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UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
Washington, D.C. 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, 2020

☐ **TRANSITION REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934**

Commission File No. 001-34186

VANDA PHARMACEUTICALS INC.
(Exact name of registrant as specified in its charter)

Delaware	**03-0491827**
(State or other jurisdiction of incorporation or organization)	**(I.R.S. Employer Identification No.)**

2200 Pennsylvania Avenue NW, Suite 300 E
Washington DC 20037
(202) 734-3400
(Address and telephone number, including area code, of registrant's principal executive offices)

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

Title of each class	Trading Symbol(s)	Name of each exchange on which registered
Common Stock, par value $0.001 per share	VNDA	The Nasdaq Global Market

Securities registered pursuant to Section 12(g) of the Exchange 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 Exchange 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, a 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. Yes ☒ No ☐

Indicate by check mark whether the registrant is a shell company (as defined in Rule 12b-2 of the Securities Exchange Act of 1934). Yes ☐ No ☒

As of June 30, 2020, the last business day of the registrant's last completed second quarter, the aggregate market value of the Common Stock held by non-affiliates of the registrant was approximately $609.8 million based on the closing price of the registrant's Common Stock, as reported by The Nasdaq Global Market, on such date. Shares of Common Stock held by each executive officer and director and stockholders known by the registrant to own 10% or more of the outstanding stock based on public filings and other information known to the registrant have been excluded since such persons may be deemed affiliates. This determination of affiliate status is not necessarily a conclusive determination for other purposes.

The number of shares of the registrant's Common Stock, par value $0.001 per share, outstanding as of February 4, 2021 was 54,882,710.

The exhibit index as required by Item 601(a) of Regulation S-K is included in Item 15 of Part IV of this report.

DOCUMENTS INCORPORATED BY REFERENCE

Specified portions of the registrant's proxy statement with respect to the registrant's 2021 Annual Meeting of Stockholders, which is to be filed pursuant to Regulation 14A within 120 days after the end of the registrant's fiscal year ended December 31, 2020, are incorporated by reference into Part III of this Form 10-K.

Vanda Pharmaceuticals Inc.
Form 10-K

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PART I

CAUTIONARY NOTE REGARDING FORWARD-LOOKING STATEMENTS

This annual report on Form 10-K (Annual Report) contains "forward-looking statements" within the meaning of Section 27A of the Securities Act of 1933, as amended (Securities Act) and Section 21E of the Securities Exchange Act of 1934, as amended (Exchange Act). Words such as, but not limited to, "believe," "expect," "anticipate," "estimate," "intend," "plan," "project," "target," "goal," "likely," "will," "would," and "could," or the negative of these terms and similar expressions or words, identify forward-looking statements. Forward-looking statements are based upon current expectations and assumptions that involve risks, changes in circumstances and uncertainties. If the risks, changes in circumstances or uncertainties materialize or the assumptions prove incorrect, the results of Vanda Pharmaceuticals Inc. (we, our, the Company or Vanda) may differ materially from those expressed or implied by such forward-looking statements. All statements other than statements of historical fact are statements that could be deemed forward-looking statements. The forward-looking statements in this Annual Report may include, among other things, statements about:

- our ability to continue to commercialize HETLIOZ® (tasimelteon) capsules for the treatment of Non-24-Hour Sleep-Wake Disorder (Non-24) in the United States (U.S.) and Europe and HETLIOZ® capsules and oral suspension (HETLIOZ LQ™) for the treatment of nighttime sleep disturbances in Smith-Magenis Syndrome (SMS) in the U.S.;
- our ability to increase market awareness of Non-24 and SMS and market acceptance of HETLIOZ®;
- our ability to continue to generate U.S. sales of Fanapt® (iloperidone) oral tablets for the treatment of schizophrenia;
- the impact of the novel coronavirus (COVID-19) on our business and operations, including our revenue, our supply chain, our commercial activities, our ongoing and planned clinical trial and our regulatory activities;
- our dependence on third-party manufacturers to manufacture HETLIOZ®, HETLIOZ LQ™, and Fanapt® in sufficient quantities and quality;
- our level of success in commercializing HETLIOZ® and Fanapt® in new markets;
- our ability to reach agreement with the U.S. Food and Drug Administration (FDA) regarding our regulatory approval strategy, preclinical animal testing requirements or proposed path to approval for tradipitant;
- our ability to prepare, file, prosecute, defend and enforce any patent claims and other intellectual property rights;
- our ability to maintain rights to develop and commercialize our products under our license agreements;
- our ability to obtain and maintain regulatory approval of our products, and the labeling for any approved products;
- our ability to obtain approval from the FDA for HETLIOZ® for the treatment of jet lag disorder;
- our expectations regarding the timing and success of preclinical studies and clinical trials;
- the safety and efficacy of our products;
- regulatory developments in the U.S., Europe and other jurisdictions;
- limitations on our ability to utilize some or all of our prior net operating losses and orphan drug and research and development credits;
- the size and growth of the potential markets for our products and our ability to serve those markets;
- our expectations regarding trends with respect to our revenues, costs, expenses, liabilities and cash, cash equivalents and marketable securities;
- our ability to identify or obtain rights to new products;
- our ability to attract and retain key scientific or management personnel;
- the cost and effects of litigation;
- our ability to obtain the capital necessary to fund our research and development or commercial activities;
- potential losses incurred from product liability claims made against us; and
- the use of our existing cash, cash equivalents and marketable securities.

All written and verbal forward-looking statements attributable to us or any person acting on our behalf are expressly qualified in their entirety by the cautionary statements contained throughout this report. We caution you not to rely too heavily

on the forward-looking statements we make or that are made on our behalf. Each forward-looking statement speaks only as of the date of this Annual Report, and we undertake no obligation, and specifically decline any obligation, to update or revise publicly any forward-looking statements, whether as a result of new information, future events or otherwise, except as required by law.

We encourage you to read Part II, Item 7, *Management's Discussion and Analysis of Financial Condition and Results of Operations,* and our consolidated financial statements contained in this Annual Report. We also encourage you to read *Summary of Principal Risk Factors* below and Part I, Item 1A of this Annual Report, entitled *Risk Factors*, which contains a more complete discussion of the risks and uncertainties associated with our business. In addition to the risks described in this Annual Report, other unknown or unpredictable factors also could affect our results. Therefore, the information in this report should be read together with other reports and documents that we file with the Securities and Exchange Commission from time to time, including on Form 10-Q and Form 8-K, which may supplement, modify, supersede or update those risk factors. As a result of these factors, we cannot assure you that the forward-looking statements in this report will prove to be accurate. Furthermore, if our forward-looking statements prove to be inaccurate, the inaccuracy may be material. In light of the significant uncertainties in these forward-looking statements, you should not regard these statements as a representation or warranty by us or any other person that we will achieve our objectives and plans in any specified time frame, or at all.

