Liquidity and Capital Resources," we estimate we have working capital to fund our current business plans through at least the next twelve months.

Key Developments and Trends in Liquidity and Capital Resources

We estimate that we have working capital to fund our current business plans for at least the next twelve months from the date of filing. At December 31, 2021, we had approximately $798.8 million in cash and investments in marketable securities.

Results of Operations

Years Ended December 31, 2021 and 2020

The results of operations for the years ended December 31, 2021 and 2020 is presented below. Additional information required by Item 7 for the year ended December 31, 2019 can be found in Item 7 in our Annual Report on Form 10-K for the year December 31, 2020, filed with the SEC on February 26, 2021 and is incorporated herein by reference.

Revenue (in thousands, except percentages)

	Year Ended December 31,		Increase/ (Decrease)	Percentage Increase/ (Decrease)
	2021	2020	2021 vs. 2020	2021 vs. 2020
Product sales	$ 23,725	$ 17,504	$ 6,221	36 %
Royalty revenue	—	30,999	(30,999)	(100)%
Non cash royalty revenue related to sale of future royalties	77,746	48,563	29,183	60 %
License, collaboration and other revenue	436	55,849	(55,413)	(99)%
Total revenue	$ 101,907	$ 152,915	$ (51,008)	(33)%

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. We recognize revenue 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 development or 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.

As noted above, dependent on whether one of more of our registrational studies in bempegaldesleukin in combination with Opdivo® meet their primary endpoints, we may file a BLA and/or MAA for bempegaldesleukin in one or more indications. We are entitled to milestones of $35.0 million and $25.0 million for the acceptance of our BLA and MAA filings, respectively, for bempegaldesleukin in the first indication and $30.0 million in aggregate per indication for the acceptance of our BLA and MAA for up to three additional indications. If approved, we are entitled to milestones of $250.0 million in the US and $250.0 million in the EU for the first commercial sale of bempegaldesleukin in the first indication and $100.0 million in each of the US and EU for the first commercial sale of bempegaldesleukin in up to three additional indications.

Accordingly, the recognition of these milestones, if any, and product sales for bempegaldesleukin, if approved, is dependent upon the timing of the readouts of our registrational trials and, if the results are positive, the timelines for regulatory filing submissions and reviews.

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 increased for the year ended December 31, 2021, as compared to the year ended December 31, 2020, due to increased demand from our collaboration partners.

Other than the potential for sales of bempegaldesleukin, if approved and as described above, we expect product sales in 2022 to decrease compared to 2021 due to decreased demand from our collaboration partners.

Royalty Revenue

On December 16, 2020, we entered into the 2020 Purchase and Sale Agreement with HCR, under which we sold to HCR certain of our rights to receive royalty payments arising on worldwide net sales of MOVANTIK®, ADYNOVATE® and REBINYN® beginning October 1, 2020. As a result, we recognized royalty revenue for these products for the nine months ended September 30, 2020, and recognized these royalties as non-cash royalty revenue for the three months ended December

31, 2020 and for the year ended December 31, 2021. Please see Note 8 to our Consolidated Financial Statements for additional information on the 2020 Purchase and Sale Agreement.

We did not recognize any royalty revenue during 2021 because we recognized all such royalties as non-cash royalty revenue as a result of the 2020 Purchase and Sale Agreement, and we expect this presentation to continue through the end of the HCR royalty sale arrangement.

Non-cash Royalty Revenue Related to Sales of Future Royalties

For a discussion of our Non-cash royalty revenue, please see our discussion below "Non-Cash Royalty Revenue and Non-Cash Interest Expense."

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.

During the year ended December 31, 2020, pursuant to the BMS Collaboration Agreement, we recognized $25.0 million for the achievement of the first patient, first visit in the registrational muscle-invasive bladder cancer trial, which was achieved on January 30, 2020, and $25.0 million for the achievement of the first patient, first visit in the registrational adjuvant melanoma trial, which we achieved on July 27, 2020. We did not achieve any additional milestones during the year ended December 31, 2021.

Other than the potential for the recognition of milestones under our BMS Collaboration Agreement, we expect license, collaboration and other revenue for 2022 to be consistent with 2021.

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 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,	
	2021	2020
United States	$ 10,114	$ 64,966
Rest of World	91,793	87,949
Total revenue	$ 101,907	$ 152,915

Revenue attributable to the U.S. for the year ended December 31, 2021 was lower than for the year ended December 31, 2020 primarily due to the recognition of $50.0 million of milestones during the year ended December 31, 2020, from the BMS Collaboration Agreement as described above.

Cost of goods sold (in thousands, except percentages)

	Year Ended December 31,		Increase/ (Decrease) 2021 vs. 2020	Percentage Increase/ (Decrease) 2021 vs. 2020
	2021	2020		
Cost of goods sold	$ 24,897	$ 19,477	$ 5,420	28 %
Product gross profit (loss) (1)	$ (1,172)	$ (1,973)	$ 801	41 %
Product gross margin	(5)%	(11)%		

(1) Percentage change represents an improvement since the negative gross margin has decreased.

Our strategy is to manufacture and supply polymer reagents to support our drug candidates or our third-party collaborators where we have a strategic development and commercialization relationship or where we derive substantial economic benefit. Typically, we have elected to 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.

Product gross margin improved for the year ended December 31, 2021 compared to the year ended December 31, 2020 primarily due to a more favorable product mix in 2021 compared to 2020. We have a manufacturing arrangement with a partner that includes a fixed price which is less than the fully burdened manufacturing cost for the polymer reagent, and we expect this arrangement to continue with this partner in future years. We also receive royalty revenue from this collaboration. In each of the years ended December 31, 2021 and 2020, 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. Other than the potential for sales of bempegaldesleukin, which, if approved and as described above, would improve our product gross margin, we expect product gross margin to remain negative in 2022 and to be approximately consistent with 2021 as a result of the collaborative arrangement described above.

Research and development expense (in thousands, except percentages)

	Year Ended December 31,		Increase/ (Decrease) 2021 vs. 2020	Percentage Increase/ (Decrease) 2021 vs. 2020
	2021	2020		
Research and development expense	$ 400,269	$ 408,678	$ (8,409)	(2)%

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 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. Under the BMS Collaboration Agreement, BMS generally bears 67.5% of development costs for bempegaldesleukin in combination with Opdivo® and 35% of costs for manufacturing bempegaldesleukin.

We utilize our employee and infrastructure resources across multiple development and research programs. The following table presents 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 Status(1)	Year Ended December 31,	
		2021	2020
Bempegaldesleukin (CD122-preferential IL-2 pathway agonist)(2)	Phase 1/2/3	$ 107,928	$ 131,900
NKTR-358 (cytokine Treg stimulant)	Phase 1/2	9,376	20,153
NKTR-255 (IL-15 receptor agonist)	Phase 1/2	25,390	14,542
NKTR-262 (toll-like receptor agonist)	Phase 1/2	4,320	8,928
Discovery research, manufacturing and other costs	Various	29,880	19,576
Total clinical development, contract manufacturing and other third party costs		176,894	195,099
Personnel, overhead and other costs(3)		158,732	147,200
Stock-based compensation and depreciation		64,643	66,379
Research and development expense		$ 400,269	$ 408,678

(1) Clinical Study Status definitions are provided in the chart found in Part I, Item 1. Business.
(2) Development expenses for bempegaldesleukin include expenses under the BMS Collaboration Agreement, other collaboration agreements and our own independent studies. The amounts for the years ended December 31, 2021 and 2020 include net reductions of $64.3 million and $90.4 million, respectively, of development cost reimbursements from BMS under our collaboration, net of our share of BMS's costs.
(3) The amounts for the year ended December 31, 2021 and 2020 include reductions of $37.2 million and $37.8 million of employee cost reimbursements from BMS under our collaboration.

Research and development expense was consistent between the year ended December 31, 2021 and December 31, 2020. Research and development expense increased for our independent development of bempegaldesleukin outside of the BMS Collaboration Agreement, including our registrational Phase 2/3 trial in head and neck cancer under our co-development agreement with SFJ and our Phase 1b trial in COVID-19. Research and development expense decreased under our BMS Collaboration Agreement because we have fully enrolled our registrational trials in first-line cisplatin ineligible, PD-L1 low, locally advanced or metastatic urothelial cancer and first-line metastatic renal cell carcinoma and because we completed certain manufacturing activities for bempegaldesleukin in 2020. These decreases were partially offset by an increase in expense for our Phase 3 adjuvant melanoma trial under the BMS Collaboration Agreement. As a result of the decrease in expense under the BMS Collaboration Agreement, the net reductions recorded to research and development expense for BMS's reimbursements of our costs decreased from $128.2 million for the year ended December 31, 2020 to $101.5 million for the year ended December 31, 2021. Please see Note 11 to our Consolidated Financial Statements for additional information regarding our BMS Collaboration Agreement..

Additionally, research and development expense increased for our development of NKTR-255 in our Phase 1/2 studies in liquid and solid tumors, partially offset by a decrease in development costs for NKTR-358. We completed certain Phase 1 clinical development and drug product development deliverables for NKTR-358 in 2020, for which we were responsible for 100% of costs. Phase 1B and Phase 2 development continues, for which we are responsible for 25% of costs and Lilly is responsible for 75% of costs.

We expect research and development expense to increase for 2022 compared to 2021. We expect our development expense for bempegaldesleukin to increase as we continue our registrational trial in adjuvant melanoma and our Phase 2/3 study in head and neck cancer under our co-development agreement with SFJ. We expect research and development expense to increase for our continued development of Phase 1/2 dose-escalation and expansion studies for NKTR-255 in multiple myeloma, non-Hodgkin lymphoma, relapsed or refractory head and neck squamous cell carcinoma, and colorectal cancer. In addition, we are collaborating with Lilly to develop NKTR-358, and Lilly will be conducting the recently started Phase 2 studies and other ongoing studies in 2022, for which we are responsible for 25% of costs. 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 additional clinical development programs and potential clinical collaboration partnerships (if any) for these programs.

In addition to our drug candidates that we plan to evaluate in clinical development during 2022 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 across a wide range of molecule classes, including small molecules and large proteins, peptides and antibodies, across multiple therapeutic areas. We also plan from time to time to evaluate opportunities to in-license potential drug candidates from third parties to add to our drug discovery and development pipeline. 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 bempegaldesleukin, NKTR-358, or clinical collaborations where we would share costs and operational responsibility with a partner such as we have done with NKTR-255. 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 timing and outcomes of our clinical studies could be impacted by the uncertainties of the COVID-19 pandemic. Please see discussion above on effects of the COVID-19 pandemic. 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) 2021 vs. 2020	Percentage Increase/ (Decrease) 2021 vs. 2020
	2021	2020		
General and administrative expense	$ 122,844	$ 104,682	$ 18,162	17 %

General and administrative expense includes the cost of administrative staffing, business development, sales and marketing, finance, and legal activities as well as certain overhead allocations consisting of support and facilities-related costs. General and administrative expense increased for the year ended December 31, 2021 compared with the year ended December 31, 2020 primarily due to increased personnel costs as we begin a stage appropriate build of our commercial capability to co-commercialize bempegaldesleukin with BMS.

We expect general and administrative expense to increase for 2022 compared to 2021, as we continue to build our commercial capabilities. However, we will only incur our most significant commercialization expenditures, if the results of at

least one of our registrational studies in bempegaldesleukin in combination with Opdivo® meets its primary endpoints. BMS and we share commercial costs, using a ratio of 35% to BMS and 65% to Nektar, and each party bears its own costs for non-product specific core commercialization infrastructure.

Impairment of Assets and Other Costs for Terminated Program

On January 14, 2020, the joint FDA Anesthetic Drug Products Advisory Committee and Drug Safety and Risk Management Committee did not recommend approval of our NDA for NKTR-181. As a result, we withdrew our NDA and decided to make no further investments in this program. On February 26, 2020, the Audit Committee of our Board of Directors approved management's plan for the wind-down of the NKTR-181 program.

As a result, in the three months ended March 31, 2020, we wrote off $19.7 million of advance payments to contract manufacturers for commercial batches of NKTR-181. We also incurred $25.5 million of additional costs, primarily for non-cancellable commitments to our contract manufacturers and severance costs.

Change in Fair Value of Development Derivative Liability

As discussed in Note 6 to our Consolidated Financial Statements, we remeasure the development derivative liability under our co-development agreement with SFJ to fair value at each reporting date. The change in fair value recorded for the year ended December 31, 2021 primarily reflects the accretion of the scenario-based probability-adjusted discounted cash flows of our obligation to potentially pay Success Payments to SFJ using our imputed borrowing rate of 12.7%, net of the accretion of SFJ's obligation to fund the SCCHN Clinical Trial, using SFJ's estimated borrowing rate of 1.5%. We review our estimates at each reporting period, and, in particular, in future periods, as information becomes available, such as the applicable clinical trial results and FDA approval decisions, we will re-evaluate our probability of success estimates related to achieving FDA approval for bempegaldesleukin in the Melanoma Indication, the SCCHN Indication and one additional indication, and will record a corresponding increase or decrease in the fair value of the development derivative liability. Additionally, in future periods, we may adjust our estimate of the probability of a successful interim futility analysis and we will record a corresponding increase or decrease to the fair value of the development derivative liability, reflecting the decrease or increase (as applicable) in the likelihood of SFJ's resulting obligation to complete the full SCCHN Clinical Trial. Such changes in the probabilities of success may result in a material expense or benefit in the period when the information is received.

For 2022, we expect that we will record a significant remeasurement adjustment when we receive the results of our registrational study in the Melanoma Indication. If the Melanoma Clinical Trial meets its primary endpoints, our probability of paying Success Payments to SFJ will significantly increase, which will significantly increase the fair value of the development derivative liability. Conversely, if the Melanoma Clinical Trial does not meet its primary endpoints, our probability of paying Success Payments to SFJ will significantly decrease, which will significantly decrease the fair value of the development derivative instrument.

Non-Cash Royalty Revenue, Non-Cash Interest Expense and Loss on Revaluation of Liability (in thousands, except percentages)

	Year Ended December 31,		Increase/ (Decrease) 2021 vs. 2020	Percentage Increase/ (Decrease) 2021 vs. 2020
	2021	2020		
Non-cash royalty revenue related to the sales of future royalties	$ 77,746	$ 48,563	$ 29,183	60 %
			(Increase)/ Decrease 2021 vs. 2020	Percentage Increase/ (Decrease) 2021 vs. 2020
Non-cash interest expense on liabilities related to the sales of future royalties	$ (47,313)	$ (30,267)	$ (17,046)	56 %
Loss on revaluation of liability related to the sale of future royalties	$ (24,410)	$ —	$ (24,410)	>100%

As discussed in Note 8 to our Consolidated Financial Statements, we continue to recognize non-cash royalty revenue for the 2012 Purchase and Sale Agreement and the 2020 Purchase and Sale Agreement.

2012 Purchase and Sale Agreement

Non-cash royalty revenue for the 2012 Purchase and Sale Agreement resulting from net sales of CIMZIA® and MIRCERA® for the year ended December 31, 2021 was consistent with the year ended December 31, 2020. Non-cash interest expense for the 2012 Purchase and Sales Agreement decreased for the year ended December 31, 2021 compared to the year ended December 31, 2020 due to the lower interest rate used in the three months ended December 31, 2021 as a result of the revaluation of the liability.

As discussed in Note 8 to our Consolidated Financial Statements, to resolve UCB's challenges to our patents and their resulting obligation to pay us the royalties on net sales of CIMZIA® which we had sold to RPI, RPI and UCB negotiated a reduction in the royalty term and decreased royalty rates over the remaining term, which was implemented through the Settlement Agreement between UCB and us. As a result of accounting for the Settlement Agreement as a debt modification, we remeasured the liability to fair value based on the present value of the royalty payments to RPI after the modification, discounted at a rate of 16%. The recognition of the loss on the revaluation has no effect on our cash flows, and the net income statement effect over the term of 2012 Purchase and Sale Agreement remains unchanged.

Over the term of this arrangement, the net proceeds of the transaction of $114.0 million, consisting of the original proceeds of $124.0 million, net of $10.0 million in payments from us to RPI, is amortized as the difference between the non-cash royalty revenue and the sum of the non-cash interest expense and the loss on the revaluation of the liability. To date, we have amortized $35.7 million of the net proceeds. There are a number of factors that could materially affect our estimated interest rate, in particular, the amount and timing of royalty payments from future net sales of CIMZIA® and MIRCERA®. As a result, future interest rates could differ significantly. After the modification, we will continue to periodically assess future non-cash royalty revenues, and we will adjust any such change in our estimated interest rate prospectively based on our best estimates of future non-cash royalty revenue such that future non-cash interest expense will amortize the remaining $78.3 million of the net proceeds, since all changes in the royalties are absorbed by RPI.

Before the modification, we had increased our forecasts of future non-cash royalties at various intervals, primarily due to sales of CIMZIA® exceeding previous expectations. Due to these increases in estimated future royalties, we increased the prospective effective interest rate from 17% at inception to 48% as of the modification date. In connection with the modification and the reduction in the royalty rate and the royalty term, the net present value of the modified royalty stream, discounted at the current fair market value discount rate of 16%, is higher than the prior liability balance. The difference of $23.5 million was reported as a loss on the revaluation of the liability.

2020 Purchase and Sale Agreement

As discussed in Note 8 to the Consolidated Finance Statements and above under Royalty Revenue, we began recognizing non-cash royalty revenue for the 2020 Purchase and Sale Agreement in the three months ended December 31, 2020. Non-cash royalty revenue and non-cash interest expense increased for 2021 as we recognized them for the full year.

The 2020 Purchase and Sale Agreement provides for a capped return sale arrangement under which the 2020 Purchase and Sale Agreement will automatically expire, and HCR's right to receive the sold royalties will cease when HCR has received payments equaling $210.0 million (the 2025 Threshold), if the 2025 Threshold is achieved on or prior to December 31, 2025, or $240.0 million, if the 2025 Threshold is not achieved on or prior to December 31, 2025. Our estimate of the imputed interest rate reflects that our estimates for sales of MOVANTIK®, ADYNOVATE® and REBINYN® are sufficient to achieve the 2025 Threshold. As a result, we expect the interest rate to remain consistent between 2021 and 2022. However, if sales estimates decline and we conclude that the 2025 Threshold will not be achieved, we expect that the interest rate would increase modestly.