SUMMARY OF PRINCIPAL RISK FACTORS

This summary briefly lists the principal risks and uncertainties facing our business, which are only a select portion of those risks. A more complete discussion of those risks and uncertainties is set forth in Part I, Item 1A of this Annual Report, entitled *Risk Factors*. Additional risks not presently known to us or that we currently deem immaterial may also affect us. If any of these risks occur, our business, financial condition or results of operations could be materially and adversely affected.

Our business is subject to the following principal risks and uncertainties:

Risks Related to our Business and Industry

- We are dependent on the commercial success of HETLIOZ® and Fanapt®.
- Growth of HETLIOZ® and Fanapt® may be slow or limited for a variety of reasons including competing products or unanticipated safety issues.
- Global economic conditions may have an adverse effect on our business.
- Global health crises and pandemics, such as the global outbreak of COVID-19, may adversely impact our business.
- The FDA may not accept for filing the New Drug Applications (NDAs) that we may submit for tradipitant for the treatment of gastroparesis, motion sickness, atopic dermatitis, and COVID-19 pneumonia, or the FDA may determine that our clinical trial results for tradipitant for these indications do not demonstrate adequate safety and efficacy.
- The FDA may not approve our supplemental New Drug Application (sNDA) for HETLIOZ® for the treatment jet lag disorder.
- We may be unable to enter into third-party collaborations to develop and commercialize our products, or collaborations we enter into with any such third party may not be commercially successful.
- Even after we obtain regulatory approvals of a product, acceptance of the product in the marketplace is uncertain.
- We rely and will continue to rely on outsourcing arrangements for many of our activities, including preclinical and clinical development and supply of HETLIOZ®, HETLIOZ LQ™, Fanapt® and our other products.
- We may experience disruptions to our HETLIOZ®, HETLIOZ LQ™ or Fanapt® supply chains.
- We may fail to comply with government regulations regarding the sale and marketing of our products.
- We may fail to comply with regulations and obligations related to the ongoing oversight of our products regarding, among other things, development, manufacturing, labeling, recording keeping and reporting.
- We may not market or distribute our products in a manner compliant with federal or state healthcare fraud and abuse laws.
- We rely on a limited number of specialty pharmacies for distribution of HETLIOZ® in the U.S., and the loss of one or more of these specialty pharmacies or their failure to distribute HETLIOZ® effectively would materially harm our business.
- Our revenues from Fanapt® are substantially dependent on sales through a limited number of wholesalers.
- We face substantial competition, which may result in others developing or commercializing products before or more successfully than we do.
- FDA and foreign regulatory approval of our products is uncertain.
- Our products may cause undesirable side effects or have other properties that could delay, prevent or result in the revocation of their regulatory approval or limit their marketability.
- Clinical trials for our products are expensive and their outcomes are uncertain.
- Our ability to use net operating loss carryforwards and tax credit carryforwards to offset future taxable income is dependent on generating future taxable income and may be limited, including as a result of transactions involving our common stock.
- Our contract research organizations (CROs) may not successfully carry out their duties or we may lose our relationships with CROs.

- We rely on a limited number of third-party manufacturers to formulate and manufacture our products and these manufacturers may not able to satisfy our demand and alternative sources may not be available.
- Materials necessary to manufacture our products may not be available on commercially reasonable terms, or at all.
- We may lose key scientists or management personnel or fail to recruit additional highly skilled personnel.
- We may be subject to product liability lawsuits.
- European Union (E.U.) Member States tend to impose strict price controls, which may delay or prevent the further commercial launch or impede the commercial success of HETLIOZ® in Europe and adversely affect our future results of operations.
- We may not be able to effectively market and sell our future products, if approved, in the U.S.
- Healthcare legislative reform measures or developments arising from changes in political climate may have a material adverse effect on our business and results of operations.

Risks Related to Intellectual Property and Other Legal Matters

- Our rights to develop and commercialize our products are subject in part to the terms and conditions of licenses or sublicenses granted to us by other pharmaceutical companies.
- Our efforts to protect the proprietary nature of the intellectual property related to our products may not be adequate.
- We are, have been, and may continue to be, involved in lawsuits to protect or enforce our patents, which could be expensive, time-consuming and unsuccessful, and third parties may challenge the validity or enforceability of our patents and they may be successful.
- We may not be able to obtain protection under the Hatch-Waxman Act and similar foreign legislation to extend our patents and to obtain market exclusivity for our products.
- We may not be successful in the development of products for our own account.
- Litigation or third-party claims of intellectual property infringement could require us to divert resources and may prevent or delay our drug discovery and development efforts.

ITEM 1. BUSINESS

Overview

Vanda Pharmaceuticals Inc. (we, our, the Company or Vanda) is a leading global biopharmaceutical company focused on the development and commercialization of innovative therapies to address high unmet medical needs and improve the lives of patients.

We strive to advance novel approaches to bring important, new medicines to market through responsible innovation. We are committed to the use of technologies that support sound science, including genetics and genomics, in drug discovery, clinical trials and the commercial positioning of our products.

Our commercial portfolio is currently comprised of two products, HETLIOZ® for the treatment of Non-24-Hour Sleep-Wake Disorder (Non-24) and nighttime sleep disturbances in Smith-Magenis Syndrome (SMS) and Fanapt® for the treatment of schizophrenia. HETLIOZ® is the first treatment for patients with Non-24 and SMS approved by the FDA. In addition, we have a number of drugs in development, including:

- HETLIOZ® (tasimelteon) for the treatment of jet lag disorder, pediatric Non-24, delayed sleep phase disorder (DSPD) and autism spectrum disorder (ASD);
- Fanapt® (iloperidone) for the treatment of bipolar disorder and Parkinson's disease psychosis (PDP) and a long acting injectable (LAI) formulation for the treatment of schizophrenia;
- Tradipitant (VLY-686), a small molecule neurokinin-1 receptor (NK-1R) antagonist, for the treatment of gastroparesis, motion sickness, atopic dermatitis, and COVID-19 pneumonia;
- VTR-297, a small molecule histone deacetylase (HDAC) inhibitor for the treatment of hematologic malignancies and with potential use as a treatment for several oncology indications;
- Portfolio of Cystic Fibrosis Transmembrane Conductance Regulator (CFTR) activators and inhibitors, including VSJ-110 for the treatment of dry eye and ocular inflammation and BPO-27 for the treatment of secretory diarrhea disorders, including cholera; and
- VQW-765, a small molecule nicotinic acetylcholine receptor partial agonist, with potential use for the treatment of psychiatric disorders.

We were incorporated in 2003 and are headquartered in Washington, D.C.

Our Strategy

Our goal is to further solidify our position as a leading global biopharmaceutical company focused on developing and commercializing innovative therapies addressing high unmet medical needs through the application of our drug development expertise and our pharmacogenetics and pharmacogenomics expertise. The key elements of our strategy to accomplish this goal are to:

- *Maximize the commercial success of HETLIOZ® and Fanapt®;*
- *Enter into strategic partnerships to supplement our capabilities and to extend our commercial reach;*
- *Pursue the clinical development and regulatory approval of our products, including tradipitant;*
- *Apply our pharmacogenetics and pharmacogenomics expertise to differentiate our products;*
- *Expand our product portfolio through the identification and acquisition of additional products; and*
- *Utilize novel and innovative approaches in pursuit of each of these strategies.*

Commercialized Products

Our commercial product portfolio consists of:

Product	Indication	2020 Net Sales (in millions)	Geography
Hetlioz® (tasimelteon) capsules 20 mg Hetlioz LQ™ (tasimelteon) Oral Suspension 4mg/mL	Non-24 (capsules) Nighttime sleep disturbances in SMS (capsules and HETLIOZ LQ™ oral suspension)	$160.7	United States Europe (Non-24 Only)
Fanapt® (iloperidone) tablets 1 mg, 2 mg, 4 mg, 6 mg, 8 mg, 10 mg, 12 mg	Schizophrenia (tablets)	$87.5	United States Israel

HETLIOZ® for Non-24 (capsules)

In January 2014, HETLIOZ® capsules were approved in the U.S. for the treatment of adults with Non-24. Non-24 is a serious, rare and chronic circadian rhythm sleep-wake disorder characterized by the inability to entrain (synchronize) the master body clock with the 24-hour day-night cycle. HETLIOZ® is the first FDA approved treatment for Non-24. HETLIOZ® is a melatonin agonist of the human MT1 and MT2 receptors, with greater specificity for MT2. These receptors are thought to be involved in the control of circadian rhythms. HETLIOZ® is believed to reset the master body clock in the suprachiasmatic nucleus, located in the hypothalamus, resulting in the entrainment and alignment of the body's melatonin and cortisol rhythms to the 24-hour day-night cycle.

Most people have a master body clock that naturally runs longer than 24 hours and light is the primary environmental cue that resets it to 24 hours each day. Individuals with Non-24 have a master body clock that is not reset, and continually delays, resulting in prolonged periods of misalignment between their circadian rhythms and the 24-hour day-night cycle, including the timing of melatonin and cortisol secretion. As a result of this misalignment, Non-24 is associated with significant disruption of the sleep-wake cycle and impairments in social and occupational functioning, and marked subjective distress. Individuals with Non-24 cycle in and out of phase and suffer from disrupted nighttime sleep patterns and/or excessive daytime sleepiness.

HETLIOZ® was launched commercially in the U.S. in April 2014. In addition, in July 2015, the European Commission (EC) granted centralized marketing authorization with unified labeling for HETLIOZ® for the treatment of Non-24 in totally blind adults and included post-marketing commitments related to a pediatric investigation plan. This authorization was renewed in July 2020 for an unlimited duration, and is valid in the 27 countries that are members of the European Union (E.U.), as well as European Economic Area members Iceland, Liechtenstein and Norway. HETLIOZ® was launched commercially in Germany in August 2016.

In January 2010, the FDA granted orphan drug designation status for HETLIOZ® in Non-24 in blind individuals. The FDA grants orphan drug designation to drugs that may provide significant therapeutic advantage over existing treatments and target conditions affecting 200,000 or fewer U.S. patients per year. Orphan drug designation provides potential financial and regulatory incentives, including study design assistance, tax credits, waiver of FDA user fees, and up to seven years of market exclusivity upon marketing approval. In February 2011, the European Medicines Agency (EMA) designated HETLIOZ® as an orphan medicinal product for the same indication.

Non-24 affects a majority of totally blind individuals, or approximately 80,000 people in the U.S. Blind individuals who develop Non-24 lack the light sensitivity necessary to synchronize the master body clock in the brain with the 24-hour day-night cycle. Non-24 also can affect sighted individuals. As with the totally blind, Non-24 in sighted individuals appears to be a comorbidity with certain other conditions. For example, a comorbidity has been established between psychiatric mood disorders and Non-24. Hospitalized individuals with neurological and psychiatric disorders can become insensitive to social cues, which

may predispose them to the development of Non-24. This recognition of comorbidity led Vanda to an initiative to engage with the psychiatric community. Patients diagnosed with traumatic brain injury, including concussions, frequently suffer from sleep disorders, some of which may be circadian rhythm sleep-wake disorders, including Non-24.

While there are no FDA or EC approved treatments for Non-24 other than HETLIOZ®, there are a number of drugs approved and prescribed for patients with sleep disorders. The most commonly prescribed drugs are hypnotics. See *Competition* below for a discussion of commonly prescribed drugs for patients with sleep disorders.

HETLIOZ® for SMS (capsules and oral suspension)

In December 2020, HETLIOZ® capsules and oral suspension (HETLIOZ LQ™) were approved in the U.S. for the treatment of adults and children, respectively, with nighttime sleep disturbances in SMS. SMS is a developmental disorder that is caused by a small deletion of human chromosome 17p. In more rare cases, SMS is caused by a point mutation in the RAI1 gene, which resides in the deleted region. HETLIOZ® is the first FDA-approved medication for patients with SMS.

In April 2010, the FDA granted orphan drug designation status for HETLIOZ® in the treatment of sleep disorder in SMS. SMS is estimated to affect 1/15,000-25,000 births in the U.S. SMS is not usually inherited but rather is caused by a de-novo deletion. Patients with SMS present with a number of physical, mental and behavioral problems. The most common symptom of SMS is a severe sleep disorder associated with significant disruption in the lives of patients and their families.

While there are no FDA approved treatments for patients with SMS other than HETLIOZ®, there are a number of drugs approved and prescribed for patients with sleep disorders that may be used to treat patients with SMS. The most commonly prescribed drugs are hypnotics. See *Competition* below for a discussion of commonly prescribed drugs for patients with sleep disorders.

Fanapt® for schizophrenia (tablets)

Fanapt® is a product for the treatment of schizophrenia. In May 2009, the FDA granted U.S. marketing approval of Fanapt® for the acute treatment of schizophrenia in adults. At that time, we had certain worldwide exclusive rights relating to Fanapt®, which we obtained pursuant to a sublicense agreement entered into with Novartis Pharma AG (Novartis) in June 2004. In October 2009, we amended and restated our sublicense agreement with Novartis pursuant to which Novartis retained exclusive commercialization rights to all formulations of Fanapt® in the U.S. and Canada. In January 2010, Novartis launched Fanapt® in the U.S. On December 31, 2014, Novartis transferred all the U.S. and Canadian commercial rights to the Fanapt® franchise to us as part of a settlement agreement. Additionally, our distribution partners launched Fanapt® in Israel in 2014. In May 2016, the FDA approved a supplemental New Drug Application (sNDA) for Fanapt® for the maintenance treatment of schizophrenia in adults.