Interest Income and Other Income (Expense), net (in thousands, except percentages)

	Year Ended December 31,		Increase/ (Decrease) 2021 vs. 2020	Percentage Increase/ (Decrease) 2021 vs. 2020
	2021	2020		
Interest income and other income (expense), net	$ 2,569	$ 18,282	$ (15,713)	(86)%

Interest income and other income (expense), net decreased for the year ended December 31, 2021 compared to the year ended December 31, 2020, primarily due to decreases in market interest rates and lower investment balances which have been utilized to fund our operations and the repayment of our senior notes on April 13, 2020. The effective interest rate earned on investments which we purchased after the COVID-19 pandemic began has been significantly lower than historical interest rates. We expect that our interest income and other income (expense), net will decrease for 2022 compared to 2021 due to lower investments balances as we fund our operations and continued low interest rates.

Interest expense (in thousands, except percentages)

	Year Ended December 31,		(Increase)/ Decrease 2021 vs. 2020	Percentage Increase/ (Decrease) 2021 vs. 2020
	2021	2020		
Interest expense	$ —	$ (6,851)	$ 6,851	(100)%

Interest expense during the year ended December 31, 2020 consisted of interest from our senior secured notes. In October 2015, we issued $250.0 million in aggregate principal amount of 7.75% senior secured notes, which we repaid on April 13, 2020. As a result, we incurred no interest expense after the repayment date.

Income Tax Expense (in thousands, except percentages)

	Year Ended December 31,		Increase/ (Decrease) 2021 vs. 2020	Percentage Increase/ (Decrease) 2021 vs. 2020
	2021	2020		
Provision for income taxes	$ 557	$ 493	$ 64	13

For the years ended December 31, 2021 and 2020, our income tax expense primarily results from our foreign operations. Due to our expected net loss in 2022, we expect income tax expense to be consistent with 2021 and reflect taxable income for our foreign operations.

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 and private placements of debt and equity securities. At December 31, 2021, we had approximately $798.8 million in cash and investments in marketable securities.

We estimate that we have working capital to fund our current business plans for at least the next twelve months from the date of filing. We expect the clinical development of our drug candidates including bempegaldesleukin, NKTR-358, and NKTR-255 will continue to require significant investment to continue to advance in clinical development with the objective of obtaining regulatory approval or entering into one or more collaboration partnerships. Additionally, we have begun to invest in a stage appropriate build for commercialization of bempegaldesleukin. If the results of one or more of our registrational trials in bempegaldesleukin meet their primary endpoints to support health authority filings, we expect to increase our commercialization investment significantly to prepare for the commercial launch of bempegaldesleukin. The preparation for our potential first commercial drug launch requires a significant investment in building a commercial infrastructure, hiring a commercial sales force and incurring other third-party costs, which we will incur before we begin to receive any revenues from the sale of bempegaldesleukin, if approved. Even if our BLA or MAA for bempegaldesleukin is approved, we cannot be assured that the gross margin from sales of bempegaldesleukin will be sufficient to recover the costs of these investments in the near-term period following commercial launch. Under our BMS Collaboration Agreement, we share commercialization costs, using a ratio of 35% to BMS, 65% to Nektar, but each parties bears its own costs for non-product specific core commercialization infrastructure. If bempegaldesleukin is approved, we will share the net commercial profits and losses in the same manner of 35% to BMS and 65% to Nektar.

In the past, we have received a number of significant payments from collaboration agreements and other significant transactions, including $1.9 billion in total consideration received under our arrangement with BMS and a $150.0 million upfront payment from Lilly for our collaboration agreement for NKTR-358. In the future, we expect to receive substantial

payments from our collaboration agreements with BMS and Lilly. In particular, under the BMS Collaboration Agreement, as discussed above, we are entitled to approximately $1.4 billion of potential future milestones for the acceptance of our regulatory submissions and commercial launch of bempegaldesleukin in the US, EU and Japan in up to four indications. Of these milestones, $560.0 million are associated with the acceptance of our regulatory submissions and commercial launches of bempegaldesleukin in its first indication in the U.S. and EU, subject to regulatory approval. As a result, whether and when bempegaldesleukin 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.

On February 12, 2021, we entered into a co-development agreement with SFJ Pharmaceuticals (SFJ), pursuant to which SFJ will pay up to $150.0 million in committed funding to support a Phase 2/3 study of bempegaldesleukin in combination with pembrolizumab (Keytruda®) for first-line treatment of patients with metastatic or unresectable recurrent squamous cell carcinoma of the head and neck (the SCCHN Clinical Trial) whose tumors express PD-L1 (the SCCHN Indication). In exchange for funding the SCCHN Clinical Trial, SFJ is entitled to a series of contingent success-based payments with the first payment due after substantial completion of the SCCHN Clinical Trial which we currently expect to occur in late 2024 or early 2025 as follows: (i) if bempegaldesleukin receives FDA approval for first line metastatic melanoma or the SCCHN Indication, we would pay SFJ $450.0 million over a series of five annual payments with the first annual payment being $30.0 million; (ii) if bempegaldesleukin receives FDA approval in both the Melanoma Indication and the SCCHN Indication, we would pay SFJ an additional $150.0 million paid over a series of seven annual payments; and (iii) if bempegaldesleukin receives FDA approval in an indication other than the Melanoma Indication or the SCCHN Indication, we would pay SFJ a one-time payment of $37.5 million. See Note 6 to our Consolidated Financial Statements for additional information.

In the short term, we do not anticipate that the effects of the COVID-19 pandemic will have a material effect on our results of operations or financial position since we do not generate significant cash flows from recurring revenues and our revenues are generally less affected by shelter-in place or similar orders. However, if delays caused by the COVID-19 pandemic in commencing and enrolling patients in our clinical trials or those run by our partners result in a delay in completing these trials, our ability to file for regulatory approval and commercialize these products (if approved) and receive associated milestone payments may also be delayed.

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. 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 and the effect of the COVID-19 pandemic on the financial markets, 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 bempegaldesleukin, 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, if and when they are approved, 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.

We currently have an effective shelf registration statement on Form S-3 (the 2021 Shelf Registration Statement) on file with the Securities and Exchange Commission, which expires in March 2024. The 2021 Shelf Registration Statement currently permits the offering, issuance and sale by us of up to an aggregate offering price of $300.0 million of common stock, preferred stock, debt securities and warrants in one or more offerings and in any combination, all of which may be offered, issued and sold in “at-the-market” sales pursuant to an equity distribution agreement with Cowen and Company, LLC (the Equity Distribution Agreement). No securities have been sold under the 2021 Shelf Registration Statement or the Equity Distribution Agreement.

Our only significant noncancellable contractual commitments relate to our leases. Please see Note 7 to our Consolidated Financial Statements for additional information.

Cash flows from operating activities

Cash flows used in operating activities for the year ended December 31, 2021 totaled $412.7 million.

Cash flows used in operating activities for the year ended December 31, 2020 totaled $313.3 million, which includes $353.6 million of net operating cash uses and $9.7 million for interest payments on our senior secured notes, partially offset by $50.0 million in milestones under the BMS Collaboration Agreement.

We expect that cash flows used in operating activities, excluding upfront, milestone and other contingent payments received, if any, will increase in 2022 compared to 2021 primarily as a result of increased research and development expenses. If the results of one or more of our registrational trials for bempegaldesleukin in combination with Opdivo® meets their primary endpoints, we expect our cash flows used in preparing for the commercial launch of bempegaldesleukin will significantly increase. However, we are entitled to milestones for the acceptance of our BLA or MAA filing by the FDA and EMA, respectively, and the commercial launch of bempegaldesleukin, the receipt of which is dependent upon if and when our BLA or MAA is accepted, our filings are approved and we are able to complete a first commercial sale of bempegaldesleukin. A substantial portion of these milestones are based on the first commercial sale of bempegaldesleukin in the U.S. and EU and there is therefore uncertainty regarding the timing of achievement of this portion of the milestones depending on health authority review timelines.

Cash flows from investing activities

We paid $15.0 million and $7.3 million to purchase or construct property, plant and equipment in the years ended December 31, 2021 and 2020, respectively.

Cash flows from financing activities

As described in Note 5 to our Consolidated Financial Statements, in the second quarter of 2020, we redeemed the senior secured notes at par and therefore repaid the principal of $250.0 million.

On December 16, 2020, we entered into a purchase and sale agreement (the 2020 Purchase and Sale Agreement) with entities managed by Healthcare Royalty Management, LLC, pursuant to which we sold our rights to receive royalty payments arising from the worldwide net sales of MOVANTIK®, ADYNOVATE® and REBINYN®, beginning on October 1, 2020. We received proceeds of $146.3 million, representing the selling price of $150.0 million, net of transaction costs. See Note 8 for additional details on the 2020 Purchase and Sale Agreement, including the capped nature of the arrangement.

We received proceeds from issuance of common stock related to our employee option and stock purchase plans of $33.2 million and $23.4 million in the years ended December 31, 2021 and 2020, respectively.

Critical Accounting Policies and Estimates

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.

Development Derivative Liability

As described above and in Note 6 to our Consolidated Financial Statements, in February 2021, we entered into a co-development agreement with SFJ (the SFJ Agreement), pursuant to which SFJ will provide up to $150.0 million in committed funding for a Phase 2/3 registrational clinical study of bempegaldesleukin plus Keytruda® in patients with head and neck cancer whose tumors express PD-L1 (the SCCHN Indication). In exchange for funding the SCCHN Clinical Trial, SFJ is entitled to a series of contingent success-based payments as follows: (i) if bempegaldesleukin receives FDA approval for first line metastatic melanoma (the Melanoma Indication) or the SCCHN Indication, we would pay SFJ $450.0 million over a series of five annual

payments with the first payment due after substantial completion of the SCCHN Clinical Trial which we currently expect to occur in late 2024 or early 2025; (ii) if bempegaldesleukin receives FDA approval in both the Melanoma Indication and the SCCHN Indication, we would pay SFJ an additional $150.0 million paid over a series of seven annual payments; and (iii) if bempegaldesleukin receives FDA approval in an indication other than first line metastatic melanoma or the SCCHN Indication, would pay SFJ a one-time payment of $37.5 million.

The SCCHN Clinical Trial provides for an interim futility analysis, and unless the futility criteria are met, SFJ is required to complete the SCCHN Clinical Trial. However, if the futility criteria are met, SFJ has the responsibility to wind down the SCCHN Clinical Trial at its sole cost. and the Success Payments, if any, for the Melanoma Indication and/or the additional bempegaldesleukin indication are reduced pro rata based on the costs incurred by SFJ for the SCCHN Clinical Trial over the aggregate commitment of $150.0 million.

We account for the SFJ Agreement as a derivative instrument, which we measure based on the scenario-based discounted cash flows of our obligation to pay the Success Payments to SFJ, net of the scenario-based discounted cash flows of SFJ's obligation to fund the SCCHN Clinical Trial. Accordingly, we record increases to the derivative liability as SFJ funds the SCCHN Clinical Trial as non-cash research and development expense or as we receive cash payments from SFJ, and we record adjustments to the derivative as the net present value of these two scenario-based discounted cash flows changes over time as the Change in fair value of development derivative liability line in our Consolidated Financial Statements. Our discounted cash flow methodology makes a number of complex assumptions requiring significant management judgment about the probability and timing of cash flows and the risk-adjusted rate we use to discount such cash flows to present value. The key inputs to the valuation include our estimates of the following: (i) the probability and timing of achieving FDA approval in the Melanoma Indication, the SCCHN Indication and any other bempegaldesleukin indication, (ii) the timing of the substantial completion of the SCCHN Clinical Trial that SFJ must achieve before receiving a Success Payment, (iii) the probability of termination of the study due to meeting the interim futility criteria, (iv) the amount of costs incurred by SFJ if the success criterion for the interim futility analysis is not met, (v) SFJ's cost of borrowing (1.5% as of December 31, 2021), and (vi) the Company's imputed cost of borrowing for debt with similar terms (12.7% as of December 31, 2021).

Substantially all of these inputs are considered Level 3 inputs in the fair value hierarchy because no market data exists which we can directly or indirectly observe to assist us in developing these estimates. Additionally, the inputs which have the most significant effect on the valuation of this derivative instrument are our estimates related to the probability and timing of the SCCHN Clinical Trial meeting the futility criteria, the results of the registrational trials in the Melanoma Indication, the SCCHN Indication and another bempegaldesleukin indication meeting their primary endpoints, and the FDA approval of bempegaldesleukin in one or more indications. We generally do not believe we will have information to adjust these probabilities until these clinical results are released to us, and therefore when we adjust these assumptions in the period when the information becomes available to us, we expect that such adjustment will have a material effect on our financial condition and results of operations.

Debt Modification

As discussed in Note 8 to our Consolidated Financial Statements, to resolve UCB's challenges to our patents and their resulting obligation to pay us the royalties on net sales of CIMZIA® which we had sold to RPI, RPI and UCB negotiated a reduction in the royalty term and decreased royalty rates over the remaining term. This negotiation was implemented through the Letter Agreement between RPI and us, which permitted us to enter into the Settlement Agreement with UCB. When we initially sold our rights to receive royalties to RPI, we concluded that we should account for the transaction as debt under ASC 450-10 *Debt* (ASC 450-10) due to our continuing involvement in the generation of the royalties due to our obligation to manufacture the polymer reagent purchased by UCB for the production of CIMZIA®. Since this obligation remained unchanged as a result of the Settlement Agreement, we concluded that we should account for the Letter Agreement within the scope of ASC 450-10.

In our assessment, we concluded that the Letter Agreement represented a modification of the 2012 Purchase and Sale Agreement, since RPI had agreed to reduced royalty payments. Since our estimates of the present value of the reduction in the future royalties exceeded 10% of our estimates of the present value of the royalties before the modification (including the royalties from MIRCERA® which remain unchanged as a result of these agreements), we concluded that we should treat the modification as an extinguishment of the prior liability and recognize a new liability based on the revised royalty payments and term, discounted to fair value. The estimation of the fair value required us to develop estimates of the future sales of CIMZIA® and MIRCERA® over the remaining royalty terms, as well as estimate an appropriate discount rate. Since no active, traded markets exist for arrangements of this nature, we concluded that the 2020 Purchase and Sale Arrangement was economically similar enough to the modified 2012 Purchase and Sale Agreement to use as a basis for the discount rate because the products under both arrangements are well established drugs and the duration of the arrangements are similar. Accordingly,

we utilized our estimated imputed interest rate of 16% from the inception of the 2020 Purchase and Sale Agreement as the discount rate to estimate the fair value of the modified 2012 Purchase and Sale Agreement.

If our estimates of the future royalties to be received by RPI under the modified 2012 Purchase and Sale Agreement had been higher or lower, our estimated fair value of the new liability would have been higher or lower as well, resulting in a larger or smaller loss on the revaluation. Similarly, if our estimated discount rate had been lower or higher, the estimated fair value of the liability would have been higher or lower, resulting in a larger or smaller loss on revaluation.

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.

We have concluded that our collaboration agreements with BMS and Lilly fall within the scope of ASC 808. We concluded that the upfront and milestone payments under these arrangements fall within the scope of ASC 606 and therefore recognize these payments as revenue in License, collaboration and other revenue. However, due to the collaborative nature of our joint development and commercialization of bempegaldesleukin, we recognize the reimbursements we receive from BMS for their share of the costs that we incur for the development, manufacturing and commercialization of bempegaldesleukin as a reduction of research and development expense or general and administrative expense, as applicable.

Revenue Recognition

We recognize license, collaboration and other research revenue, including the upfront fees and milestone payments based on the facts and circumstances of each contractual agreement. 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 and commercial launch milestones. These milestones include the $1.7 billion clinical, regulatory and commercial launch milestones under our collaboration agreements with BMS and Lilly. We must use judgment to determine when to include the variable consideration for these milestones 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. To date, we have not included these remaining milestones from BMS and Lilly in the respective transaction prices due to the significant uncertainties involved with clinical development and regulatory approval. We generally do not believe that we would update the transaction price before events that are outside of our control occur, such as the release of clinical trial results, regulatory acceptance of a BLA or similar filing or regulatory approval. However, if these results are positive, we may conclude that certain milestones meet the recognition requirements for inclusion in the transaction price and therefore we would recognize them as revenue before the milestone event occurs and the payment becomes due to us, provided that the achievement of the milestone is within our control.

Accrued Clinical Trial Expenses

We record an accrued expense for the estimated unbilled 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 recognize costs associated with the start-up and reporting phases of the clinical trials as incurred. We generally accrue costs associated with the treatment phase of clinical trials based on the estimated activities performed by our third party vendors, including our contract research organizations. We may also accrue expenses based on the total estimated cost of the treatment phase on a per patient basis and expense the per patient cost ratably over the estimated patient treatment period. In specific circumstances, such as for certain time-based costs, we recognize clinical trial expenses ratable over the service period, as we believe that this methodology may be more reflective of the timing of costs incurred.

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.

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 $1.8 million decrease, less than 1%, in the fair value of our available-for-sale securities at December 31, 2021. This potential change is based on sensitivity analyses performed on our investment securities at December 31, 2021. Actual results may differ materially. The same hypothetical 50 basis point increase in interest rates would have resulted in an approximate $2.5 million decrease, less than 1%, in the fair value of our available-for-sale securities at December 31, 2020.

As of December 31, 2021, we held $762.6 million of available-for-sale investments, excluding money market funds, with an average time to maturity of six 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, the timing of the maturities of our investments 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.

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, and incur costs from sites in a variety of international locations which are compensated in their respective local currencies. Additionally, a portion of our operations consists of research and development activities outside the United States, with transactions in the Indian Rupee. 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
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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, 2021 and 2020, the related consolidated statements of operations, comprehensive loss, stockholders' equity and cash flows for each of the three years in the period ended December 31, 2021, and the related notes (collectively referred to as the “consolidated financial statements”). In our opinion, the consolidated financial statements present fairly, in all material respects, the financial position of the Company at December 31, 2021 and 2020, and the results of its operations and its cash flows for each of the three years in the period ended December 31, 2021, 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, 2021, 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, 2022 expressed an unqualified opinion thereon.

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.