In July 2017, the EMA's Committee for Medicinal Products for Human Use (CHMP) issued a negative opinion recommending against approval of Fanaptum® (oral iloperidone tablets) for the treatment of schizophrenia in adult patients in the E.U. The CHMP was of the opinion that the benefits of Fanaptum® did not outweigh its risks and recommended against marketing authorization. The negative opinion was upheld upon appeal in November 2017. (See Note 17, *Legal Matters,* to the consolidated financial statements in Part II, Item 8 of this Annual Report, which is incorporated herein by reference, for information relating to subsequent proceedings in this matter.)

Schizophrenia is a chronic, debilitating mental disorder characterized by hallucinations, delusions, racing thoughts and other psychotic symptoms (collectively referred to as "positive symptoms"), as well as moodiness, anhedonia (inability to feel pleasure), loss of interest, eating disturbances and withdrawal (collectively referred to as "negative symptoms"), and attention and memory deficits (collectively referred to as "cognitive symptoms"). Schizophrenia develops in late adolescence or early adulthood in approximately 1% of the world's population. Most schizophrenia patients today are treated with drugs known as "atypical" antipsychotics, which were first approved in the U.S. in the late 1980s. These antipsychotics have been named "atypical" for their ability to treat a broader range of negative symptoms than the first-generation "typical" antipsychotics, which were introduced in the 1950s and are now generic. Atypical antipsychotics are generally regarded as having improved side effect profiles and efficacy relative to typical antipsychotics. See *Competition* below for a discussion of commonly prescribed atypical antipsychotics in addition to Fanapt®.

Research and Development

We have built a research and development organization that includes extensive expertise in the scientific disciplines of pharmacogenetics and pharmacogenomics. We operate cross-functionally and are led by an experienced research and development management team. We use rigorous project management techniques to assist us in making disciplined strategic research and development program decisions and to help limit the risk profile of our product pipeline. We also access relevant market information and key opinion leaders in creating target product profiles and, when appropriate, as we advance our programs towards commercialization. We engage third parties to conduct portions of our preclinical research. In addition, we utilize multiple clinical sites to conduct our clinical trials; however, we are not substantially dependent upon any one of these sites for our clinical trials nor do any of them conduct a major portion of our clinical trials.

Our product pipeline currently consists of the following products in clinical development or under regulatory review:

HETLIOZ® for jet lag disorder

In March and May 2018, respectively, we announced the results of our JET8 and JET studies for the treatment of jet lag disorder. In the JET8 clinical study, HETLIOZ® demonstrated significant and clinically meaningful benefits in nighttime and daytime symptoms of jet lag disorder, including improvement in sleep time and benefits in measurements of next day alertness.

The JET study showed effectiveness in treating travelers who traveled either five or eight time zones from Washington, DC to London and San Francisco or Los Angeles to London, respectively. The results support the previously reported pivotal JET5 and JET8 Phase III studies, which demonstrated improvements in patients who experienced circadian advances of five and eight hours, respectively.

Additionally, in September 2018, we announced results from a driving study, which demonstrated that tasimelteon did not impair measures of driving performance.

The FDA accepted the filing of our sNDA for HETLIOZ® for the treatment of jet lag disorder in December 2018. The FDA determined the action target date under the Prescription Drug User Fee Act Amendments of 2017 (PDUFA-VI) to be August 16, 2019, and on that date, we received a complete response letter (CRL) from the FDA. The FDA asserted in the CRL that the measures demonstrating improved sleep were of unclear clinical significance. We met with the FDA to discuss the CRL in a Post Action meeting and we are determining our next steps.

Jet lag disorder is a common circadian disorder frequently observed in millions of travelers who cross multiple time zones. Jet lag disorder is characterized by nighttime sleep disruption, a decrease in daytime alertness and impairment to social and occupational functioning. Jet lag disorder symptoms are more severe during eastward travel. U.S. Department of Commerce, International Trade Administration reports state that more than 20 million U.S. residents make trips abroad each year to overseas destinations in Europe, the Middle East and Asia.

HETLIOZ® for pediatric Non-24

We plan to develop HETLIOZ® for the treatment of pediatric Non-24. A pharmacokinetic study of the HETLIOZ® pediatric liquid formulation was completed in the first quarter of 2018.

HETLIOZ® for DSPD

A clinical program of HETLIOZ® in DSPD is ongoing. DSPD is a circadian rhythm disorder in which a person's sleep is delayed beyond the socially acceptable or conventional bedtime. This delay in falling asleep causes difficulty in waking up at the desired time and affects social and occupational functioning.

HETLIOZ® for ASD

A clinical program of HETLIOZ® for the treatment of sleep disturbances in ASD is expected to be initiated in the first quarter of 2021. Sleep disturbances in ASD are a high unmet medical need in people with ASD and have been characterized in the literature to include difficulties falling and staying asleep.

Fanapt® for bipolar disorder

A Phase III study of Fanapt® in bipolar disorder is ongoing. Bipolar disorders are brain disorders that cause changes in a person’s mood, energy and ability to function. Bipolar disorder is a category that includes three different conditions - bipolar I, bipolar II and cyclothymic disorder.

People with bipolar disorders have extreme and intense emotional states that occur at distinct times, called mood episodes. These mood episodes are categorized as manic, hypomanic or depressive. People with bipolar disorders generally have periods of normal mood as well.

Fanapt® for schizophrenia (LAI)

In October 2018, we enrolled our first patient in a pharmacokinetic study of the LAI formulation of Fanapt®. This pharmacokinetic study is ongoing and will serve to inform the dosing for a later clinical study of Fanapt® LAI for the treatment of schizophrenia.

Fanapt® for PDP

A clinical program of Fanapt® in PDP is expected to begin in 2021. Parkinson's disease is a neurodegenerative disorder that affects predominately dopaminergic neurons in a specific area of the brain called substantia nigra.

People with Parkinson's disease experience a combination of hallucinations and delusions and the disease is associated with significant caregiver burden.

Tradipitant for gastroparesis

We announced results in December 2018 from a Phase II randomized clinical study (2301) of tradipitant as a monotherapy in the treatment of gastroparesis. Several symptom severity scales were used to assess gastroparesis symptoms, including the Gastroparesis Symptom Index (GCSI), Patients Assessment of Upper Gastrointestinal Disorders-Symptoms

(PAGI-SYM), and Patient Global Impression of Change (PGI-C) as well as a Clinician Global Impression of Severity (CGI-S). Tradipitant met the primary endpoint of the study of change in nausea score as measured by patient daily diaries and also met the related endpoint of improvement in the number of nausea free days. Tradipitant also showed significant improvement in most of the secondary endpoints studied, including several key scales reflecting overall gastroparesis symptoms, specifically GCSI, PAGI-SYM, CGI-S, and PGI-C. We are currently enrolling patients in a Phase III study of tradipitant in the treatment of both diabetic and idiopathic gastroparesis. This Phase III study is a 12-week study of similar design to the Phase II study in both target population and endpoints.