Critical Audit Matters

The critical audit matters communicated below are matters arising from the current period audit of the financial statements that were communicated or required to be communicated to the audit committee and that: (1) relate to accounts or disclosures that are material to the financial statements and (2) involved our especially challenging, subjective or complex judgments. The communication of critical audit matters does not alter in any way our opinion on the consolidated financial statements, taken as a whole, and we are not, by communicating the critical audit matters below, providing separate opinions on the critical audit matters or on the accounts or disclosures to which they relate.

Accounting for accrued research and development expenses

Description of the Matter

As more fully described in Note 1 to the consolidated financial statements, the Company records expenses and accruals for estimated costs of research and development activities, including third party contract services costs for clinical research and contract manufacturing. Clinical trial and contract manufacturing activities performed by third parties are expensed based upon estimates of work completed in accordance with agreements with the respective Clinical Research Organization ("CRO") or Contract Manufacturing Organization ("CMO"). Billing terms and payments are reviewed by management to ensure estimates of outstanding obligations are appropriate as of period end. Tracking the progress of completion for clinical trial and contract manufacturing activities performed by third parties allows the Company to record the appropriate expense and accruals under the terms of the agreements. During 2021, the Company incurred $400.3 million of research and development expenses. The Company recorded an accrued liability of $26.8 million and $4.6 million for clinical trial and contract manufacturing expenses, respectively, as of December 31, 2021.

Auditing the accounting for accrued clinical trial and contract manufacturing expenses is complex because of the high volume of data used in management's estimates, the assumptions used by management to develop their estimates and verifying the cost and extent of unbilled work performed during the reporting period.

How We Addressed the Matter in Our Audit

We obtained an understanding, evaluated the design and tested the operating effectiveness of controls over the accounting for accrued research and development expenses, including the Company's assessment and estimation of accrued costs for clinical trial and contract manufacturing activities performed by third parties. This assessment was done with the Company's financial and operational personnel to determine the appropriate project status and estimated accrual of costs.

To test the Company's accounting for accrued clinical trial and contract manufacturing expenses, our audit procedures included, among others, obtaining supporting evidence from third parties of the research and development activities performed for significant clinical trials and contract manufacturing services. We agreed, on a sample basis, the Company schedules to key milestones and completion terms, activities, timing, and costs to signed CMO and CRO contracts in order to evaluate the status of completion and accuracy of invoices received from the vendors. We met with clinical and manufacturing personnel to understand the status of significant research and development activities. We also tested a sample of subsequent payments by agreeing the invoice to the original accrual and the invoice payments to bank statements.

Accounting for cost-sharing under the Bristol-Myers Squibb (BMS) Collaboration Agreement

Description of the Matter

The Company and Bristol-Myers Squibb Company (BMS) both conduct research and development activities under a Strategic Collaboration Agreement for bempegaldesleukin (NKTR-214). As more fully explained in note 11 to the consolidated financial statements, the Company and BMS share certain internal and external development costs under the collaboration agreement. The Company's research and development costs include external actual and estimated Clinical Research Organizations ("CRO") and Contract Manufacturing Organization ("CMO") costs in addition to internal employee costs. BMS provides reports to support their research and development activities performed and costs incurred in the relevant period under the terms of the agreement. Estimates included in each party's research and development costs are trued up to actuals by each party when known. Eligible costs incurred by each party during the reporting period are offset and the net amount is owed to the party with the excess costs. The Company has a net receivable of $21.4 million from BMS under the collaboration as of December 31, 2021. During a reporting period in which there is a net receivable to the Company, the net amount of BMS' reimbursement of collaboration expense is recorded as a reduction of research and development expense. For the year ended December 31, 2021, the Company recorded $101.5 million as a reduction of research and development expenses for BMS' share of the Company's research and development expenses, net of the Company's share of BMS' research and development expenses.

Auditing the cost-sharing under the collaboration agreement was especially challenging because of the complexity of the data used by the Company for determining the actual and estimated research and development activities that are eligible for reimbursement under the collaboration agreement. The research and development expenses include management's judgment regarding the estimated third party contract service costs for clinical research and contract manufacturing incurred during the reporting period. Additionally, the Company evaluates the costs incurred and activities performed by BMS to assess their eligibility for reimbursement under the agreement.

How We Addressed the Matter in Our Audit

We evaluated the design and tested the operating effectiveness of controls over the accounting for the cost-sharing conducted under the collaboration agreement, including the Company's assessment and measurement of its and BMS's activities performed and costs incurred that are eligible for reimbursement. This includes conducting meetings with program management, clinical operations and manufacturing personnel to determine the progress to date under the collaboration and substantiating the calculation of eligible costs and activities.

Our audit procedures included, among others, testing the eligibility of the Company's research and development costs against the terms of the agreement. We met with Company personnel and reviewed meeting minutes to understand discussions held with BMS during various committee meetings to corroborate our knowledge of the collaboration activities that have occurred to date. We tested the activities reported by the Company and BMS for appropriate classification and disclosure under the collaboration agreement. We obtained an external confirmation from BMS for the net amount owed to the Company.

Accounting for the Co-Development Agreement with SFJ Pharmaceuticals and Development Derivative Liability

Description of the Matter	As discussed in note 6 to the consolidated financial statements, on February 12, 2021, the Company entered into a co-development funding agreement ("SFJ Arrangement") with SFJ Pharmaceuticals Group company ("SFJ") under which SFJ agreed to pay up to $150 million in committed funding to support a phase 2/3 study of bempegaldesleukin in combination with Keytruda in squamous cell cancer of the head and the neck ("SCCHN"). In return the Company will pay SFJ a series of success-based annual payments in the event of FDA approval of bempegaldesleukin for the Melanoma indication, the SCCHN indication, or both, and in the event of one additional bempegaldesleukin indication. The SFJ Agreement is presented as a development derivative liability whose fair value is based on unobservable inputs and is remeasured at each reporting date. As SFJ conducts the SCCHN clinical trial, the Company records non-cash research and development expense with a corresponding increase to the development derivative liability, and as SFJ remits funding to support the Company's internal cost of conducting the trial, the Company also records a corresponding increase to the development derivative liability. The change in the fair value between reporting periods is recorded as a gain or loss in the Company's Consolidated Statement of Operations. For the year ended December 31, 2021, the Company recorded $16.7 million of non-cash research and development expense and a loss of $8.0 million reflecting the change in the fair value of the development derivative liability. The fair value of the development derivative liability as of December 31, 2021 was $27.7 million. We identified the a) initial accounting, and b) valuation of the development derivative liability as a critical audit matter. The development derivative liability is valued using several unobservable inputs in a scenario-based discounted cash flow method, whereby each scenario makes assumptions about the probability and timing of cash flows, and such cash flows are present valued using risk-adjusted discount rates. Auditing this model required a high degree of auditor judgment as well as analysis by our fair value specialists.
How We Addressed the Matter in Our Audit	We evaluated the design and tested the operating effectiveness of controls over management's initial accounting and valuation of the development derivative liability. This included conducting meetings with the Company's financial and operational personnel to determine the progress to date of the ongoing clinical studies and their process and procedures around the development of the unobservable inputs utilized in the estimation of the fair value of the development derivative liability. Our audit procedures included, among others, testing and evaluating the reasonableness of management's assumptions by comparing the assumptions within the model to internal communications among management and the Company's Board of Directors, information included in the Company's earnings releases, analyst reports for the Company and life science industry third-party research reports. We also conducted inquiries with those responsible for clinical trials regarding the progress of ongoing trials. With the assistance of our fair value specialists, we evaluated the reasonableness of the valuation methodology including the discount rates used by testing the source information and the mathematical accuracy of the calculation.

/s/ Ernst & Young LLP

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

Redwood City, California
February 28, 2022

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, 2021, 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, 2021, 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, 2021 and 2020, the related consolidated statements of operations, comprehensive loss, stockholders' equity and cash flows for each of the three years in the period ended December 31, 2021, and the related notes and our report dated February 28, 2022 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, 2022

NEKTAR THERAPEUTICS
CONSOLIDATED BALANCE SHEETS
(In thousands, except par value information)

	December 31, 2021	December 31, 2020
ASSETS		
Current assets:		
Cash and cash equivalents	$ 25,218	$ 198,955
Short-term investments	708,737	862,941
Accounts receivable	22,492	38,889
Inventory	15,801	15,292
Other current assets	23,333	21,928
Total current assets	795,581	1,138,005
Long-term investments	64,828	136,662
Property, plant and equipment, net	60,510	59,662
Operating lease right-of-use assets	117,025	126,476
Goodwill	76,501	76,501
Other assets	2,744	1,461
Total assets	$ 1,117,189	$ 1,538,767
LIABILITIES AND STOCKHOLDERS' EQUITY		
Current liabilities:		
Accounts payable	9,747	22,139
Accrued compensation	15,735	14,532
Accrued clinical trial expenses	26,809	44,207
Other accrued expenses	15,468	20,986
Operating lease liabilities, current portion	17,441	13,915
Total current liabilities	85,200	115,779
Operating lease liabilities, less current portion	125,736	136,373
Development derivative liability	27,726	—
Liabilities related to the sales of future royalties, net	195,427	200,340
Other long-term liabilities	3,592	8,980
Total liabilities	437,681	461,472
Commitments and contingencies		
Stockholders' equity:		
Preferred stock, $0.0001 par value; 10,000 shares authorized; no shares designated, issued or outstanding at December 31, 2021 or 2020	—	—
Common stock, $0.0001 par value; 300,000 shares authorized; 185,468 shares and 180,091 shares issued and outstanding at December 31, 2021 and 2020, respectively	19	18
Capital in excess of par value	3,516,641	3,388,730
Accumulated other comprehensive loss	(4,157)	(2,295)
Accumulated deficit	(2,832,995)	(2,309,158)
Total stockholders' equity	679,508	1,077,295
Total liabilities and stockholders' equity	$ 1,117,189	$ 1,538,767

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,		
	2021	2020	2019
Revenue:			
Product sales	$ 23,725	$ 17,504	$ 20,117
Royalty revenue	—	30,999	41,222
Non-cash royalty revenue related to the sales of future royalties	77,746	48,563	36,303
License, collaboration and other revenue	436	55,849	16,975
Total revenue	101,907	152,915	114,617
Operating costs and expenses:			
Cost of goods sold	24,897	19,477	21,374
Research and development	400,269	408,678	434,566
General and administrative	122,844	104,682	98,712
Impairment of assets and other costs for terminated program	—	45,189	—
Total operating costs and expenses	548,010	578,026	554,652
Loss from operations	(446,103)	(425,111)	(440,035)
Non-operating income (expense):			
Change in fair value of development derivative liability	(8,023)	—	—
Non-cash interest expense on liabilities related to the sales of future royalties	(47,313)	(30,267)	(25,044)
Loss on revaluation of liability related to the sale of future royalties	(24,410)	—	—
Interest income and other income (expense), net	2,569	18,282	46,335
Interest expense	—	(6,851)	(21,310)
Total non-operating expense, net	(77,177)	(18,836)	(19)
Loss before provision for income taxes	(523,280)	(443,947)	(440,054)
Provision for income taxes	557	493	613
Net loss	$ (523,837)	$ (444,440)	$ (440,667)
Basic and diluted net loss per share	$ (2.86)	$ (2.49)	$ (2.52)
Weighted average shares outstanding used in computing basic and diluted net loss per share	183,298	178,581	174,993

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

NEKTAR THERAPEUTICS
CONSOLIDATED STATEMENTS OF COMPREHENSIVE LOSS
(In thousands)

	Year Ended December 31,		
	2021	2020	2019
Net loss	$ (523,837)	$ (444,440)	$ (440,667)
Other comprehensive income (loss):			
Net unrealized gain (loss) on available-for-sale investments	(1,568)	(927)	5,693
Net foreign currency translation gain (loss)	(294)	(363)	(382)
Other comprehensive income (loss)	(1,862)	(1,290)	5,311
Comprehensive loss	$ (525,699)	$ (445,730)	$ (435,356)

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 Loss	Accumulated Deficit	Total Stockholders' Equity
Balance at December 31, 2018	173,530	$ 17	$ 3,147,925	$ (6,316)	$ (1,424,051)	$ 1,717,575
Shares issued under equity compensation plans	2,975	—	23,377	—	—	23,377
Stock-based compensation	—	—	99,795	—	—	99,795
Comprehensive loss	—	—	—	5,311	(440,667)	(435,356)
Balance at December 31, 2019	176,505	17	3,271,097	(1,005)	(1,864,718)	1,405,391
Shares issued under equity compensation plans	3,586	1	23,372	—	—	23,373
Stock-based compensation	—	—	94,261	—	—	94,261
Comprehensive loss	—	—	—	(1,290)	(444,440)	(445,730)
Balance at December 31, 2020	180,091	18	3,388,730	(2,295)	(2,309,158)	1,077,295
Shares issued under equity compensation plans	5,377	1	33,237	—	—	33,238
Stock-based compensation	—	—	94,674	—	—	94,674
Comprehensive loss	—	—	—	(1,862)	(523,837)	(525,699)
Balance at December 31, 2021	185,468	$ 19	$ 3,516,641	$ (4,157)	$ (2,832,995)	$ 679,508

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,		
	2021	**2020**	**2019**
Cash flows from operating activities:			
Net loss	$ (523,837)	$ (444,440)	$ (440,667)
Adjustments to reconcile net loss to net cash used in operating activities:			
Non-cash royalty revenue related to the sales of future royalties	(77,746)	(48,563)	(36,303)
Non-cash interest expense on liabilities related to sales of future royalties	47,313	30,267	25,044
Loss on revaluation of liability related to the sale of future royalties	24,410	—	—
Change in fair value of development derivative liability	8,023	—	—
Non-cash research and development expense	16,703	—	—
Stock-based compensation	94,674	94,261	99,795
Depreciation and amortization	14,146	14,182	13,156
Impairment of advance payments to contract manufacturers and equipment for terminated program	—	20,351	—
Amortization of premiums (discounts), net and other non-cash transactions	6,730	3,943	(11,394)
Changes in operating assets and liabilities			
Accounts receivable	12,397	1,913	6,411
Inventory	(509)	(2,627)	(1,284)
Operating leases, net	2,340	2,743	13,090
Other assets	(2,688)	4,476	1,190
Accounts payable	(11,690)	2,382	12,967
Accrued compensation	1,203	4,697	1,530
Other accrued expenses	(23,524)	8,644	4,349
Deferred revenue	(605)	(5,516)	(16,565)
Net cash used in operating activities	(412,660)	(313,287)	(328,681)
Cash flows from investing activities:			
Purchases of investments	(960,689)	(987,533)	(1,380,865)
Maturities of investments	1,166,951	1,449,304	1,614,036
Sales of investments	11,504	41,700	—
Purchases of property, plant and equipment	(14,989)	(7,258)	(26,285)
Net cash provided by investing activities	202,777	496,213	206,886
Cash flows from financing activities:			
Proceeds from sale of future royalties, net of $3.8 million of transaction costs	—	146,250	—
Repayment of senior notes	—	(250,000)	—
Cash receipts from development derivative liability	3,000	—	—
Proceeds from shares issued under equity compensation plans	33,238	23,396	23,355
Net cash provided by (used in) financing activities	36,238	(80,354)	23,355
Effect of foreign exchange rates on cash and cash equivalents	(92)	20	(102)
Net increase (decrease) in cash and cash equivalents	(173,737)	102,592	(98,542)
Cash and cash equivalents at beginning of year	198,955	96,363	194,905
Cash and cash equivalents at end of year	$ 25,218	$ 198,955	$ 96,363
Supplemental disclosure of cash flow information:			
Cash paid for interest	$ —	$ 9,742	$ 19,199
Cash paid for income taxes	$ 325	$ 539	$ 555
Operating lease right-of-use assets recognized in exchange for lease liabilities	$ 1,057	$ 2,133	$ 57,691
Accounts receivable recognized in exchange for long-term liabilities	$ —	$ 4,000	$ —

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

NEKTAR THERAPEUTICS

NOTES TO CONSOLIDATED FINANCIAL STATEMENTS
December 31, 2021

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 investigational treatments for cancer, autoimmune disease and viral infections.

Our research and development activities have required significant ongoing investment to date and are expected to continue to require significant investment. As a result, 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, 2021, we had approximately $798.8 million in cash and investments in marketable securities.

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 Europe GmbH, Nektar Therapeutics (India) Private Limited (Nektar India), Inheris Biopharma, Inc. (Inheris) and certain other entities in Europe. We have eliminated all intercompany accounts and transactions 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. We include translation gains and losses in accumulated other comprehensive loss in the stockholders' equity section of our Consolidated Balance Sheets. To date, such cumulative currency translation adjustments have not been significant to our consolidated financial position.

Our comprehensive loss consists of our net loss plus our foreign currency translation gains and losses and unrealized holding gains and losses on available-for-sale securities. There were no significant reclassifications out of accumulated other comprehensive loss to the statements of operations during the years ended December 31, 2021, 2020 and 2019.

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 the selling prices of performance obligations and amounts of variable consideration in collaboration agreements, royalty revenue, and other assumptions 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; non-cash royalty revenue and non-cash interest expense from our liabilities related to our sales of future royalties; assumptions used in the valuation of our development derivative liability as further described in Note 6; our assumptions used in 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, we assess estimates each period, update them to reflect current information, and will generally reflect any changes in estimates in the period first identified.

Reclassifications

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

Fair Value of Financial Instruments

The recorded amounts of certain financial instruments, including cash and cash equivalents, accounts receivable, accounts payable and accrued liabilities approximate their fair values due to their relatively short maturities. Investments that are classified as available-for-sale are recorded at estimated fair value. 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. Development derivative liability is recorded at its estimated fair value based on management's estimates of several unobservable inputs, including the probabilities of success of ongoing clinical trials and various other inputs described above and in Note 6.

The fair value of our financial assets and liabilities are determined in accordance with the fair value hierarchy established in ASC 820-10, *Fair Value Measurements and Disclosures* (ASC 820). ASC 820 defines fair value as the exchange price that would be received for an asset or paid to transfer a liability (an exit price) in the principal or most advantageous market for the asset or liability in an orderly transaction between market participants on the measurement date. The fair value hierarchy of ASC Topic 820 requires an entity to maximize the use of observable inputs when measuring fair value and classifies those inputs into three levels:

Level 1 — Quoted prices in active markets for identical assets or liabilities.