We believe that tradipitant has a well-established safety profile, as demonstrated by the results of extensive testing in animals and humans. Despite these results, however, the FDA informed us in December 2018 that in order to treat patients beyond 12 weeks, we will have to conduct a 9-month non-rodent chronic toxicity study, which currently limits our ability to collect safety data in humans for more than 12 weeks. The non-rodent study required by the FDA necessitates the sacrifice of dozens of animals and we have disputed the necessity of a 9-month non-rodent chronic toxicity study. In February 2019, we filed a lawsuit in the U.S. District Court for the District of Columbia (DC District Court) challenging the FDA's position, but ultimately did not prevail. Despite our disagreement with the FDA, the preclinical package has allowed us to continue to conduct all of the efficacy studies necessary for NDA filing. Moreover, in July 2020, the FDA approved the use of tradipitant for up to six months with an option of renewal for an individual patient who requested expanded access. Since then, other patients who experienced a unique benefit in tradipitant studies have requested expanded access. The expanded access program is ongoing and a number of patients have initiated treatment. Although this expanded access program is not intended for data collection, we will collect safety data from this cohort of expanded access patients and include this data in its NDA for tradipitant for the treatment of gastroparesis; however, the FDA may disregard such safety data when reviewing the NDA. The lack of long-term (>12 weeks in humans) safety data would likely impact the FDA's willingness to approve tradipitant for a chronic indication. However, because long-term safety data is not normally a requirement for short-term indications, and with a preclinical profile that has not precluded clinical development, we believe the package is complete for any NDA filing to treat patients for 12 weeks or less. In gastroparesis, for example, the FDA has communicated to us that it is considering an indication for the short-term relief of nausea in gastroparesis. While this short-term indication is not preferred, we would consider accepting this limited indication while continuing to pursue a chronic indication.

Gastroparesis is a serious medical condition characterized by delayed gastric emptying associated with the symptoms of nausea, vomiting, bloating, fullness after meals and abdominal pain, along with significant impairment of social and occupational functioning. A paper by Rey et al published in the January 2012 Journal of Neurogastroenterology and Motility estimated the prevalence of gastroparesis in the U.S. to be over 5 million patients, many of whom remain undiagnosed.

Tradipitant for motion sickness

In July 2019, we reported tradipitant was effective in treating motion sickness in a Phase II clinical study conducted in the Pacific Ocean. In the study, 126 people with a prior history of motion sickness were subjected to sea travel in the Pacific Ocean. Study participants were randomized to receive either tradipitant or placebo in a blinded fashion. The study had two primary endpoints: percentage of participants vomiting, and Motion Sickness Severity Scale (MSSS) Worst score. In the overall population, a significantly higher percentage of participants experienced vomiting in the placebo arm as compared to the tradipitant arm. The MSSS Worst score endpoint also favored tradipitant, but the difference did not reach statistical significance. The protocol for a pivotal Phase III motion sickness study was discussed with the FDA at the end of Phase II meeting, and the FDA agreed with the adequacy of the program design to support an NDA. Preparations for this study have begun with the boat trip portion of the study expected to commence as soon as local restrictions related to the COVID-19 pandemic are lifted.

Motion sickness is a disorder that arises often as a response to real or perceived movement, as occurring during vehicular travel. Vomiting is the most disturbing symptom of motion sickness, although the disorder is often accompanied by a constellation of symptoms that includes nausea, sweating, pallor, headache and anorexia. Motion sickness is one of the most prevalent episodic disorders in the world, whose prevalence has dramatically increased with world population mobility over the last 100 years. It is reported that approximately 30% of the general population suffers from motion sickness under ordinary travel conditions that include sea, air and land travel.

Tradipitant for atopic dermatitis

We announced results in September 2017 from a randomized Phase II clinical study of tradipitant as a monotherapy in the treatment of patients with atopic dermatitis. Tradipitant was shown to improve the intensity of the worst itch patients experienced, as well as atopic dermatitis disease severity. On the pre-specified primary endpoint of Average Itch Visual Analog

Scale (VAS), tradipitant showed improvement over placebo, but this improvement was not significant due to high placebo effect and the lack of sensitivity of this measure.

In June 2018, we initiated EPIONE, a Phase III study of tradipitant for pruritus in atopic dermatitis. In October 2019, we began enrolling patients in EPIONE 2, a second Phase III clinical study of tradipitant in atopic dermatitis. We announced results of EPIONE in February 2020. The EPIONE study did not meet its primary endpoint in reduction of pruritus across the overall study population. However, the antipruritic effect of tradipitant was robust in the mild atopic dermatitis population. The EPIONE study continued to demonstrate that tradipitant is safe and well-tolerated. The ongoing EPIONE 2 study was placed on hold due to the COVID-19 pandemic.

Atopic dermatitis is a chronic, relapsing inflammatory skin disorder characterized by the symptom of intense and persistent pruritus or itch. Other clinical features include erythema, excoriation, edema, lichenification, oozing and xerosis. Atopic dermatitis is a common skin disorder affecting millions of people worldwide. Currently, there are very few safe systemic treatments available for atopic dermatitis, representing a significant unmet medical need in this population. A 2015 Decision Resources Group report estimated that 9.8 million individuals were diagnosed with atopic dermatitis in the U.S., of which approximately 6.4 million were drug-treated atopic dermatitis patients.

Tradipitant for COVID-19 pneumonia

In April 2020, we announced the initiation of clinical study, ODYSSEY VLY-686-3501, in hospitalized patients with COVID-19. We received permission from the FDA to proceed with the study for the treatment and prevention of pneumonia associated with COVID-19. Enrollment in our Phase III clinical study of VLY-686-3501 is ongoing.

COVID-19 is associated with a lower respiratory tract inflammation that often progresses to acute respiratory distress syndrome requiring mechanical ventilation. Tradipitant targets the neurokinin-1 receptor, which is coded by the TACR1 gene and is the main receptor for substance P, an 11 amino acid neuropeptide with a diverse set of functions. It has been shown that the substance P NK-1R system is involved in the neuroinflammatory processes that leads to significant lung injury following a number of insults, including viral challenges.

VTR-297

VTR-297 is a small molecule HDAC inhibitor with potential use as a treatment for several oncology indications. The FDA accepted an Investigational New Drug (IND) application for VTR-297 in 2017 and provided authorization to proceed with the treatment of patients with relapsed and/or refractory hematologic malignancies. We initiated a clinical study in patients with hematologic malignancies in the fourth quarter of 2018. Enrollment in the Phase I clinical study (1101) of VTR-297 in hematologic malignancies is ongoing.