Level 2 — Inputs 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. For the years ended December 31, 2021 and 2020, there were no transfers between Level 1 and Level 2 of the fair value hierarchy.

Level 3 — Unobservable inputs that are supported by little or no market activity and that are significant to the fair value of the assets or liabilities.

Cash, Cash Equivalents, and Investments in Marketable Securities

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.

Our cash and investments are held or issued by financial institutions that management believes are of high credit quality. However, they are exposed to credit risk in the event of default by the third parties that hold or issue such assets. 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.

For our available-for-sale securities, we have significant concentrations of issuers in the banking and financial services industry. While our investment policy requires that we only invest in highly-rated securities and limit our exposure to any single issuer, the COVID-19 pandemic may materially affect the financial condition of issuers. Additionally, pursuant to our investment policy, we may sell securities before maturity if the issuer's credit rating has been downgraded below our minimum credit rating requirements, which may result in a loss on the sale. As a result of the COVID-19 pandemic, we have seen credit downgrades for certain of our securities. Accordingly, if the COVID-19 pandemic or other factors result in downgrades below our minimum credit rating requirements and if we decide to sell these securities, we may experience losses on such sales.

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). We review our portfolio of available-for-sale debt securities, using both quantitative and qualitative factors, to determine if declines in fair value below amortized cost have resulted from a credit-related loss or other factors. If the decline in fair value is due to credit-related factors, we recognize a loss in our Consolidated Statement of Operations, whereas if the decline in fair value is not due to credit-related factors, we recognize the loss in other comprehensive income (loss).

We include coupon interest on securities classified as available-for-sale, as well as amortization of premiums and accretion of discounts to maturity, in interest income. The cost of securities sold is based on the specific identification method.

Accounts Receivable and Significant Customer Concentrations

Our customers are primarily pharmaceutical and biotechnology companies that are primarily 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 (to the extent that they have been achieved and are due from the counterparty), other contingent payments, as well as reimbursable costs from collaborative research and development agreements. Our accounts receivable included $21.4 million and $38.7 million for unbilled net expense reimbursements from our collaboration partner Bristol-Myers Squibb Company (BMS) as of December 31, 2021 and December 31, 2020, respectively. The remaining accounts receivable related primarily to product sales. We perform a regular review of our partners' credit risk and payment histories when circumstances warrant, 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.

Inventory and Significant Supplier Concentrations

We generally manufacture inventory upon receipt of firm purchase orders from our collaboration partners, and we may manufacture certain intermediate work-in-process materials and purchase raw materials based on purchase forecasts from our collaboration partners. Inventory includes direct materials, direct labor, and manufacturing overhead, and we determine cost on a first-in, first-out basis for raw materials and on a specific identification basis for work-in-process and finished goods. We value inventory at the lower of cost or net realizable value, and we write down defective or excess inventory to net realizable value based on historical experience or projected usage. We expense inventory related to our research and development activities when we purchase or manufacture it. Before the regulatory approval of our drug candidates, we recognize research and development expense for the manufacture of drug products that could potentially be available to support the commercial launch of our drug candidates, if approved.

We are dependent on our suppliers and contract manufacturers to provide raw materials and drugs 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, including as a result of the COVID-19 pandemic, our ability to develop and produce our drug candidates, our ability to supply comparator drugs for our clinical trials, 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

We state property, plant and equipment at cost, net of accumulated depreciation. We capitalize major improvements and expense maintenance and repairs as incurred. We generally recognize depreciation on a straight-line basis. We depreciate manufacturing, laboratory and other equipment over their estimated useful lives of generally three to ten years, depreciate buildings over the estimated useful life of generally twenty years and amortize leasehold improvements over the shorter of the estimated useful lives or the remaining term of the related 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 and right-of-use assets for our leases, 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.

Leases

We determine if an arrangement contains a lease at the inception of the arrangement. Right-of-use assets represent our right to use an underlying asset for the lease term, and lease liabilities represent our obligation to make lease payments arising from the lease. We recognize operating lease right-of-use assets and liabilities at the lease commencement date based on the present value of lease payments over the expected lease term. In determining the present value of lease payments, we use our incremental borrowing rate based on the information available at the lease commencement date. We have elected the practical expedient to account for the lease and non-lease components, such as common area maintenance charges, as a single lease component for our facilities leases, and elected the short-term lease recognition exemption for our short-term leases, which allows us not to recognize lease liabilities and right-of-use assets for leases with an original term of twelve months or less.

Our expected lease terms may include options to extend or terminate the lease when it is reasonably certain that we will exercise any such options. We recognize lease expense for our operating leases on a straight-line basis over the expected lease term. We have elected to recognize lease incentives, such as tenant improvement allowances, at the lease commencement date as a reduction of the right-of-use asset and lease liability until paid to us by the lessor to the extent that the lease provides a specified fixed or maximum level of reimbursement and we are reasonably certain to incur reimbursable costs at least equaling such amounts.

Please see Note 7 for additional information regarding our leases.

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 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 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 and regulatory 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 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 of the arrangement. 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* (ASC 606). 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 customers. 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 invoice. We test our products for adherence to technical specifications before shipment; accordingly, we have not experienced any significant returns from our customers. We recognize costs related to shipping and handling of product to customers in cost of goods sold.

Royalty revenue, including Non-cash royalty revenue

Generally, for our collaboration arrangements that include sales-based royalties, we have granted our collaboration partner a license to our intellectual property. Pursuant to these arrangements, our collaboration partners are typically obligated to pay a royalty that is based on the net sales of their approved drugs that are sold in the countries where we have intellectual property rights covering their drugs. As of December 30, 2021, we have sold our rights to receive sales-based royalties for CIMZIA®, MIRCERA®, MOVANTIK®, ADYNOVATE® and REBINYN® as further described in Note 8. For collaboration arrangements that include sales-based royalties, we have concluded that the license is the predominant item to which the royalties relate, which include commercial milestone payments based on the level of sales. Accordingly, we recognize royalty revenue when the underlying sales occur based on our best estimates of sales of the drugs. Our aggregate royalty and non-cash royalty revenue of $77.7 million, $79.6 million and $77.5 million for the years ended December 31, 2021, 2020 and 2019, respectively, represents revenue for granting licenses for which we had satisfied in prior periods. 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, filing for or receipt of regulatory approval or the first commercial sale of a product, 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. As described further in Note 11, we recognized $50.0 million of milestones in the year ended December 31, 2020 because we had previously satisfied the performance obligation. If we update the transaction price before the triggering event, we recognize the increase in the transaction price as a contract asset. 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.

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 activities for our drug candidates and technology development and for certain third parties under collaboration agreements. For our 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 joint development collaboration, such as our collaboration with BMS, we record the cost reimbursement from our partner 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 unbilled 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 recognize costs associated with the start-up and reporting phases of the clinical trials as incurred. We generally accrue costs associated with the treatment phase of clinical trials based on the estimated activities performed by our third party vendors, including our contract research organizations. We may also accrue expenses based on the total estimated cost of the treatment phase on a per patient basis and expense the per patient cost ratably over the estimated patient treatment period. In specific circumstances, such as for certain time-based costs, we recognize clinical trial expenses ratable over the service period, as we believe that this methodology may 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 to be sufficiently defined such that the resulting product can be considered the delivery of a good, as evidenced by predictive or contractually required yields in the production process or payment terms based on the actual yield, 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.

We capitalize advance payments for goods or services that will be used or rendered for future research and development activities and recognize expense as the related goods are delivered or services performed. We base our estimates on the best information available at the time. However, additional information may become available to us in the future 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. We generally consider such increases or decreases in cost as changes in estimates and reflect them in research and development expenses in the period identified.

Impairment of Assets and Other Costs for Terminated Program

On January 14, 2020, the joint FDA Anesthetic Drug Products Advisory Committee and Drug Safety and Risk Management Committee did not recommend approval of our NDA for NKTR-181. As a result, we withdrew our NDA and decided to make no further investments in this program. On February 26, 2020, the Audit Committee of our Board of Directors approved management's plan for the wind-down of Inheris and the NKTR-181 program. As a result, in the three months ended March 31, 2020, we wrote off $19.7 million of advance payments to contract manufacturers for commercial batches of NKTR-181. We also incurred $25.5 million of additional costs, primarily for non-cancellable commitments to our contract manufacturers and certain severance costs.

Stock-Based Compensation

Stock-based compensation arrangements include grants of stock options, restricted stock units (RSUs), performance stock units (PSUs) 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 expense the grant date fair value of options, RSUs, PSUs and ESPP shares on a straight-line basis over the requisite service periods in our Consolidated Statements of Operations and recognize forfeitures of options, RSUs and PSUs as they occur. For options and RSUs that vest upon the achievement of performance milestones, we recognize expense provided that we believe that the performance milestones are probable of achievement, and we estimate the vesting period based on our evaluation of the estimated date of achievement of these milestones. For PSUs, we recognize expense based on the grant date fair value regardless of whether the market condition is met. Additionally, we do not adjust the expense based on the number of shares ultimately issued, which may be higher or lower than the grant amount. We report expense amounts 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 have no effect on our reported cash flows. We estimate the grant date fair value of our stock-based compensation awards as follows:

- 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, including but not limited to, our stock price volatility over the term of the awards, and actual and projected employee stock option exercise behaviors.

- The number of shares issuable under PSUs is based on our total shareholder return as compared to other companies within the Nasdaq biotechnology index over the measurement period and may be capped based on our absolute total shareholder return over such period. We use the Monte Carlo simulation model to determine the estimated grant date fair value. The Monte Carlo simulation model incorporates assumptions such as the volatility of our stock, the volatility of the stock of other peer companies within the index, and the correlation of both our stock and our peer companies' stock to the index.

- The fair value of an RSU is equal to the closing price of our common stock on the grant date.

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.

Net Loss Per Share

For all periods presented in the Consolidated Statements of Operations, the net loss available to common stockholders is equal to the reported net loss. We calculate basic net loss per share based on the weighted-average number of common shares outstanding during the periods presented. For the years ended December 31, 2021, 2020 and 2019, 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, RSUs and PSUs totaling 18.4 million, 17.4 million and 17.9 million for the years ended December 31, 2021, 2020 and 2019, respectively.

Comprehensive Loss

Comprehensive 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 comprehensive loss includes our net loss, gains and losses from the foreign currency translation of the assets and liabilities of our foreign subsidiaries, and unrealized gains and losses on investments in available-for-sale securities.

Recent Accounting Pronouncements

We have reviewed recent accounting pronouncements and concluded they are either not applicable to us or that we do not expect adoption to have a material effect on our consolidated financial statements.

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, 2021	December 31, 2020
Cash and cash equivalents	$ 25,218	$ 198,955
Short-term investments	708,737	862,941
Long-term investments	64,828	136,662
Total cash and investments in marketable securities	$ 798,783	$ 1,198,558

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, 2021 and 2020 had maturities between one and two years.

During the year ended December 31, 2021 and 2020, we sold available-for-sale securities totaling $11.5 million and $41.7 millions, respectively. We did not sell any available-for-sale securities in the year ended December 31, 2019. Gross realized gains and losses on those sales were not significant.

We report our accrued interest receivable, which totaled $1.4 million and $5.1 million at December 31, 2021 and December 31, 2020, respectively, in other current assets on our Consolidated Balance Sheets.

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

		December 31, 2021				December 31, 2020
	Fair Value Hierarchy Level	Amortized Cost	Gross Unrealized Gains	Gross Unrealized Losses	Fair Value	Fair Value
Corporate notes and bonds	2	$ 278,475	$ 7	$ (361)	$ 278,121	$ 687,469
Corporate commercial paper	2	478,932	5	(308)	478,629	313,497
Obligations of U.S. government agencies	2	5,880	—	(5)	5,875	2,382
Available-for-sale investments		763,287	12	(674)	762,625	1,003,348
Money market funds	1				23,968	179,302
Certificates of deposit	2				10,940	9,623
Cash	N/A				1,250	6,285
Total cash and investments in marketable securities					$ 798,783	$ 1,198,558

At December 31, 2020, our gross unrealized gains and losses totaled $1.1 million and $0.2 million, respectively.

At both December 31, 2021 and 2020, we had letter of credit arrangements in favor of our landlords and certain vendors totaling $8.1 million. These letters of credit are secured by investments of similar amounts.

Note 3 — Inventory

Inventory consists of the following (in thousands):

	December 31,	
	2021	2020
Raw materials	$ 3,166	$ 2,422
Work-in-process	9,342	10,703
Finished goods	3,293	2,167
Total inventory	$ 15,801	$ 15,292

Note 4 — Property, Plant and Equipment

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

	December 31,	
	2021	2020
Building and leasehold improvements	$ 97,385	$ 92,977
Laboratory equipment	42,704	40,121
Computer equipment and software	28,829	28,684
Manufacturing equipment	22,374	21,796
Furniture, fixtures, and other	10,094	9,872
Depreciable property, plant and equipment at cost	201,386	193,450
Less: accumulated depreciation	(148,039)	(138,488)
Depreciable property, plant and equipment, net	53,347	54,962
Construction-in-progress	7,163	4,700
Property, plant and equipment, net	$ 60,510	$ 59,662

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 expense for property, plant and equipment for the years ended December 31, 2021, 2020, and 2019 was $13.0 million, $12.5 million, and $11.0 million, respectively.

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 bore interest at a rate of 7.75% per annum and were to mature on October 5, 2020. On April 13, 2020, we redeemed the Notes at par and therefore repaid the principal of $250.0 million and accrued interest of $4.8 million.

Note 6 — Co-Development Agreement with SFJ Pharmaceuticals and Development Derivative Liability

On February 12, 2021, we entered into a co-development agreement (the SFJ Agreement) with SFJ Pharmaceuticals XII, L.P., a SFJ Pharmaceuticals Group company (SFJ), pursuant to which SFJ will pay up to $150.0 million in committed funding to support a Phase 2/3 study of bempegaldesleukin in combination with Keytruda® (pembrolizumab) for first-line treatment of patients with metastatic or unresectable recurrent squamous cell carcinoma of the head and neck (the SCCHN Clinical Trial) whose tumors express PD-L1 (the SCCHN Indication). SFJ Pharmaceuticals is a global drug development company backed by Blackstone Life Sciences and Abingworth. On February 11, 2021, we entered into a collaboration agreement with MSD International GmbH (MSD), an affiliate of Merck, Sharp & Dohme, pursuant to which MSD will provide Keytruda® at no cost for use in the SCCHN Clinical Trial but will not bear any other costs of the trial.

SFJ will have primary responsibility for the clinical trial management of the SCCHN Clinical Trial, and we will be the sponsor of the SCCHN Clinical Trial and will also have sole responsibility for regulatory interactions and filings for bempegaldesleukin.

Other than the opportunity to receive Success Payments as outlined below, SFJ has no right to reimbursement of costs incurred by SFJ for the SCCHN Clinical Trial in the event that the Melanoma Clinical Trial and the SCCHN Clinical Trial do not achieve FDA approval. We will pay SFJ a series of success-based annual payments (collectively, the Success Payments) in the event of FDA approval of bempegaldesleukin for the Melanoma Indication, the SCCHN Indication, or both, and in the event of FDA approval of one additional bempegaldesleukin indication. The Success Payments do not begin until the substantial completion of the SCCHN Clinical Trial. The total success-based annual payments for the first indication approved by FDA, whether for the Melanoma Indication or the SCCHN Indication, is an aggregate of $450.0 million, paid in annual contractual payments over five years, with the first payment being $30.0 million, with the earliest possible payment expected to occur in late 2024 or early 2025, subject to the substantial completion of the SCCHN Clinical Trial. The total success-based payments for the second indication approved by FDA, whether for the Melanoma Indication or the SCCHN Indication, is an aggregate of $150.0 million, paid in annual contractual payments over seven years. Finally, in the event of FDA approval for

bempegaldesleukin for any indication other than the Melanoma Indication or the SCCHN Indication, we will make a one-time payment of $37.5 million to SFJ.

The SCCHN Clinical Trial provides for an interim futility analysis, and unless the futility criteria are met, SFJ is required to complete the SCCHN Trial, but if the futility criteria are met, SFJ has the responsibility to wind down the SCCHN Clinical Trial at its sole cost. We and BMS, pursuant to the BMS Collaboration Agreement, remain solely responsible for conducting the Phase 3 clinical trials of bempegaldesleukin in combination with Opdivo®, including the treatment of previously untreated unresectable or metastatic melanoma (the "Melanoma Indication" and the "Melanoma Clinical Trial"). If the success criterion for the interim futility analysis is not met and SFJ winds down the SCCHN Clinical Trial, then the Success Payments, if any, for the Melanoma Indication and/or the additional bempegaldesleukin indication are reduced pro rata based on the costs incurred by SFJ for the SCCHN Clinical Trial over the aggregate commitment of $150.0 million.

The SFJ Agreement provides for certain positive and negative covenants, including restrictions on our ability to incur liens on our intellectual property related to bempegaldesleukin (the bempegaldesleukin IP), or assign or convey any right to receive income with respect to the bempegaldesleukin IP (other than royalty and other license fee obligations to licensors), except for the issuance of senior secured debt secured by all or substantially all of our assets, including the bempegaldesleukin IP.

The SFJ Agreement expires upon the payment of all Success Payments to SFJ, unless earlier terminated as provided under the SFJ Agreement. The SFJ Agreement may be terminated by either party for a safety or health concern for the patients, whether by the independent data monitoring committee or by mutual agreement of both parties. The SFJ Agreement may also be terminated by either party for material breach or insolvency of the counterparty.

We present the SFJ Agreement as a Development derivative liability in our Consolidated Balance Sheets, which we remeasure to fair value at each reporting date. As SFJ conducts the SCCHN Clinical Trial, we record non-cash research and development expense with a corresponding increase to the development derivative liability, and as SFJ remits funding to us to support our internal costs of conducting the trial, we also record a corresponding increase to the development derivative liability. We present the gain (loss) from the remeasurement as Change in fair value of development derivative liability in our Consolidated Statements of Operations. The following table presents the changes in the development derivative liability for the year ended December 31, 2021:

	Fair Value Hierarchy Level	Year ended December 31,
Fair value at inception on February 12, 2021	3	$
Non-cash research and development expense		$ 1(
Cash receipts from SFJ		$
Change in the fair value of development derivative liability		$
Fair value at end of period	3	$ 2

We valued the derivative using a scenario-based discounted cash flow method, whereby each scenario makes assumptions about the probability and timing of cash flows, and we discount such cash flows to present value using a risk-adjusted rate. The key inputs to the valuation include our estimates of the following: (i) the probability of the Melanoma Clinical Trial, the SCCHN Clinical Trial and another bempegaldesleukin trial meeting their primary endpoints, (ii) the probability and timing of achieving FDA approval in the Melanoma Indication, the SCCHN Indication and any other bempegaldesleukin indication, (iii) the timing of the substantial completion of the SCCHN Clinical Trial that SFJ must achieve before receiving a Success Payment, (iv) the probability of termination of the study due to meeting the interim futility criteria, (v) the amount of costs incurred by SFJ if the success criterion for the interim futility analysis is not met, (vi) SFJ's cost of borrowing, currently estimated at 1.5%, and (vii) the Company's imputed cost of borrowing for debt with similar terms, currently estimated at 12.7%.

Note 7 — Operating Leases

Our leases consist of a Lease Agreement (the Mission Bay Lease) with ARE-San Francisco No. 19, LLC (ARE) for our 155,215 square foot corporate office and R&D facility located at 455 Mission Bay Boulevard, San Francisco, California (the Mission Bay Facility) and a Lease Agreement (the Third Street Lease) with Kilroy Realty Finance Partnership, L.P. (Kilroy) for an additional 135,936 square foot facility to support our R&D operations at 360 Third Street, San Francisco,

California (the Third Street Facility). The following table presents key information regarding these leases (dollars in thousands):

	Mission Bay Facility	Third Street Facility
Lease commencement	September 2017	June 2018
Lease term	January 2030	January 2030
Space delivered during the year ended December 31, 2020		
Square footage	4,940	—
Right-of-use asset and lease liability recognized	$ 2,133	$ —
Space delivered during the year ended December 31, 2021		
Square footage	2,012	—
Right-of-use asset and lease liability recognized	$ 1,057	$ —
Renewal terms	Two consecutive five-year terms	One five-year term

- The monthly base rent for both facilities will escalate over the term of the lease at various intervals.
- Both leases include various covenants, indemnities, defaults, termination rights, security deposits and other provisions customary for lease transactions of this nature.
- During the term of the Mission Bay Lease, we are responsible for paying our share of operating expenses specified in the lease, including utilities, common area maintenance, insurance costs and taxes.
- For the Third Street Lease, our fixed annual base rent on an industrial gross lease basis includes certain expenses and property taxes paid directly by the landlord. We have a one-time right of first offer with respect to certain additional rental space at the Third Street Facility.

We recognize rent expense for these operating leases on a straight-line basis over the lease period. The components of lease expense, which we include in operating expenses in our Consolidated Statements of Operations, were as follows (in thousands):

	Year Ended December 31,		
	2021	2020	2019
Operating lease expense	$ 19,153	$ 18,985	$ 14,697
Variable lease expense	8,974	8,179	6,408
Total lease expense	$ 28,127	$ 27,164	$ 21,105

During the years ended December 31, 2021, 2020 and 2019, we paid $16.8 million, $16.2 million and $8.4 million, respectively, of operating lease payments related to our lease liabilities, which we include in net cash used in operating activities in our Consolidated Statements of Cash Flows.

As of December 31, 2021, the maturities of our operating lease liabilities were as follows (in thousands):

Year ending December 31,		
2022	$	18,626
2023		20,909
2024		21,572
2025		22,255
2026		22,957
2027 and thereafter		75,411
Total lease payments		181,730
Less: portion representing interest		(37,900)
Less: lease incentives		(653)
Operating lease liabilities		143,177
Less: current portion		(17,441)
Operating lease liabilities, less current portion	$	125,736

As of December 31, 2021, the weighted-average remaining lease term is 8.1 years and the weighted-average discount rate used to determine the operating lease liability was 5.8%.

Note 8 — Liabilities Related to the Sales of Future Royalties

On February 24, 2012, we entered into a purchase and sale agreement (the 2012 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 2012 Transaction Royalties) 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 2012 Transaction Royalties. 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 continue to account for these royalties as revenue. We recorded the $124.0 million in proceeds from this transaction as a liability (the 2012 Royalty Obligation) that is amortized using the effective interest method over the estimated life of the 2012 Purchase and Sale Agreement as royalties from the CIMZIA® and MIRCERA® products are remitted directly to RPI.

On June 5, 2020, UCB served notice of a Declaratory Judgment of Patent Invalidity, filed in the United States District Court for the District of Delaware, seeking a declaration of invalidity of certain of our patents that we had licensed to UCB and pursued similar actions in other jurisdictions. On October 14, 2021, RPI and we entered into a Letter Agreement which permitted us to enter into a Settlement Agreement, effective October 13, 2021, with UCB to effect the negotiation between RPI and UCB in which UCB and RPI agreed to a reduction in the royalty term and annual decreases in the royalty rate over the remaining royalty term in exchange for UCB's withdrawal of all of UCB's litigation and challenges.

We concluded that we should account for the decrease in royalty payments to RPI as a result of these agreements as a modification of our liability. Due to the significance of the change in the estimated royalty payments, we concluded that we should treat the modification as an extinguishment of the prior liability and recognize a new liability based on the revised royalty payments and term, discounted to fair value. Accordingly, we estimated the fair value to be approximately $84.7 million, reflecting a discount rate of 16.0%, and we began amortizing the liability prospectively at this rate commencing in the three months ended December 31, 2021. As a result, we recognized a loss of $23.5 million on the revaluation of the prior liability in the three months ended December 31, 2021, and we wrote off of the remaining $0.9 million of unamortized transaction costs. We present these charges in Loss on revaluation of liability related to the sale of future royalties line in our Consolidated Statement of Operations.

On December 16, 2020, we entered into a purchase and sale agreement (the 2020 Purchase and Sale Agreement) with entities managed by Healthcare Royalty Management, LLC (collectively, HCR). Pursuant to the 2020 Purchase and Sale Agreement, we agreed to sell to HCR certain of our rights to receive royalty payments (the 2020 Transaction Royalties) arising from the worldwide net sales, from and after October 1, 2020 until such time that certain return thresholds are met as described below, of (a) MOVANTIK® under that certain License Agreement, dated September 20, 2009, by and between Nektar and AstraZeneca AB, as amended, (b) ADYNOVATE® under that certain Exclusive Research, Development, License and Manufacturing and Supply Agreement, dated September 26, 2005, by and among Nektar, Baxalta US Inc. and Baxalta GmbH,

as amended, (c) REBINYN® under that certain Settlement and License Agreement, dated December 21, 2016, by and among Nektar, Novo Nordisk Inc., Novo Nordisk A/S and Novo Nordisk A/G and (d) licensed products under that certain Right to Sublicense Agreement, dated October 27, 2017, by and among Nektar, Baxalta Incorporated, Baxalta US Inc. and Baxalta GmbH.

The 2020 Purchase and Sale Agreement will automatically expire, and the payment of the 2020 Transaction Royalties to HCR will cease, when HCR has received payments of the 2020 Transaction Royalties equal to $210.0 million (the 2025 Threshold), if the 2025 Threshold is achieved on or prior to December 31, 2025, or $240.0 million, if the 2025 Threshold is not achieved on or prior to December 31, 2025 (or, if earlier, the date on which the last royalty payment under the relevant license agreements is made). If HCR has received payments of the 2020 Transaction Royalties equal to at least $208.0 million on or prior to December 31, 2025, we have the option to pay the difference between the 2025 Threshold and such 2020 Transaction Royalties, and the 2025 Threshold will be met and the 2020 Purchase and Sale Agreement will expire. After the 2020 Purchase and Sale Agreement expires, all rights to receive the 2020 Transaction Royalties return to Nektar.

On December 30, 2020, we received aggregate cash proceeds of $150.0 million for the 2020 Transaction Royalties. As part of the sale, we incurred approximately $3.8 million in transaction costs, which will be amortized to interest expense over the estimated life of the 2020 Purchase and Sale Agreement. Although we sold all of our rights to receive royalties from these products, as a result of the limits on the 2020 Transaction Royalties to be received by HCR and our ongoing manufacturing and supply obligations related to the generation of these royalties, we will continue to account for these non-cash royalties as revenue, commencing with royalties for the three months ended December 31, 2020, to be received by HCR in the first quarter of 2021. We recorded the $150.0 million in proceeds from this transaction as a liability (the 2020 Royalty Obligation) that will be amortized using the effective interest method over the estimated life of the 2020 Purchase and Sale Agreement. As of December 31, 2021, our prospective effective interest rate used to amortize the liability is 15%.

The following table shows the activity within the liability account of each arrangement (in thousands):

	Year-Ended December 31, 2021			Period from inception to December 31, 2021		
	2012 Purchase and Sale Agreement	2020 Purchase and Sale Agreement	Total	2012 Purchase and Sale Agreement	2020 Purchase and Sale Agreement	Total
Liabilities related to the sales of future royalties—beginning balance	$ 65,880	$ 139,375	$ 205,255	$ —	$ —	$ —
Royalty monetization proceeds	—	—	—	124,000	150,000	274,000
Non-cash royalty revenue	(37,578)	(40,168)	(77,746)	(282,658)	(50,793)	(333,451)
Non-cash interest expense	26,458	20,855	47,313	223,418	20,855	244,273
Payments to RPI	—	—	—	(10,000)	—	(10,000)
Loss on revaluation of liability related to the sale of future royalties	23,522		23,522	23,522	—	23,522
Liabilities related to the sales of future royalties – ending balance	78,282	120,062	198,344	78,282	120,062	198,344
Less: unamortized transaction costs	—	(2,917)	(2,917)	—	(2,917)	(2,917)
Liabilities related to the sales of future royalties, net	$ 78,282	$ 117,145	$ 195,427	$ 78,282	$ 117,145	$ 195,427

Pursuant to the 2012 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 2012 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.

As royalties are remitted to RPI and HCR by our licensees, the balances of the respective Royalty Obligations will be effectively repaid over the lives of the agreements. To determine the amortization of the Royalty Obligations, we are required to estimate the total amount of future royalty payments to be received by RPI and HCR, respectively. The sum of these amounts less the net proceeds we received will be recorded as non-cash interest expense, as well as the loss on the revaluation described above, over the lives of the respective Royalty Obligations. We periodically assess the estimated royalty payments to RPI and

HCR from our licensees and to the extent the amount or timing of such payments is materially different than our original estimates, we will prospectively adjust the imputed interest rate and the related amortization of the appropriate Royalty Obligation.

There are a number of factors that could materially affect the amount and timing of royalty payments from our licensees, 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 or HCR are made in U.S. dollars (USD) while significant portions of the underlying sales of the products of our licensees are made in currencies other than USD, and other events or circumstances that could result in reduced royalty payments from our licensees, all of which would result in a reduction of non-cash royalty revenues and the non-cash interest expense over the life of the respective Royalty Obligation. Conversely, for the 2012 Purchase and Sale Agreement, if sales of these products 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 2012 Royalty Obligation.

Note 9 — 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, 2021, these commitments were approximately $8.2 million, all of which we expect to pay in 2022.

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 for that period and on our cash flows and liquidity.

In October 2018, we and certain of our executives were named in a putative securities class action complaint filed in the U.S. District Court for the Northern District of California (Case No. 18-cv-06607, which we refer to as the Mulquin action). The Mulquin plaintiffs have challenged public statements Nektar made, between January 2017 and June 2018, about the clinical trials of bempegaldesleukin. The Mulquin complaint was amended in May 2019. The defendants moved to dismiss and the court granted the motion without prejudice in July 2020. The Mulquin plaintiffs again amended their complaint and the defendants again moved to dismiss. In December 2020, the court dismissed the action with prejudice. The plaintiffs filed a notice of appeal in January 2021 and appellate briefing in the U.S. Court of Appeals for the Ninth Circuit was completed in September 2021. Oral argument occurred on December 10, 2021, and the matter remains pending with the court.

A second putative securities class action was filed against the Company and certain of our executives in the U.S. District Court for the Northern District of California in August 2019 (Case No. 4-19-cv-05173, which we refer to as the Damiba action). The Damiba plaintiffs challenged public statements Nektar made, between February 2019 and May 2019, about its bempegaldesleukin clinical trials and collaboration with Bristol-Myers Squibb. After the Damiba plaintiffs filed an amended complaint and the defendants moved to dismiss, the court dismissed the action without prejudice in January 2021. The Damiba plaintiffs subsequently voluntarily dismissed the action, with prejudice, in March 2021.

In addition to the two securities actions (the Mulquin action and the Damiba action), three additional sets of derivative actions have been filed against certain of the Company's current and former officers and directors, purportedly on the Company's behalf. These derivative actions are based on the allegations in the securities actions and on the premise that the Company's officers and directors breached their fiduciary duties by exposing the Company to one or both of the securities actions. The first derivative action was filed in the U.S. District Court for the District of Delaware in February 2019 (Case No. 1:19-cv-00322-MN-JLH). After amending their complaint several times, the plaintiffs in that action voluntarily dismissed their claims without prejudice in April 2021.

A second set of derivative actions was filed in February 2020 in the U.S. District Court for the Northern District of California (Case No. 4:20-cv-01088-JSW). The derivative actions in California were consolidated and the Company moved to dismiss on the basis that the plaintiffs had neither made a demand on the Company's board of directors nor shown that a demand would be futile. On September 1, 2021, the court dismissed the action with prejudice.

A third derivative complaint was filed in February 2021 in the Court of Chancery of the State of Delaware (C.A. No. 2021-0118-PAF). The parties agreed to stay further proceedings in this action until thirty days after the U.S. Court of Appeals for the Ninth Circuit's final resolution of the appeal in the Mulquin action.

Given the nature and status of these securities class action lawsuits and derivative complaints, we cannot reasonably estimate a potential future loss or a range of potential future losses. However, an unfavorable resolution could potentially have a material adverse effect on our business, financial condition, and results of operations or prospects, and potentially result in paying monetary damages. We have recorded no liability for these matters in our Consolidated Balance Sheets at either December 31, 2021 or December 31, 2020.

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 in our Consolidated Balance Sheets at either December 31, 2021 or December 31, 2020.

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 and PEGylation materials 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. The term of these indemnification obligations is generally perpetual commencing after execution of the agreement. There is generally no limitation on the potential amount of future payments we could be required to make under these indemnification obligations.

From time to time, we enter into other strategic agreements such as divestitures and financing transactions pursuant to which we are required to make representations and warranties and undertake to perform or comply with certain covenants. For example, we made certain intellectual property representations in connection with our RPI and HCR transactions, however, the time limitation we have to indemnify RPI with respect to any breach of these intellectual property-based representations and warranties has passed. In the event it is determined that we breached certain of the representations and warranties or covenants made by us in any such agreements or certain express indemnification provisions are applicable, we could incur substantial indemnification liabilities depending on the timing, nature, and amount of any such claims.

To date, we have not incurred any costs to defend lawsuits or settle claims related to these indemnification obligations, nor any breaches of representations or warranties or covenants. 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.

Indemnification of Underwriters and Initial Purchasers of our Securities

In connection with our sale of equity 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 retention of up to $10.0 million per incident for merger and acquisition related claims, $10.0 million per incident for securities related claims and $10.0 million per incident for non-securities related claims 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 10 — Stockholders' Equity

As discussed in Note 11, 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.

We currently have an effective shelf registration statement on Form S-3 (the 2021 Shelf Registration Statement) on file with the SEC, which expires in March 2024. The 2021 Shelf Registration Statement currently permits the offering, issuance and sale by us of up to an aggregate offering price of $300.0 million of common stock, preferred stock, debt securities and warrants in one or more offerings and in any combination, all of which may be offered, issued and sold in "at-the-market" sales pursuant to an equity distribution agreement with Cowen and Company, LLC (the Equity Distribution Agreement). No securities have been sold under the 2021 Shelf Registration Statement or the Equity Distribution Agreement.

As of December 31, 2021, shares of common stock reserved for future issuance are as follows (in thousands):

Stock options, RSUs and PSUs outstanding	
Shares available for future grant under the 2017 Performance Incentive Plan	
Shares available for issuance under the employee stock purchase plan	
Total common stock reserved for issuance	

Note 11 — 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. We generally include our costs of performing these services in research and development expense, except for costs for product sales to our collaboration partners which we include in cost of goods sold. We analyze our agreements to determine whether we should account for the agreements within the scope of ASC 808, and, if so, we analyze whether we should account for any elements under ASC 606.

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

		Year Ended December 31,		
Partner	**Agreement**	**2021**	**2020**	**2019**
Bristol-Myers Squibb	Bempegaldesleukin	$ —	$ 50,000	$ —
Eli Lilly and Company	NKTR-358	—	1,259	7,019
Amgen, Inc.	Neulasta®	—	4,167	5,000
Other		436	423	4,956
License, collaboration and other revenue		$ 436	$ 55,849	$ 16,975

As of December 31, 2021, our collaboration agreements with partners included potential future payments for development and regulatory milestones totaling approximately $1.7 billion, including amounts from our agreements with BMS and Eli Lilly and Company 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.

There have been no material changes to our collaboration agreements for the year ended December 31, 2021, except as

described below.

Bristol-Myers Squibb (BMS): Bempegaldesleukin (previously referred to as NKTR-214)

On February 13, 2018, we entered into a Strategic Collaboration Agreement (the BMS Collaboration Agreement) and a Share Purchase Agreement with BMS, both of which became effective on April 3, 2018. Pursuant to the BMS Collaboration Agreement, we and BMS are jointly developing bempegaldesleukin, including, without limitation, in combination with BMS's Opdivo®, and other compounds of BMS, us or any third party. The parties have agreed to jointly commercialize bempegaldesleukin on a worldwide basis. We retained the right to record all worldwide sales for bempegaldesleukin. We will share global commercialization profits and losses with BMS for bempegaldesleukin, with Nektar sharing 65% and BMS sharing 35% of the net profits and losses. The parties share the internal and external development costs for bempegaldesleukin 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 share development costs for bempegaldesleukin in combination with Opdivo®, 67.5% of costs to BMS and 32.5% to Nektar. The parties share costs for the manufacturing and joint commercialization of bempegaldesleukin, 35% of the costs to BMS and 65% to Nektar. On January 9, 2020, we and BMS entered into Amendment No. 1 (the First Amendment) to the BMS Collaboration Agreement, pursuant to which, we and BMS agreed to update the Collaboration Development Plan under which we are collaborating and developing bempegaldesleukin. BMS has the right, at its sole discretion, to terminate co-funding its share of the development costs for the adjuvant melanoma collaboration study if the metastatic melanoma collaboration study fails to meet the primary endpoint of progression free survival. If BMS exercises such right, we have the right, in our sole discretion, to continue the adjuvant melanoma study. On January 12, 2022, we and BMS entered into an Amendment No. 2 to the BMS Collaboration Agreement, pursuant to which we and BMS allocated certain responsibilities for price negotiations and promotion, market access, patient support and related activities to each party. The cost sharing for the development, manufacturing and commercialization under our collaboration remains unchanged as a result of these amendments.