Portfolio of CFTR activators and inhibitors

In October 2020, the FDA accepted the IND application to evaluate CFTR activator VSJ-110 and provided authorization to proceed with clinical development. We are evaluating VSJ-110 for the treatment of allergic conjunctivitis. In November 2020, we initiated a study in human volunteers that will evaluate the acute anti-inflammatory effects of VSJ-110 in an ocular allergic challenge model, and will evaluate the prosecretory effects using standard tear production assessments. The results from the study will help guide further development of VSJ-110 to treat a variety of ocular inflammatory conditions, including dry eye, which has an estimated worldwide prevalence of 5-20%, with about 16 million affected individuals in the U.S. VSJ-110 (previously known as CFTRact-K267) is a small molecule nanomolar potency CFTR activator. VSJ-110 has shown efficacy in a dry eye model and exhibited anti-inflammatory properties in both in vitro and in vivo assays.

In addition, an early stage CFTR inhibitor program is planned for BPO-27 for the treatment of secretory diarrhea disorders, including cholera.

Other products

VQW-765

VQW-765 is a Phase II alpha-7 nicotinic acetylcholine receptor partial agonist that we licensed from Novartis on December 31, 2014 pursuant to a settlement agreement. The FDA accepted an IND application for VQW-765 in January 2020 and provided authorization to proceed with clinical development. We are evaluating VQW-765 for the treatment of psychiatric disorders.

For more detailed information regarding our clinical trial results and regulatory activities for our products please refer to our SEC filings and press releases, which can be found on the SEC Edgar system and on our website www.vandapharma.com.

License Agreements

Our rights to develop and commercialize our products are subject to the terms and conditions of licenses granted to us by other pharmaceutical companies.

HETLIOZ®

In February 2004, we entered into a license agreement with Bristol-Myers Squibb (BMS) under which we received an exclusive worldwide license under certain patents and patent applications, and other licenses to intellectual property, to develop and commercialize HETLIOZ®. We have paid BMS $37.5 million in upfront fees and milestone obligations. We have no remaining milestone obligations to BMS. Additionally, we are obligated to make royalty payments on HETLIOZ® net sales to BMS in any territory where we commercialize HETLIOZ® for a period equal to the greater of 10 years following the first commercial sale in the territory or the expiry of the new chemical entity (NCE) patent in that territory. During the period prior to the expiry of the NCE patent in a territory, we are obligated to pay a 10% royalty on net sales in that territory. The royalty rate is decreased by half for countries in which no NCE patent existed or for the remainder of the 10 years after the expiry of the NCE patent. We are also obligated under the license agreement to pay BMS a percentage of any sublicense fees, upfront payments and milestone and other payments (excluding royalties) that we receive from a third party in connection with any sublicensing arrangement, at a rate which is in the mid-twenties. We have agreed with BMS in the license agreement for HETLIOZ® to use commercially reasonable efforts to develop and commercialize HETLIOZ®.

Either party may terminate the HETLIOZ® license agreement under certain circumstances, including a material breach of the agreement by the other. In the event we terminate our license, or if BMS terminates our license due to our breach, all rights licensed and developed by us under this agreement will revert or otherwise be licensed back to BMS on an exclusive basis.

Fanapt®

Pursuant to the terms of a settlement agreement with Novartis, Novartis transferred all U.S. and Canadian rights in the Fanapt® franchise to us on December 31, 2014. We paid directly to Sanofi S.A. (Sanofi) a fixed royalty of 3% of net sales through December 2019 related to manufacturing know-how. No further royalties on manufacturing know-how are payable by us. We are also obligated to pay Sanofi a fixed royalty on Fanapt® net sales equal up to 6% on Sanofi know-how not related to manufacturing under certain conditions for a period of up to 10 years in markets where the NCE patent has expired or was not issued. We are obligated to pay this 6% royalty on net sales in the U.S. through November 2026. No further royalties on know-how not related to manufacturing will be payable by us for net sales in the U.S. after November 2026. We may lose our rights to develop and commercialize Fanapt® if we fail to comply with certain requirements in the Titan license agreement regarding our financial condition, or if we fail to comply with certain diligence obligations regarding our development or commercialization activities.

Tradipitant (VLY-686)

In April 2012, we entered into a license agreement with Eli Lilly and Company (Lilly) pursuant to which we acquired an exclusive worldwide license under certain patents and patent applications, and other licenses to intellectual property, to develop and commercialize an NK-1R antagonist, tradipitant, for all human indications. Lilly is eligible to receive future payments based upon achievement of specified development, regulatory approval and commercialization milestones as well as tiered-royalties on net sales at percentage rates up to the low double digits. We have paid Lilly $3.0 million in upfront fees and development milestones, including a $2.0 million milestone payment as a result of enrolling the first subject into a Phase III study for tradipitant in July 2018. As of December 31, 2020, remaining milestones include a $2.0 million development milestone due upon the filing of the first marketing authorization for tradipitant in either the U.S. or the E.U, $10.0 million and $5.0 million for the first approval of a marketing authorization for tradipitant in the U.S. and E.U., respectively, and up to $80.0 million for sales milestones. We are obligated to use commercially reasonable efforts to develop and commercialize tradipitant.

Either party may terminate the agreement under certain circumstances, including a material breach of the agreement by the other. In the event that we terminate the agreement, or if Lilly terminates the agreement due to our breach or for certain other reasons set forth in the agreement, all rights licensed and developed by us under the agreement will revert or otherwise be

licensed back to Lilly on an exclusive basis, subject to payment by Lilly to us of a royalty on net sales of products that contain tradipitant.

Portfolio of CFTR activators and inhibitors

In March 2017, we entered into a license agreement with the University of California San Francisco (UCSF), under which we acquired an exclusive worldwide license to develop and commercialize a portfolio of CFTR activators and inhibitors. Pursuant to the license agreement, we will develop and commercialize the CFTR activators and inhibitors and are responsible for all development costs under the license agreement, including current pre-investigational new drug development work. UCSF is eligible to receive future payments based upon achievement of specified development, regulatory approval and commercialization milestones as well as single-digit tiered-royalties on net sales. To date, we have paid UCSF $1.2 million in upfront fees and development milestones. As of December 31, 2020, remaining milestones include $12.2 million for development milestones and $33.0 million for future regulatory approval and sales milestones. Included in the $12.2 million in development milestones is a $350,000 milestone due upon the conclusion of a Phase I study for each licensed product, not to exceed $1.1 million in total for the CFTR portfolio. In the fourth quarter of 2020, we determined the $350,000 milestone to be probable and accrued it as a current liability as of December 31, 2020.

Either party may terminate the agreement under certain circumstances. In the event that we terminate the agreement, or if UCSF terminates the agreement due to our breach or for certain other reasons set forth in the agreement, all rights licensed and developed by us under the agreement will revert or otherwise be licensed back to UCSF. Termination will not relieve us of our obligation to pay royalties or other payments owed, if any, to UCSF under the terms of the agreement.

VQW-765

In connection with the settlement agreement with Novartis relating to Fanapt®, we received an exclusive worldwide license under certain patents and patent applications, and other licenses to intellectual property, to develop and commercialize VQW-765, a Phase II alpha-7 nicotinic acetylcholine receptor partial agonist. Pursuant to the license agreement, we are obligated to use commercially reasonable efforts to develop and commercialize VQW-765 and are responsible for all development costs. We have no milestone obligations, but Novartis is eligible to receive tiered-royalties on net sales at percentage rates up to the mid-teens.