Upon the effective date of the BMS Collaboration Agreement in April 2018, BMS paid us a non-refundable upfront cash payment of $1.0 billion and purchased 8,284,600 shares of our common stock pursuant to the Share Purchase Agreement for total additional cash consideration of $850.0 million. Pursuant to Amendment No. 1 described below, we received a non-refundable, creditable milestone payment of $25.0 million for the first patient, first visit in the registrational muscle-invasive bladder cancer trial, which was achieved on January 30, 2020, and also received a non-refundable, non-creditable milestone payment of $25.0 million for the first patient, first visit in the registrational adjuvant melanoma trial, which we achieved on July 27, 2020. We are eligible to receive potential future payments for development and regulatory milestones of approximately $1.4 billion (which reflects the reduction for the creditable milestone for the muscle-invasive bladder cancer trial) and up to a total of $350.0 million upon the achievement of certain sales milestones.

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 years ended December 31, 2021, 2020 and 2019, we recorded $101.5 million, $128.2 million and $105.4 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, 2021 and 2020, we have recorded an unbilled receivable of $21.4 million and $38.7 million, respectively, from BMS in accounts receivable in our Consolidated Balance Sheet.

Our share of development costs is limited to an annual cap of $125.0 million. To the extent this annual cap is exceeded, BMS reimburses us for the excess, which we must repay to the extent that our share of development costs are less than the annual cap in a future year. For the year-ended December 31, 2020, our share of the development costs exceeded the annual cap and therefore we included the $4.0 million reimbursement in our accounts receivable as of December 31, 2020 and recorded an off-setting liability in Other long-term liabilities. For the year-ended December 31, 2021, our share of the development costs was sufficiently lower than the cap such that we are required to repay the $4.0 million and therefore have reclassified the liability as a reduction of our accounts receivable as of December 31, 2021.

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

During 2018, 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. We allocated the remaining $1,059.8 million to the transaction price of the collaboration agreement, which we recognized in 2018. During the year ended December 31, 2020, we received $50.0 million in aggregate for the achievements of the first patient, first visit in the registrational muscle-invasive bladder cancer trial and the registrational adjuvant melanoma trial, which we recognized as revenue in 2020 because we had previously satisfied our performance obligation of granting the licenses. We continue to exclude the variable consideration of the potential future development, regulatory and sales milestones of up to approximately $1.8 billion from the transaction price as of December 31, 2021 due to the significant uncertainties involved with clinical development and regulatory approval. We re-evaluate the transaction price at each reporting period and as uncertain events are resolved or other changes in circumstances occur.

Eli Lilly and Company (Lilly): *NKTR-358*

On July 23, 2017, we entered into a worldwide license agreement with Eli Lilly and Company (Lilly), which became effective on August 23, 2017, 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, for which we were responsible for completing Phase 1 clinical development and certain drug product development and supply activities, (iii) will share with Lilly Phase 1B and 2 development costs with 75% of those costs borne by Lilly and 25% of the costs borne by us, (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 a royalty rate up to the low twenties 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 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 Phase 1 clinical development obligation and our drug product development obligation as the significant performance obligations in the arrangement. 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 our portion of the Phase 1 clinical development and $6.5 million to the drug product development. We 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 recognized revenue for our portion of the Phase 1 clinical development and drug product development through the three months ended March 31, 2020. As of December 31, 2021, we have no deferred revenue related to this agreement.

We continue to exclude the other milestones from the transaction price as of December 31, 2021 due to the significant uncertainties involved with clinical development.

Baxalta Incorporated/Takeda: *Hemophilia*

We are a party to an exclusive research, development, license and manufacturing and supply agreement with Baxalta Inc. (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 for 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 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. We are entitled to royalties based on worldwide net sales of ADYNOVATE® and an sales milestone upon achievement of an annual worldwide net sales target.

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, we are entitled to single digit royalty payments based upon net sales of the products covered under the sublicense throughout the term of the agreement. As described in Note 8, we sold our rights to receive these royalties to HCR pursuant to the 2020 Purchase and Sale Agreement.

***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 costs and related decisions for MOVANTIK®. In September 2014 and December 2014, MOVANTIK® /MOVENTIG® was approved in the US and EU, respectively. 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. In April 2020, AstraZeneca announced that it had sublicensed its global commercialization rights for MOVANTIK®, excluding Europe, Canada and Israel, to RedHill Biopharma. These sublicenses did not change our rights under the agreement with AstraZeneca, and our royalty rate, royalty term and future potential sales milestones remain unchanged.

For net sales of MOVANTIK® from AstraZeneca and RedHill Biopharma, we are entitled to significant and escalating double-digit royalty payments and sales milestones. For the net sales of MOVANTIK® under the sublicense to Kirin, we are entitled to 40% of the royalties and sales milestones received by AstraZeneca. AstraZeneca is entitled to deduct a portion of its costs for a post-marketing study required by the FDA, subject to certain limits, only through a reduction of the royalties due to us. As of December 31, 2021, our cumulative share of these costs was not significant.

As described in Note 8, we sold our rights to receive these royalties to HCR pursuant to the 2020 Purchase and Sale Agreement, and HCR will bear the cost of any reductions for the post-marketing study.

***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 2010 Agreement) and a license agreement with Amgen, Inc. and Amgen Manufacturing, Limited (together referred to as Amgen). Under the terms of the 2010 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 our proprietary PEGylation materials to Amgen. We recognized this revenue on a straight-line basis over the ten-year term of the 2010 Agreement through September 2021.

Other

In addition, as of December 31, 2021, we have other collaboration agreements, including with our collaboration partner UCB Pharma, under which we are entitled to up to a total of $40.0 million of development milestone payments 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 and, therefore, have excluded all development milestones from the respective transaction prices for these agreements. As of December 31, 2021, we have deferred revenue of approximately $2.0 million related to these other collaboration agreements.

Note 12 — Stock-Based Compensation

2017 Performance Incentive Plan

Our 2017 Performance Incentive Plan (2017 Plan) provides for the issuance of our common stock to members of the Board of Directors, officers or employees, certain consultants and advisors and our subsidiaries. Our 2017 Plan has been amended and restated such that an aggregate 34,200,000 shares have been authorized for issuance as of December 31, 2021, including 5,000,000 shares that were approved on June 10, 2021. Under the 2017 Plan, we may issue stock options, restricted stock, performance stock, stock units, stock appreciation rights and other similar types of awards. When the 2017 Plan was approved on June 14, 2017, any shares of our common stock that were available for issuance under our 2012 Performance Incentive Plan (the 2012 Plan) ceased to be available for future grants. However, options and RSUs granted under the 2012 Plan

remained outstanding, and any options or RSUs that were cancelled or forfeited became available for issuance under the 2017 Plan. Shares issued for RSUs, PSUs or any other "full-value award" will be counted against the share limit as 1.5 shares for every one share actually issued in connection with the award.

We have granted or issued non-qualified stock options, RSUs and PSUs to employees, officers, and non-employee directors. For our employees, the requisite service period is generally four years for stock options, and three years for RSUs and PSUs. For our directors, the requisite service is generally one year for stock options and RSUs. The maximum term of a stock option or stock appreciation right 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.

Under our Change in Control Plan (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) within twelve months following a change of control, our employees are entitled to full acceleration of their unvested equity awards. Our Chief Executive Officer, Senior Vice Presidents and Vice Presidents (including Principal Fellows) are also entitled to full acceleration of unvested equity awards if the termination is initiated by the employee for a Good Reason Resignation (as defined in the CIC Plan) within twelve months following a change of control. Additionally, 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.

Employee Stock Purchase Plan

Under the terms of our the Employee Stock Purchase Plan (ESPP), employees may purchase shares of our common stock based on a percentage of their compensation subject to certain limits. Shares are purchased at 85% of the lower of the closing price on either the first day or last day of each six-month offering period. An aggregate 3,500,000 shares have been authorized for issuance under our ESPP, including 1,000,000 shares approved on June 17, 2020.

Stock-Based Compensation Expense

We recognize total stock-based compensation expense in our Consolidated Statements of Operations as follows (in thousands):

	Year Ended December 31,		
	2021	2020	2019
Cost of goods sold	$ 2,779	$ 2,825	$ 4,294
Research and development	54,821	57,116	63,224
General and administrative	37,074	33,295	32,277
Impairment of assets and other costs for terminated program	—	1,025	—
Total stock-based compensation	$ 94,674	$ 94,261	$ 99,795

The stock-based compensation expense reported in impairment of assets and other costs for terminated program results from executive severance. Stock-based compensation expense resulting from PSUs and our ESPP was not significant in the years ended December 31, 2021, 2020, and 2019.

As of December 31, 2021, total unrecognized compensation costs of $187.4 million related to unvested stock-based compensation arrangements are expected to be recognized as expense over a weighted-average period of 2.6 years.

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, as well as the resulting grant-date fair value:

	Year Ended December 31,		
	2021	2020	2019
Average risk-free interest rate	1.2 %	0.4 %	1.8 %
Dividend yield	0.0 %	0.0 %	0.0 %
Average volatility factor	63.8 %	64.1 %	62.2 %
Weighted-average expected life	5.5 years	5.6 years	5.6 years
Weighted-average grant-date fair value of options granted	$ 8.07	$ 10.70	$ 12.25

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, 2020	13,637	$ 24.30		
Options granted	2,890	14.45		
Options exercised	(2,481)	12.08		
Options forfeited & canceled	(504)	46.25		
Outstanding at December 31, 2021	13,542	$ 23.62	4.66	$ 2,711
Exercisable at December 31, 2021	8,236	26.94	3.08	$ 2,267

(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, 2021.

The intrinsic value of options exercised during the years ended December 31, 2021, 2020 and 2019 totaled $17.3 million, $15.9 million and $30.6 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
Unvested at December 31, 2020	7,094	$ 22.46
Granted	6,544	14.68
Vested and released	(2,617)	25.04
Forfeited and canceled	(1,091)	21.13
Unvested at December 31, 2021	9,930	$ 16.80

The weighted-average grant-date fair values of RSUs granted during the years ended December 31, 2021, 2020 and 2019 were $14.68, $19.24 and $23.32, respectively. The fair value of restricted stock that vested in the years ended December 31, 2021, 2020 and 2019 totaled $45.3 million, $33.3 million and $32.4 million, respectively.

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, 2021, 2020, and 2019, we recognized $3.6 million, $3.5 million, and $3.5 million, respectively, of compensation expense in connection with our 401(k) retirement plan.

Note 13 — Income Taxes

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

	Year Ended December 31,		
	2021	2020	2019
Domestic	$ (524,440)	$ (445,370)	$ (441,494)
Foreign	1,160	1,423	1,440
Loss before provision for income taxes	$ (523,280)	$ (443,947)	$ (440,054)

Provision for Income Taxes

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

	Year Ended December 31,		
	2021	2020	2019
Current:			
Federal	$ —	$ —	$ —
State	50	165	139
Foreign	609	364	495
Total current income tax expense	659	529	634
Deferred:			
Federal	—	—	—
State	—	—	—
Foreign	(102)	(36)	(21)
Total deferred income tax expense	(102)	(36)	(21)
Provision for income taxes	$ 557	$ 493	$ 613

Our income tax provision related to continuing operations differs from the amount computed by applying the statutory income tax rate of 21% to our pretax loss as follows (in thousands):

	Year Ended December 31,		
	2021	2020	2019
Income tax benefit at federal statutory rate	$ (109,889)	$ (93,229)	$ (92,411)
Research credits	(4,727)	(3,081)	(10,511)
Change in valuation allowance	97,914	87,060	104,440
Non-cash interest expense on liability related to sales of future royalties	9,936	6,356	5,259
Non-cash royalty revenue related to sales of future royalties	(7,891)	(7,967)	(7,624)
Loss on revaluation of liability related to the sale of future royalties	4,940	—	—
Stock-based compensation	6,627	7,929	(672)
Other	3,647	3,425	2,132
Provision for income taxes	$ 557	$ 493	$ 613

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 measure deferred tax assets and liabilities based on the rates at which they are expected to reverse in the future. Significant components of our deferred tax assets for federal and state income taxes are as follows (in thousands):

	December 31,	
	2021	2020
Deferred tax assets:		
Net operating loss carryforwards	$ 564,712	$ 456,284
Research and other credits	139,996	132,994
Operating lease liabilities	34,680	35,672
Stock-based compensation	33,408	32,517
Liability related to the sale of future royalties	23,757	32,737
Development derivative liability	6,639	—
Other	10,651	11,688
Deferred tax assets before valuation allowance	813,843	701,892
Valuation allowance for deferred tax assets	(785,748)	(670,103)
Total deferred tax assets	28,095	31,789
Deferred tax liabilities:		
Operating lease right-of-use assets	(27,204)	(29,707)
Other	(564)	(1,856)
Total deferred tax liabilities	(27,768)	(31,563)
Net deferred tax assets	$ 327	$ 226

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, we have fully reserved our net U.S. deferred tax assets with a valuation allowance. The valuation allowance increased by $115.6 million and $95.0 million during the years ended December 31, 2021 and 2020, respectively. The increase in the valuation allowance is consistent with the increase in net operating loss carryforwards in the respective periods.

Net Operating Loss and Tax Credit Carryforwards

As of December 31, 2021, we had a net operating loss carryforward for federal income tax purposes of approximately $2.4 billion, portions of which will begin to expire in 2022 and a total state net operating loss carryforward of approximately $1.5 billion, portions of which will begin to expire in 2026. We have federal research credits of approximately $103.3 million, which will begin to expire in 2023 and state research credits of approximately $47.0 million which have no expiration date. We have federal orphan drug credits of $19.4 million which will begin to expire in 2026. 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.

Unrecognized tax benefits

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

	Year Ended December 31,		
	2021	2020	2019
Beginning balance	$ 78,665	$ 77,410	$ 27,419
Tax positions related to current year:			
Additions	2,371	2,512	49,858
Reductions	—	—	—
Tax positions related to prior years:			
Additions	58	193	277
Reductions	(490)	(1,450)	(144)
Settlements	—	—	—
Lapses in statute of limitations	—	—	—
Ending balance	$ 80,604	$ 78,665	$ 77,410

If we are eventually able to recognize our uncertain tax 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 carryforwards rather than resulting in a cash outlay.

We file income tax returns in the U.S., California, Alabama, certain other states and India. As a result of our net operating loss and research credit carryforwards, substantially all of our domestic tax years remain open and subject to examination. We may be subject to examination in India from time to time, but we do not believe that any liability resulting from such an examination would have a material effect on our financial position or results of operations.

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. During the years ended December 31, 2021, 2020 and 2019, no significant interest or penalties were recognized relating to unrecognized tax benefits. Although it is reasonably possible that certain unrecognized tax benefits could change in the future, we do not anticipate any significant changes over the next twelve months.

Note 14 — 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 UCB Pharma, Baxalta / Takeda, AstraZeneca and Pfizer represented 36%, 23%, 16% and 13% of our revenue, respectively, for the year ended December 31, 2021. Revenue from BMS, UCB Pharma, Baxalta / Takeda, and AstraZeneca represented 33%, 23%, 14% and 13% of our revenue for the year-ended December 31, 2020. Revenue from UCB Pharma, Baxalta / Takeda, and AstraZeneca represented 28%, 19%, and 17% of our revenue for the year-ended December 31, 2019.

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,		
	2021	2020	2019
United States	$ 10,114	$ 64,966	$ 27,093
Rest of World	91,793	87,949	87,524
Total revenue	$ 101,907	$ 152,915	$ 114,617

At December 31, 2021, $56.1 million, or approximately 93%, of the net book value of our property, plant and equipment was located in the United States and $4.4 million, or approximately 7%, was located in India. At December 31, 2020, $54.5 million, or approximately 91%, of the net book value of our property, plant and equipment was located in the United States and $5.1 million, or approximately 9%, was located in India.

Note 15 — 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. All data is in thousands except per share information.

	Year Ended December 31, 2021				Year Ended December 31, 2020			
	Q1	Q2	Q3	Q4	Q1	Q2	Q3	Q4
Product sales	$ 4,795	$ 7,846	$ 5,194	$ 5,890	$ 3,444	$ 5,485	$ 5,691	$ 2,884
Total revenue	$ 23,647	$ 28,330	$ 24,921	$ 25,009	$ 50,573	$ 48,847	$ 30,033	$ 23,462
Cost of goods sold	$ 5,756	$ 7,667	$ 5,311	$ 6,163	$ 3,811	$ 5,773	$ 5,570	$ 4,323
Research and development expenses	$ 95,604	$ 101,313	$ 103,738	$ 99,614	$ 108,987	$ 96,436	$ 100,531	$ 102,724
Operating loss	$ (109,392)	$ (110,205)	$ (113,596)	$ (112,910)	$ (133,631)	$ (77,709)	$ (103,050)	$ (110,721)
Net loss	$ (122,967)	$ (125,519)	$ (129,706)	$ (145,645)	$ (138,651)	$ (80,000)	$ (108,586)	$ (117,203)
Net loss per share, basic and diluted(1)	$ (0.68)	$ (0.69)	$ (0.70)	$ (0.79)	$ (0.78)	$ (0.45)	$ (0.61)	$ (0.65)

(1) Quarterly loss per share amounts may not total to the year-to-date 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 rules and forms of the SEC, 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 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 our Chief Executive Officer and 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, our Chief Executive Officer and Chief Financial Officer concluded that our disclosure controls and procedures were effective.

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, 2021. 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, 2021.

The effectiveness of our internal control over financial reporting as of December 31, 2021 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, 2021, 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. Specifically, despite the fact that most of our employees are working remotely due to the COVID-19 pandemic, we do not believe that our adjustments to how we work have materially impacted our internal controls over financial reporting. We continue to monitor and assess the potential impact of the COVID-19 pandemic, and the related shelter-in-place requirements, on our internal controls and strive to minimize the impact on our internal control design and operating effectiveness.

Inherent Limitations on the Effectiveness of Controls

Our management, including our 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 errors or mistakes. 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.

Item 9C. ***Disclosure Regarding Foreign Jurisdictions that Prevent Inspections***

Not applicable.

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 "Information about our Executive Officers" and is incorporated herein by reference. The other information required by this Item is incorporated by reference from the definitive proxy statement for our 2020 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. Executive officers and directors can only sell our stock in accordance with our securities trading policy and pursuant to a stock trading program set up under Rule 10b5-1 (wherein "exercise and hold" and stock purchases are exempted, and sales outside such a program can proceed upon approval of the Nominating and Corporate Governance Committee of our Board of Directors. Employees who are not executive officers may 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***

Our independent public accounting firm is Ernst & Young LLP, Redwood City, California, PCAOB Auditor ID 42.

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.”

(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
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.
4.4(28)	Description of Securities.
10.1(8)	2000 Equity Incentive Plan, as amended and restated.++
10.2(8)	2000 Non-Officer Equity Incentive Plan, as amended and restated.++

Exhibit Number	Description of Documents
10.3(8)	2008 Equity Incentive Plan, as amended and restated.++
10.4(8)	Discretionary Incentive Compensation Policy++
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(12)	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(13)	Employee Stock Purchase Plan, as amended and restated.++
10.11(14)	Amended and Restated Compensation Plan for Non-Employee Directors.++
10.12(15)	401(k) Retirement Plan.++
10.13(16)	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(17)	Letter Agreement, executed effective on December 10, 2009, with Stephen K. Doberstein, Ph.D.++
10.17(28)	Transition, Separation and General Release Agreement, dated as of January 9, 2020, by and between Stephen K. Doberstein and Nektar Therapeutics. ++
10.18(19)	Separation, Consulting and General Release Agreement effective as of October 15, 2019, by and between Nektar Therapeutics and John Nicholson.++
10.19(28)	Employment Agreement effective as of December 4, 2019, by and between Nektar Therapeutics and John Northcott.++
10.20(16)	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.
10.21(18)	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.

Exhibit Number	Description of Documents
10.22(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.
10.23(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.+
10.24(1)	Exclusive License Agreement, dated December 31, 2008, between Nektar Therapeutics, a Delaware corporation, and Novartis Pharma AG, a Swiss corporation.+
10.25(17)	Supply, Dedicated Suite and Manufacturing Guarantee Agreement, dated October 29, 2010, by and among Nektar Therapeutics, Amgen Inc. and Amgen Manufacturing, Limited.+
10.26(21)	License Agreement by and between AstraZeneca AB and Nektar Therapeutics, dated September 20, 2009.+
10.27(22)	Collaboration and License Agreement dated as of May 30, 2016, by and between Daiichi Sankyo Europe GmbH and Nektar Therapeutics.
10.28(18)	License Agreement effective as of August 23, 2017, by and between Eli Lilly and Company and Nektar Therapeutics.
10.29(7)	Purchase Agreement dated September 30, 2015 by and among Nektar Therapeutics and TC Lending, LLC and TAO Fund, LLC.
10.30(7)	Pledge and Security Agreement dated October 5, 2015 by and among Nektar Therapeutics and TC Lending, LLC.
10.31(23)	Purchase and Sale Agreement, dated as of February 24, 2012, between Nektar Therapeutics and RPI Finance Trust.+
10.32(24)	Amendment No. 1 to License Agreement dated effective as of August 8, 2013, by and between Nektar Therapeutics and AstraZeneca AB.+
10.33(25)	Investor Agreement, dated as of February 13, 2018, by and between Bristol-Myers Squibb and Company and Nektar Therapeutics.+
10.34(25)	Strategic Collaboration Agreement, dated as of February 13, 2018, by and between Bristol-Myers Squibb and Company and Nektar Therapeutics.+
10.35(29)	Co-Development Agreement, dated as of February 12, 2021, by and between SFJ Pharmaceuticals XII, L.P. and Nektar Therapeutics.+
10.36(28)	Amendment No. 1 to Strategic Collaboration Agreement dated as of January 9, 2020, by and between Bristol-Myers Squibb and Company and Nektar Therapeutics.+
10.37(26)	Share Purchase Agreement, dated as of February 13, 2018, by and between Bristol-Myers Squibb and Company and Nektar Therapeutics.
10.38(27)	Office Lease, effective as of May 31, 2018, by and between Kilroy Realty Finance Partnership, L.P., and Nektar Therapeutics.

Exhibit Number	Description of Documents
10.39(29)	Purchase and Sale Agreement, dated December 16, 2020, by and between entities managed by Healthcare Royalty Management, LLC and Nektar Therapeutics.+
10.40(30)	Amendment No. 2 to Strategic Collaboration Agreement dated as of January 12, 2022, by and between Bristol-Myers Squibb and Company and Nektar Therapeutics.+
21.1(30)	Subsidiaries of Nektar Therapeutics.
23.1(30)	Consent of Independent Registered Public Accounting Firm.
24	Power of Attorney (reference is made to the signature page).
31.1(30)	Certification of Nektar Therapeutics' principal executive officer required by Rule 13a-14(a) or Rule 15d-14(a).
31.2(30)	Certification of Nektar Therapeutics' principal financial officer required by Rule 13a-14(a) or Rule 15d-14(a).
32.1*	Section 1350 Certifications.
101.SCH**	Inline XBRL Taxonomy Extension Schema Document.
101.CAL**	Inline XBRL Taxonomy Extension Calculation Linkbase Document.
101.LAB**	Inline XBRL Taxonomy Extension Label Linkbase Document.
101.PRE**	Inline XBRL Taxonomy Extension Presentation Label Linkbase Document.
101.DEF**	Inline XBRL Taxonomy Extension Definition Linkbase Document.
104**	Cover Page Interactive Data File (formatted as inline XBRL with applicable taxonomy extension information contained in Exhibits 101).

+ Certain confidential portions (indicated by brackets and asterisks) have been omitted from this exhibit in accordance with the rules of the Securities and Exchange Commission.
++ 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.
** Inline 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 December 21, 2020.
(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 10-Q for the quarter ended June 30, 2021.
(12) Incorporated by reference to the indicated exhibit in Nektar Therapeutics' Annual Report on Form 10-K for the year ended December 31, 2018.
(13) Incorporated by reference to the indicated exhibit in Nektar Therapeutics' Quarterly Report on Form 10-Q for the quarter ended June 30, 2020.
(14) Incorporated by reference to the indicated exhibit in Nektar Therapeutics' Quarterly Report on Form 10-Q for the Quarter ended March 31, 2020.
(15) Incorporated by reference to the indicated exhibit in Nektar Therapeutics Quarterly Report on Form 10-Q for the quarter ended June 30, 2004.
(16) Incorporated by reference to the indicated exhibit in Nektar Therapeutics' Quarterly Report on Form 10-Q for the quarter ended September 30, 2007.
(17) Incorporated by reference to the indicated exhibit in Nektar Therapeutics' Annual Report on Form 10-K for the year ended December 31, 2010.
(18) Incorporated by reference to the indicated exhibit in Nektar Therapeutics' Quarterly Report on Form 10-Q for the quarter ended September 30, 2017.
(19) Incorporated by reference to the indicated exhibit in Nektar Therapeutics' Quarterly Report on Form 10-Q for the quarter ended September 30, 2019.
(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) Incorporated by reference to the indicated exhibit in Nektar Therapeutics' Annual Report on Form 10-K for the year ended December 31, 2019.
(29) Incorporated by reference to the indicated exhibit in Nektar Therapeutics' Annual Report on Form 10-K for the year ended December 31, 2020.
(30) 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, 2022.

By: /s/ GIL M. LABRUCHERIE
Gil M. Labrucherie
Senior Vice President, Chief Operating Officer, 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, 2022
/s/ GIL M. LABRUCHERIE **Gil M. Labrucherie**	Senior Vice President, Chief Operating Officer, and Chief Financial Officer (Principal Financial Officer)	February 28, 2022
/s/ JILLIAN B. THOMSEN **Jillian B. Thomsen**	Senior Vice President, Finance and Chief Accounting Officer (Principal Accounting Officer)	February 28, 2022
/s/ ROBERT B. CHESS **Robert B. Chess**	Director, Chairman of the Board of Directors	February 28, 2022
/s/ JEFFREY R. AJER **Jeffrey R. Ajer**	Director	February 28, 2022
/s/ DIANA M. BRAINARD **Diana M. Brainard**	Director	February 28, 2022
/s/ MYRIAM J. CURET **Myriam J. Curet**	Director	February 28, 2022
/s/ KARIN EASTHAM **Karin Eastham**	Director	February 28, 2022
/s/ R. SCOTT GREER **R. Scott Greer**	Director	February 28, 2022
/s/ ROY A. WHITFIELD **Roy A. Whitfield**	Director	February 28, 2022

[***] Certain confidential portions (indicated by brackets and asterisks) have been omitted from the exhibit in accordance with the rules of the Securities and Exchange Commission.

AMENDMENT NO. 2 TO
STRATEGIC COLLABORATION AGREEMENT

This Amendment No. 2 (this "***Amendment No. 2***") to the Agreement (as defined below) is entered into as of January 12, 2022 (the "***Amendment No. 2 Effective Date***") by and between Nektar Therapeutics, a Delaware corporation, headquartered at 455 Mission Bay Boulevard South, Suite 100, San Francisco, California 94158 ("***Nektar***"), and Bristol-Myers Squibb Company, a Delaware corporation, headquartered at 345 Park Avenue, New York, New York, 10154 ("***BMS***"). Nektar and BMS may be referred to herein individually as a "***Party***," or collectively as the "***Parties***."

RECITALS

WHEREAS, the Parties have entered into a Strategic Collaboration Agreement dated as of February 13, 2018 and effective as of April 3, 2018, as subsequently amended by Amendment No. 1 to Strategic Collaboration Agreement, dated January 9, 2020 (the "***Agreement***");

WHEREAS, the Parties have agreed to further amend the Agreement with respect to certain provisions relating to responsibility for price negotiations and certain promotional responsibilities, market access, patient support, and related activities as set forth in this Amendment No. 2;

NOW, THEREFORE, in consideration of the foregoing premises and the mutual promises and covenants contained herein, the receipt and sufficiency of which is hereby acknowledged, the Parties agree as follows:

Article 1

DEFINITIONS

1.1. New Defined Terms. The Parties shall reasonably discuss and mutually agree upon the scope and parameters of certain activities, which shall be consistent with standard industry practices, including definitions, if necessary and appropriate, relating to market access, reimbursement and patient support, as further described herein, in the Global Pricing and Reimbursement Plan and Budget.

1.2. Amended and Restated Defined Terms. The definitions set forth below are amended and restated in their entirety and incorporated into the Agreement by this reference.

"***Allowable Commercialization Expenses***" shall mean those expenses (a) incurred in connection with the Commercialization of the Products pursuant to the Commercialization Plan and Budget and the Global Pricing and Reimbursement Plan and Budget, each as mutually agreed by the Parties and approved by the JCC in accordance with Section 8.3 and (b) that are consistent with the approved budget set forth in the Commercialization Plan and Budget and the Global Pricing and Reimbursement Plan and Budget, as relevant, and are specifically attributable to Products, and shall consist of (i) Cost of Goods Sold, (ii) the market access and reimbursement and patient support costs mutually agreed by the Parties and approved by the JCC under the Global Pricing

and Reimbursement Plan and Budget, in accordance with Section 8.3, (iii) Marketing Expenses, (iv) Distribution Expenses, and (v) Post-Approval Regulatory Expenses. The JFC shall establish procedures for the calculation of Allowable Commercialization Expenses, including proper allocation of FTE costs to the extent that such FTEs promote other products (including the allocation of sales force effort between first, second and third position detail) or otherwise engage in activities not solely related to the Commercialization of the Product. For clarity, subject to Section 9.5, each Party shall be responsible for and solely bear any Commercialization expenses not contemplated in, or in excess of the agreed amounts set forth in, the approved budget set forth in the Commercialization Plan and Budget or the Global Pricing and Reimbursement Plan and Budget, as applicable."

"***Global Pricing and Reimbursement Plan and Budget***" shall mean the strategy, plan and budget setting forth the pricing, market access, and reimbursement and patient support plan for each Product in the Field in the Territory on a global basis during a given Calendar Year and the [***] succeeding Calendar Years, as developed by Nektar and approved by the JCC in accordance with Section 8.3 (subject to Nektar final decision-making authority with respect to Pricing Decisions under Section 8.6(a)), as amended from time to time in accordance with the procedures set forth in this Agreement. The Global Pricing and Reimbursement Plan and Budget shall be developed by Nektar with reasonable support and input by BMS, which Nektar shall consider in good faith, with respect to market access/reimbursement and patient support and advocacy activities. Upon adoption of the Global Pricing and Reimbursement Plan in accordance with this Agreement, such plan shall become incorporated into this Agreement.

Article 2

AMENDMENTS

2.1. Section 8.3 of the Agreement is amended and restated in its entirety and incorporated into the Agreement by this reference:

"**8.3 Responsibilities of the Joint Commercialization Committee.** Each Party shall use Commercially Reasonable Efforts to keep the JCC informed about activities performed by that Party hereunder. The JCC will be responsible for the overall oversight of the global Commercialization of the Product. Commercialization of each Product shall be pursuant to the Commercialization Plan and Budget and the Global Pricing and Reimbursement Plan and Budget, provided that Commercialization in the countries other than Major Markets shall be conducted in a manner consistent with the Commercialization Plan and Budget and the Global Pricing and Reimbursement Plan and Budget. The JCC (or in the absence of a formal JCC meeting, the JCC Co-Chairs) shall be responsible for the following, to the extent consistent with Applicable Law (including Applicable Law, antitrust, anti-monopoly or competition law or regulation, whether or not statutory) and Section 8.9(h):

(a) reviewing and providing timely comments to the initial Commercialization Plan and Budget proposed by BMS and the Global Pricing and Reimbursement Plan and Budget proposed by Nektar;

(b) updating and amending each of the Commercialization Plan and Budget and the Global Pricing and Reimbursement Plan and Budget as Regulatory Approvals for the Product are obtained (whether as a result of Collaboration Studies or Independent Studies);

(c) overseeing the Commercialization Plan and Budget and Global Pricing and Reimbursement Plan and Budget, including approving each of the Commercialization Plan and Budget and the Global Pricing and Reimbursement Plan and Budget, and any material amendments thereto;

(d) reviewing and providing timely comments to proposals from Nektar with respect to the initial post-approval Product price, any price increase/decrease ranges, annual price discounting/rebate ranges, and purchase, access and coverage conditions for Third Party payors and other purchasers (collectively, "**Pricing Decisions**"), the period for which the applicable Pricing Decisions shall apply (the "**Pricing Period**") including approving any amendments thereto; provided that all Pricing Decisions shall be subject to both Parties' legal and compliance guidelines, good faith consideration of comments and input from BMS, and Nektar final decision-making authority under Section 8.6(a);

e) overseeing the activities of the Parties with respect to the global Commercialization and pricing of the Product under each of the Commercialization Plan and Budget and the Global Pricing and Reimbursement Plan and Budget, and providing a forum for the Parties to discuss, monitor and coordinate all activities and communications regarding the global Commercialization and pricing of the Products, including payor interactions and discount/rebate range negotiations with respect to Products;

(f) Intentionally Blank

(g) reviewing and providing timely comments to proposed communication strategies and communications with any Regulatory Authority regarding the global Commercialization of the Product and, if applicable, approving such proposed communications and communication strategies;

(h) appointing working teams, to be made up of an equal number of representatives from each Party, that will hold telephone discussions at a mutually agreed-upon frequency to review global Commercialization of the Product issues that arise in the course of a study under the Commercialization Plan and Budget set forth therein, and delegating certain decision-making authority to such working teams;

(i) reviewing each Party's [***] forecast provided to the JCC for quantities of Product necessary for global Commercialization of the Products, which shall be reviewed [***], and for which [***];

(j) determining the quantities of Product, necessary for global Commercialization of the Products within a sufficient minimum lead time and

coordinating the supply of such quantities by the respective Party in accordance with Article 5 and the Supply Agreements or other arrangements;

(k) reviewing each Party's Commercialization forecast for the BMS Assets and other Nektar Assets used in Combined Therapies and advising each Party with respect to allocation of applicable available inventory; and

(l) discussing any other topics or issues relating to the global Commercialization of the Product that either Party requests that cannot be resolved at the working team level."

2.2. Section 8.5 of the Agreement is amended and restated in its entirety and incorporated into the Agreement by this reference:

"**8.5 Dispute Resolution.** The representatives of the JCC shall attempt in good faith to reach consensus on all matters properly brought before the JCC. Except as otherwise provided in this Agreement, if, after a good faith, reasonable and open discussion among the members of the JCC, the JCC is unable to agree on a matter that has been properly before it for a period of [***] and that calls for a decision, either Party may refer the dispute (a "**JCC Dispute**") to the JEC for resolution. If the JEC is unable to reach a resolution within [***] of the referral of the JCC Dispute to the JEC, either Party may refer such JCC Dispute to the Executive Officers for resolution. Subject to the following sentence, if the Executive Officers are unable to reach a resolution within [***] of such referral and such JCC Dispute is not otherwise addressed by Section 8.6 (Final Decision-Making Authority of the Parties), the dispute shall be resolved through arbitration as provided for in Article 15, whether as a Commercial/Financial Dispute or as an Arbitration Matter. If the JCC Dispute regards the Commercialization Plan and Budget and its contents for any Product or the Global Pricing and Reimbursement Plan and Budget and its contents for any Product, then such JCC Dispute shall not be subject to arbitration hereunder, no Party shall have final decision-making authority unless otherwise specified herein and the Parties shall not be deemed to be in breach of their Commercially Reasonable Efforts to Commercialize the Product, and the previous year's Commercialization Plan and Budget and Global Pricing and Reimbursement Plan and Budget shall apply until the Parties align and agree on a revised Commercialization Plan and Budget and Global Pricing and Reimbursement Plan and Budget."