Either party may terminate the agreement under certain circumstances, including a material breach of the agreement by the other. In the event that we terminate the agreement, or if Novartis terminates the agreement due to our breach or for certain other reasons set forth in the agreement, all rights licensed and developed by us under the agreement will revert or otherwise be licensed back to Novartis on an exclusive basis, subject to payment by Novartis to us of a royalty on net sales of products that contain VQW-765.

Patents and Proprietary Rights; Hatch-Waxman Protection

We will be able to protect our products from unauthorized use by others only to the extent that our products are covered through regulatory protections or by valid and enforceable patents, either licensed to us by others or generated through our activities internally, that give us sufficient proprietary rights. Accordingly, securing patents, regulatory data package protection, and other proprietary rights is an essential element of our business strategies.

HETLIOZ®, tradipitant and VQW-765 are covered by NCE and other patents and patent applications related to their respective medicinal uses. In addition, NCE patent protection has been sought for VTR-297 and CFTR. Patent applications for these active ingredients remain pending. While the NCE patents protecting Fanapt® have expired, Fanapt® remains protected by medicinal patents. For more on the license and sublicense arrangements related to these active ingredients, see *License Agreements* above. In addition, we have filed for patents based on our own discoveries that seek to provide additional protection for HETLIOZ® and Fanapt®.

A comprehensive list of patents for our U.S. commercial products is available in the *Approved Drug Products with Therapeutic Equivalence Evaluations* (Orange Book) for our commercial products and is also provided in the table below. Members of these patent families are also issued or pending in a number of territories, such as Europe and Japan.

Product	Number	Type
HETLIOZ®	US 5,856,529	New chemical entity
	US 9,060,995	Method of treatment
	US 9,539,234	Method of treatment
	US 9,549,913	Method of treatment
	US 9,730,910	Method of treatment
	US 9,855,241	Method of treatment
	US RE46604	Method of treatment
	US 10,071,977	Drug substance
	US 10,149,829	Method of treatment
	US 10,179,119	Method of treatment
	US 10,376,487	Method of treatment
	US 10,449,176	Method of treatment
	US 10,610,510	Method of treatment
	US 10,610,511	Method of treatment
	US 10,829,465	Drug substance
Fanapt®	US 8,586,610	Method of treatment
	US 8,652,776	Method of treatment
	US 8,999,638	Method of treatment
	US 9,072,742	Method of treatment
	US 9,074,254	Method of treatment
	US 9,074,255	Method of treatment
	US 9,074,256	Method of treatment
	US 9,138,432	Method of treatment
	US 9,157,121	Method of treatment

HETLIOZ®

Our rights to the NCE patent covering HETLIOZ® and related intellectual property have been acquired through a license with BMS. HETLIOZ® and its formulations, genetic markers and uses are the subject of numerous patent filings for which protection has been sought in selected countries worldwide. The NCE patent covering HETLIOZ® expires in December 2022 in the U.S., which is inclusive of a five-year extension granted under the Hatch-Waxman Act in October 2018. Corresponding NCE patent protection has expired in most other markets. The U.S. Patent and Trademark Office has issued 12 method of treatment patents for HETLIOZ® that will expire between 2033 and 2035 and two drug substance patents that will expire in 2035. We also have other pending patent applications covering methods of treatment and compositions of tasimelteon (HETLIOZ® active ingredient) oral suspensions.

In Europe, the law provides for 10 years of data exclusivity (with the potential for an additional year if a medicine is developed for a significant new indication). In addition, Europe provides for 10 years of market exclusivity for orphan indications. As such, in Europe, data or market exclusivity will provide protection for HETLIOZ® for at least 10 years from approval. It is also possible that the protection through a basic patent (i.e., a patent that protects a product as such, a process to obtain a product, or an application of a product) in Europe could be extended for up to five years by the issuance of a supplementary protection certificate (SPC). A completed Pediatric Investigation Plan (PIP) could further extend SPC protection for an additional six months or the market exclusivity in an orphan indication for two additional years. Thus, a PIP could provide a total of 12 years of market exclusivity for an orphan indication. The European Patent Office has granted our patent application directed to the 20 mg/day dose. This patent will expire in 2027 and provides the basis for an SPC. Other pending patent applications in Europe, if granted, may offer additional protection for HETLIOZ®.

Outside the U.S. and Europe, data exclusivity will protect HETLIOZ® from generic competition for varying numbers of years depending on the country.

Additional patent applications directed to specific sleep disorders and to methods of treating patients with HETLIOZ®, if issued, would provide exclusivity for such indications and methods of treatment, potentially extending the effective patent protection period in the U.S., Europe, and other markets.

Fanapt®

The NCE patent for Fanapt®, which expired in 2016 in the U.S. and in 2010 in other countries, was owned by Sanofi. Other patents and patent applications relating to Fanapt® are owned by Vanda.

Fanapt® metabolites, formulations, genetic markers and uses are the subject of numerous patent filings in which protection has been sought in the U.S., Europe, and other markets. In November 2013, a U.S. patent (U.S. 8,586,610) directed to a method of treating patients with Fanapt® based on genotype was issued to us by the U.S. Patent and Trademark Office. This patent, which was listed in the Orange Book in January 2015, is set to expire in 2027, potentially further extending the U.S. marketing exclusivity for Fanapt®. Additional method of treatment patents have been issued in the U.S. and listed in the Orange Book, with the latest expiration date in December 2031.

We have also filed and plan on filing additional patent applications covering the use of iloperidone (Fanapt® active ingredient) LAI formulations. Patents for the microsphere LAI formulation of Fanapt® expire in 2024 in the U.S. and 2022 in some markets in Europe. Patents for the aqueous microcrystals LAI formulation of Fanapt® expire in 2023 in the U.S. and in some markets in Europe. We have pending patent applications covering the use of iloperidone and plan on filing additional applications based on discoveries made throughout the development plan of this molecule.

In Europe, the law provides for 10 years of regulatory exclusivity (with the potential for an additional year if the drug is developed for a significant new indication). No generic versions of Fanapt® would be permitted to be marketed or sold during the applicable regulatory exclusivity period in most European countries. Outside the U.S. and Europe, similar regulatory package protection periods may be available and could protect Fanapt® from generic competition for varying numbers of years depending upon the country.

Tradipitant

Lilly owns an NCE patent as well as patent applications directed to polymorphic forms of, and methods of making tradipitant. This patent protection was sought in the U.S. and in other countries worldwide. These patents and patent applications have been licensed to us. The NCE patent covering tradipitant expires in April 2023, except in the U.S., where it expires normally in June 2024, subject to any extension that may be received under the Hatch-Waxman Act. We have filed additional patent applications based on discoveries made during recent studies with tradipitant.