2.3. Section 8.6 of the Agreement is amended and restated in its entirety and incorporated into the Agreement by this reference:

"**8.6 Final Decision-Making Authority of the Parties.** In the event a JCC Dispute is unresolved pursuant to Section 8.5 as set forth above:

(a) Nektar shall have final decision-making authority regarding (i) Pricing Decisions for the Product in (x) Nektar Combinations and (y) BMS Combinations, in each of (x) and (y), on a continuing, global basis, provided that the Pricing Decisions, once established for any given Pricing Period, shall not be changed during the applicable Pricing Period except as jointly agreed by the Parties through the JCC, and (ii) the Commercialization of Nektar Combinations

and any Monotherapy, and (iii) the market access, reimbursement and patient support and advocacy activities for the Product in (x) Nektar Combinations and (y) BMS Combinations, in each of (x) and (y) on a continuing, global basis, provided that the market access, reimbursement and patient support and advocacy activities, once established for any given period under the Global Pricing and Reimbursement Plan and Budget, shall not be changed during the applicable period except as jointly agreed by the Parties through the JCC.

(b) Subject to Nektar's final decision-making authority with respect to Price for the Product as set forth in Section 8.6(a), BMS shall reasonably cooperate in good faith with Nektar regarding the Commercialization (but not Pricing Decisions) of the BMS Combinations, to the extent not otherwise explicitly set forth or in conflict with any other provision in this Agreement;

provided, that the Parties expressly acknowledge and agree that nothing contained in this Section 8.6 grants any decision-making authority to Nektar with respect to any pricing decisions or activities relating to any BMS Asset"

2.4. Section 8.7 of the Agreement is amended and restated in its entirety and incorporated into the Agreement by this reference:

"**8.7 Pricing.** As a general matter and subject to the oversight of the JCC under Section 8.3, Nektar shall be responsible for price negotiations, Pricing Decisions and other industry-standard market access activities (including interactions with Third Party payors and/or purchasers regarding the purchase, coverage, and/or reimbursement of the Product), in (a) Nektar Combinations and (b) BMS Combinations, in each of (a) and (b) in all countries in the Territory, whether developed under the Joint Development Plan or an Independent Study, provided, however, that Nektar shall not engage in any price negotiations or other interactions or make any Pricing Decisions with respect to BMS Assets, which negotiations and other interactions and decisions shall be the responsibility of and controlled by BMS. For clarity, (x) Nektar will not discuss any pricing or other contracting terms that solely relate to BMS Assets as these discussions are the sole responsibility of and controlled by BMS, and further, if Nektar were to receive a question from a Third Party regarding the price or coverage terms of a BMS Asset, Nektar will direct such question to BMS, and (y) BMS will not discuss any pricing or other contracting terms that solely relate to Nektar Assets, as these discussions are the sole responsibility of and controlled by Nektar, and further, if BMS were to receive a question from a Third Party regarding the price or coverage terms of a Nektar Asset, BMS will direct such question to Nektar. BMS shall have the right to jointly participate in any such interactions led by Nektar solely for purposes of participating in discussions relating to the clinical profile, including safety and efficacy, of the Product in BMS Combinations; provided, however, that BMS may not participate in discussions specific to and negotiations of price. With respect to the foregoing, any deviation from the Pricing Decisions requires a disclosure to and approval of the JCC, subject to Nektar's final decision making authority under Section 8.6, as limited by such Section.

2.5. Section 8.9 of the Agreement is amended and restated in its entirety and incorporated into the Agreement by this reference:

[***] Certain confidential portions (indicated by brackets and asterisks) have been omitted from the exhibit in accordance with the rules of the Securities and Exchange Commission.

"**8.9 Commercialization.**

(a) The Parties shall be responsible for paying all Commercialization costs incurred by such Party set forth in the Commercialization Plan and Budget and Global Pricing and Reimbursement Plan approved by the JCC, and subject further to the Revenue Reporting and Reconciliation Procedures and Section 9.5. Each Party shall use Commercially Reasonable Efforts to Commercialize Products in the Field in the Territory in accordance with the Commercialization Plan and Budget and the terms of this Agreement.

(b) The JCC may establish standards applicable to the Parties' performance of Commercialization activities in accordance with the Commercialization Plan and Budget, the Global Pricing and Reimbursement Plan and Budget and this Agreement, which may include standards for sales representatives promoting Products in the Field. The Parties may review and discuss each Party's (and its Affiliates') performance against such standards at each meeting of the JCC. If the JCC determines that a Party or its Affiliate has failed to comply with such standards and such failure could adversely affect the Development or Commercialization of any Product in the Field, or if the JCC does not agree and one Party believes such is the case, the JCC shall (or such Party may) escalate the issue to the JEC for review and resolution.

(c) Each Party shall be responsible for day-to-day implementation of the Commercialization activities with respect to the Product for which it has or otherwise is assigned responsibility under this Agreement, the Commercialization Plan and Budget, and the Global Pricing and Reimbursement Plan and Budget and shall keep the other Party reasonably informed as to the progress of such activities, as determined by the JCC. The Commercialization Plan and Budget and the Global Pricing and Reimbursement Plan and Budget shall include a description of the respective Commercialization efforts on a country-by-country basis delegated to a Party for the Product, the Nektar Combinations and BMS Combinations.

(i) BMS shall have certain responsibility for the promotion and marketing in the Territory for BMS Combinations Developed under the Joint Development Plan or under an Independent Study as set forth in the Commercialization Plan and Budget, and BMS shall provide reasonable support and input to Nektar, which Nektar shall consider in good faith, with respect to medical support, market access/reimbursement and patient support and advocacy activities to maximize the efficiency and effectiveness of such activities.

(ii) Subject to Section 8.9(c)(i) above and the standards established by the JCC set forth in Section 8.9(b) above with respect to the performance of Commercialization activities, Nektar shall have primary responsibility for the promotion, marketing, medical support, market access/reimbursement and patient support and advocacy activities in the Territory for each of (x) the Nektar Combinations and (y) the BMS Combinations,

in each of (x) and (y) Developed under the Joint Development Plan or under an Independent Study, in accordance with the Commercialization Plan and Budget and Global Pricing and Reimbursement Plan approved by the JCC.

(d) For clarity, nothing in Section 8.9(c) shall limit either Party from promoting the Product to the extent permitted by Applicable Law outside of the scope of the Commercialization Plan and Budget, provided that (A) such promotion shall be consistent with the other provisions of this Article 8; (B) such promotion shall be consistent with the Product Brand Strategy in order to prevent counter-detailing of BMS Combinations or Nektar Combinations; (C) the Parties will not be permitted to create, disseminate or otherwise use or employ negative messaging regarding the BMS Assets and BMS Combinations, in the case of Nektar, and the Nektar Assets and Nektar Combinations, in the case of BMS; and (D) the Parties shall limit claims of efficacy and safety for any Product to those that are consistent with Applicable Laws.

(e) Unless otherwise approved by the JCC, in the performance of Commercialization (including promotion) of the Nektar Compound and Product pursuant to this Agreement, neither Party (nor any Nektar Successor or BMS Successor) shall use, other than promotional materials approved in accordance this Agreement, the trademarks, logos, promotional materials, trade dress, copyrights, corporate logos, corporate names, visual identity and branding elements of the other Party (or the other Party's other products) without the prior written consent of such other Party.

(f) The Parties shall use Commercially Reasonable Efforts to ensure commercial availability of the Nektar Assets (other than the Product) or BMS Assets, as applicable, that are used in Combined Therapies, at a level and volume of supply necessary to support achievement of the forecasted sales of the Product.

(g) Product Brand Strategy and Promotional Materials.

(i) The JCC shall appoint a joint Product brand strategy working team (the "**Product Brand Strategy Working Team**"). As set forth in the Commercialization Plan and Budget, Nektar and BMS shall develop the global brand strategy for the Product (the "**Product Brand Strategy**"), including positioning, branding, and global messaging, that will guide the development of the relevant sales, promotion and advertising materials (x) by Nektar (for the Nektar Combinations pursuant to Section 8.9(g)(ii)) and (y) by BMS (for the BMS Combinations pursuant to Section 8.9(g)(iii)). The Product Brand Strategy must comply with each Party's applicable SOPs, the Commercialization Plan and Budget, Applicable Laws and Regulatory Approvals. If the Product Brand Strategy Working Team cannot agree upon certain matters relating to the Product Brand Strategy, the matter may be referred to (A) the JCC or (B) for legal and compliance matters, the legal or compliance departments of the Parties, and then to the JCC for resolution, subject in this case to the final approval of the Parties' respective compliance officers and legal departments, provided that if the Parties'

compliance officers or legal departments are unable to reach an agreement on the matter referred to them in accordance with the immediately preceding sentence, then the Parties shall adopt the approach of the Party with the more conservative compliance or legal position regarding such matter.

(ii) Nektar shall develop the relevant sales, promotion, market access and advertising materials relating to the Nektar Combinations for use in the Territory by Nektar and its Affiliates, provided that such materials, to the extent that they relate to the Product, shall be consistent with the Product Brand Strategy. Nektar shall be responsible for compliance for such materials, including with Applicable Law and the applicable Regulatory Approvals.

(iii) BMS shall develop the relevant sales, promotion and advertising materials relating to the BMS Combinations for use in the Territory by BMS and its Affiliates, provided that such materials, to the extent that they relate to the Product, shall be consistent with the Product Brand Strategy. Nektar shall be responsible, and shall indemnify BMS, for compliance for market access materials, including with Applicable Law and the applicable Regulatory Approvals, developed by or on behalf of Nektar.

(iv) Copies of all promotional materials relating to the Nektar Combinations and BMS Combinations as set forth in Sections 8.9(g)(ii) and 8.9(g)(iii), used by Nektar and BMS and their Affiliates in the Territory will be archived by Nektar and BMS, as applicable, in accordance with Applicable Law.

(v) The JCC shall develop and approve Product packaging for use in the Territory by both Parties and their Affiliates, which shall be consistent with the Commercialization Plan and Budget and compliant with the Product Brand Strategy, each Party's applicable SOPs, Applicable Laws and Regulatory Approvals.

(h) The Parties shall establish reasonable procedures to protect the secrecy of Nektar's and BMS's competitively sensitive Confidential Information with respect to the Commercialization of Combined Therapies, including limiting access to such information to ensure that employees performing activities in connection with a Party's assets or combination of assets outside the Joint Development Plan that compete with a Product in the Field do not receive competitively sensitive Confidential Information with respect to the Commercialization of Combined Therapies."

Article 3

BMS COMBINATION COMMERCIALIZATION OPTION

3.1. The Parties acknowledge and agree that the pricing and promotional and related activities undertaken by Nektar herein shall not amend or supersede, or be deemed an exercise of, the BMS Combination Commercialization Option set forth in Section 8.12 of the Agreement.

[***] Certain confidential portions (indicated by brackets and asterisks) have been omitted from the exhibit in accordance with the rules of the Securities and Exchange Commission.

Article 4

MISCELLANEOUS

4.1. Except as amended by this Amendment No. 2, all the terms and conditions of the Agreement shall remain in full force and effect.

4.2. In the event of a conflict between the terms of this Amendment No. 2 and the terms of the Agreement, the terms of this Amendment No. 2 shall prevail.

4.3. The headings used in this Amendment No. 2 have been inserted for convenience of reference only and do not define or limit the provisions hereof.

4.4. This Amendment No. 2 may be signed in any number of counterparts (facsimile and electronic transmission included), each of which shall be deemed an original, but all of which shall constitute one and the same instrument.

4.5. This Amendment No. 2 and all claims relating to or arising out of this Amendment No. 2 or the breach thereof shall be governed and construed in accordance with the internal laws of the State of New York, USA, excluding any choice of law rules that may direct the application of the laws of another jurisdiction. The United Nations Convention on Contracts for the International Sale of Goods shall not apply to this Agreement. No part of this Amendment No. 2 changes the rights and obligations of the Parties under Article 15 of the Agreement.

4.6. This Amendment No. 2 and the Agreement (as amended by this Amendment No. 2) constitute the entire understanding between the Parties with respect to the subject matter hereof, and supersede all prior agreements whether oral or written. No amendment, modification, waiver, release or discharge to this Amendment No. 2 or the Agreement shall be binding upon the Parties unless in writing and duly executed by authorized representatives of both Parties.

4.7. This Amendment No. 2 has been prepared jointly and shall not be strictly construed against either Party. No presumption as to construction of this Amendment shall apply against either Party with respect to any ambiguity in the wording of any provision(s) of this Amendment No. 2 irrespective of which Party may be deemed to have authored the ambiguous provision(s).

[signature page follows]

IN WITNESS WHEREOF, the Parties hereto, intending to be legally bound hereby, have caused this Amendment No. 2 to be executed by their duly authorized representatives as of the Amendment No. 2 Effective Date.

Nektar Therapeutics	**Bristol-Myers Squibb Company**
By: /s/ Gil M. Labrucherie	By: /s/ Elizabeth Mily
Name: Gil M. Labrucherie	Name: Elizabeth Mily
Title: COO and CFO	Title: EVP, Strategy & Business Development
Date: January 12, 2022	Date: January 12, 2022

Exhibit 21.1

Subsidiaries of Nektar Therapeutics

Name	Jurisdiction of Incorporation or Organization
Inheris Biopharma, Inc.	United States

Exhibit 23.1

Consent of Independent Registered Public Accounting Firm

We consent to the incorporation by reference in the following Registration Statements:

(1) Registration Statement (Form S-8 No. 333-145259) pertaining to the 401(k) Retirement Plan of Nektar Therapeutics,
(2) Registration Statement (Form S-8 No. 333-153106) pertaining to the 2008 Equity Incentive Plan of Nektar Therapeutics,
(3) Registration Statement (Form S-8 No. 333-170371) pertaining to the Employee Stock Purchase Plan of Nektar Therapeutics,
(4) Registration Statement (Form S-8 No. 333-183193) pertaining to the 2012 Performance Incentive Plan of Nektar Therapeutics,
(5) Registration Statement (Form S-8 No. 333-197781) pertaining to the Employee Stock Purchase Plan of Nektar Therapeutics,
(6) Registration Statement (Form S-8 No. 333-206136) pertaining to the 2012 Performance Incentive Plan of Nektar Therapeutics,
(7) Registration Statement (Form S-8 No. 333-218777) pertaining to the 2017 Performance Incentive Plan of Nektar Therapeutics,
(8) Registration Statement (Form S-8 No. 333-226004) pertaining to the Amended and Restated 2017 Performance Incentive Plan of Nektar Therapeutics,
(9) Registration Statement (Form S-8 No. 333-242327) pertaining to the Amended and Restated 2017 Performance Incentive Plan and Amended and Restated Employee Stock Purchase Plan of Nektar Therapeutics,
(10) Registration Statement (Form S-3 No. 333-254237) of Nektar Therapeutics, and
(11) Registration Statement (Form S-8 No. 333-258900) pertaining to the Amended and Restated 2017 Performance Incentive Plan of Nektar Therapeutics;

of our reports dated February 28, 2022, with respect to the consolidated financial statements of Nektar Therapeutics and the effectiveness of internal control over financial reporting of Nektar Therapeutics included in this Annual Report (Form 10-K) of Nektar Therapeutics for the year ended December 31, 2021.

/s/ Ernst & Young LLP

Redwood City, California
February 28, 2022

Exhibit 31.1

CERTIFICATIONS

I, Howard W. Robin, certify that:

1. I have reviewed this Annual Report on Form 10-K of Nektar Therapeutics for the year ended December 31, 2021;

2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;

3. Based on my knowledge, the financial statements and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;

4. The registrant's other certifying officer(s) and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined in Exchange Act rules 13a-15(f) and 15d-15(f)) for the registrant and have:

a) Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under my supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;

b) Designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under my supervision, 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;

c) Evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and

d) Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting.

5. The registrant's other certifying officer(s) and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):

a) All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and

b) Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Date: February 28, 2022

/s/ HOWARD W. ROBIN

Howard W. Robin
Chief Executive Officer, President and Director

Exhibit 31.2

CERTIFICATIONS

I, Gil M. Labrucherie, certify that:

1. I have reviewed this Annual Report on Form 10-K of Nektar Therapeutics for the year ended December 31, 2021;

2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;

3. Based on my knowledge, the financial statements and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;

4. The registrant's other certifying officer(s) and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined in Exchange Act rules 13a-15(f) and 15d-15(f)) for the registrant and have:

a) Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under my supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;

b) Designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under my supervision, 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;

c) Evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and

d) Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting.

5. The registrant's other certifying officer(s) and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):

a) All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and

b) Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Date: February 28, 2022

/s/ GIL M. LABRUCHERIE

Gil M. Labrucherie
Senior Vice President, Chief Operating Officer, and Chief Financial Officer

Exhibit 32.1

SECTION 1350 CERTIFICATIONS*

Pursuant to the requirement set forth in Rule 13a-14(b) of the Securities Exchange Act of 1934, as amended (the "Exchange Act"), and Section 1350 of Chapter 63 of Title 18 of the United States Code (18 U.S.C. § 1350), Howard W. Robin, Chief Executive Officer, President and Director of Nektar Therapeutics (the "Company"), and Gil M. Labrucherie, Senior Vice President, Chief Operating Officer, and Chief Financial Officer of the Company, each hereby certifies that, to the best of his knowledge:

1. The Company's Annual Report on Form 10-K, for the year ended December 31, 2021, to which this Certification is attached as Exhibit 32.1 (the "Annual Report"), fully complies with the requirements of Section 13(a) or 15(d) of the Securities Exchange Act of 1934, as amended; and

2. The information contained in the Annual Report fairly presents, in all material respects, the financial condition and results of operations of the Company for the period covered by the Annual Report.

Dated: February 28, 2022

/s/ HOWARD W. ROBIN
Howard W. Robin
Chief Executive Officer, President and Director

/s/ GIL M. LABRUCHERIE
Gil M. Labrucherie
Senior Vice President, Chief Operating Officer, and Chief Financial Officer

* This certification accompanies the Annual Report on Form 10-K, to which it relates, is not deemed filed with the Securities and Exchange Commission and is not to be incorporated by reference into any filing of the Company under the Securities Act of 1933, as amended, or the Securities Exchange Act of 1934, as amended (whether made before or after the date of the Form 10-K), irrespective of any general incorporation language contained in such filing.