VTR-297

VTR-297 is a small molecule HDAC inhibitor with potential use as a treatment for several oncology indications. We have pending patent applications covering the use of VTR-297 and plan on filing additional applications based on discoveries made throughout the development plan of this molecule.

Portfolio of CFTR activators and inhibitors

Our portfolio of CFTR activators and inhibitors may have broad applicability in addressing a number of high unmet medical needs, including chronic dry eye, constipation, polycystic kidney disease, cholestasis and secretory diarrheas. We plan on filing applications based on discoveries made throughout the development plan of these product candidates.

VQW-765

Novartis owns an NCE patent as well as patent applications directed to methods of using VQW-765, VQW-765 formulations, and combinations of VQW-765 with other active pharmaceutical ingredients. In connection with the settlement agreement with Novartis relating to Fanapt®, we received an exclusive worldwide license under certain patents and patent applications, and other licenses to intellectual property, to develop and commercialize VQW-765, a Phase II alpha-7 nicotinic acetylcholine receptor partial agonist. The NCE patent expires normally in 2023 in the U.S., Europe, and other markets.

Other patents

Aside from the NCE patents and other in-licensed patents discussed above, we have obtained or filed numerous patents and patent applications, most of which have been filed in key markets including the U.S., relating to our products and product candidates. In addition, we have filed numerous other patent applications relating to drugs not presently in clinical studies. The claims in these various patents and patent applications are directed to compositions of matter, including claims covering other products, pharmaceutical compositions and methods of use.

Proprietary know-how

For proprietary know-how that is not appropriate for patent protection, processes for which patents are difficult to enforce and any other elements of our discovery process that involve proprietary know-how and technology that are not covered by patent applications, we generally rely on trade secret protection and confidentiality agreements to protect our interests. We require all of our employees, relevant consultants and advisors to enter into confidentiality agreements. Where it is necessary to share our proprietary information or data with outside parties, our policy is to make available only that information and data required to accomplish the desired purpose and only pursuant to a duty of confidentiality on the part of those parties.

Marketing and Sales

HETLIOZ® capsules were approved in the U.S. for the treatment of Non-24 in January 2014 and HETLIOZ® capsules and oral suspension were approved for the treatment of nighttime sleep disturbances in SMS in December 2020. We commercially launched HETLIOZ® in the U.S. in April 2014. Additionally, HETLIOZ® capsules were approved in the E.U. for the treatment of Non-24 in totally blind adults in July 2015 and, in August 2016, we commercially launched HETLIOZ® in Germany. Given the range of potential indications for HETLIOZ®, we may pursue one or more partnerships for the development and commercialization of HETLIOZ® worldwide.

Fanapt® oral tablets were approved in the U.S. for the treatment of schizophrenia in May 2009 and commercially launched in the U.S. in January 2010. We continue to explore the regulatory path and commercial opportunity for Fanapt® oral formulation in other regions.

Major Customers

Our revenues are generated from product sales and are concentrated with specialty pharmacies, including Diplomat Pharmacy, Inc. (a subsidiary of UnitedHealth Group) and Accredo (a subsidiary of Express Scripts), and wholesalers, including Cardinal Health, Inc., AmerisourceBergen Drug Corporation, and McKesson Corporation. These 5 major customers each accounted for more than 10% of total revenues for 2020 and, as a group, represented 95% of total revenues for the year ended December 31, 2020.

Competition

The pharmaceutical industry, in particular, is highly competitive and includes a number of established large and mid-sized companies with greater financial, technical and personnel resources than we have and significantly greater commercial infrastructures than we have. Our market segment also includes several smaller emerging companies whose activities are directly focused on our target markets and areas of expertise. Our products, once approved for commercial use, will compete with numerous therapeutic treatments offered by these competitors. While we believe that our products will have certain favorable features, existing and new treatments may also possess advantages. Additionally, the development of other drug technologies and methods of disease prevention are occurring at a rapid pace. These developments may render our products or technologies obsolete or noncompetitive.

We believe the primary competitors for HETLIOZ® and Fanapt® are as follows:

- For HETLIOZ® in the treatment of Non-24 and nighttime sleep disturbances in SMS, there are no FDA approved direct competitors. Sedative-Hypnotic treatments for certain sleep related disorders include, Ambien® (zolpidem) by Sanofi (including Ambien CR®), Lunesta® (eszopiclone) by Sunovion Pharmaceuticals Inc., Sonata® (zaleplon) by Pfizer Inc., Rozerem® (ramelteon) by Takeda Pharmaceuticals Company Limited, Silenor® (doxepin) by Pernix Therapeutics, Belsomra® (suvorexant) by Merck & Co., Inc., generic products such as zolpidem, trazodone and doxepin, and over-the-counter remedies such as Benadryl® and Tylenol PM®. The class of melatonin agonists includes Rozerem® (ramelteon) by Takeda Pharmaceuticals Company Limited, Valdoxan® (agomelatine) by Servier, Circadin® (long-acting melatonin) by Neurim Pharmaceuticals Ltd. and the food supplement melatonin.

Shift work and excessive sleepiness disorder treatments include Nuvigil® (armodafinil) and Provigil® (modafinil) both by Teva Pharmaceutical Industries Ltd.

- For Fanapt® in the treatment of schizophrenia, the atypical antipsychotics competitors are Risperdal® (risperidone), including the LAI formulation Risperdal Consta® and Invega® (paliperidone), including the LAI formulation Invega® Sustenna®, each by Ortho-McNeil-Janssen Pharmaceuticals, Inc., Zyprexa® (olanzapine), including the LAI formulation Zyprexa® Relprevv™, each by Lilly, Seroquel® and Seroquel XR® (quetiapine) by AstraZeneca PLC, Abilify® (aripiprazole) by Otsuka America Pharmaceutical Inc., Abilify Maintena® (the LAI formulation of Abilify®) by Lundbeck/Otsuka America Pharmaceutical Inc., Geodon® (ziprasidone) by Pfizer Inc., Saphris® (asenapine) by Allergan plc, Latuda® (lurasidone) by Sunovion Pharmaceuticals Inc., Rexulti® (brexpiprazole) by Lundbeck/Otsuka America Pharmaceutical, Inc., Aristada® (aripiprazole lauroxil) extended-release injectable suspension by Alkermes, plc, Vraylar® (cariprazine) by Teva Pharmaceutical Industries Ltd., Perseris® (risperidone) extended-release injectable suspension by Indivior plc, Caplyta® (lumapteperone) by Intra-Cellular Therapies, and generic clozapine, as well as the typical antipsychotics haloperidol, chlorpromazine, thioridazine, and sulpiride (all of which are generic).

Our ability to compete successfully will depend in part on our ability to utilize our pharmacogenetics and pharmacogenomics and drug development expertise to identify, develop, secure rights to and obtain regulatory approvals for promising pharmaceutical products before others are able to develop competitive products. Our ability to compete successfully will also depend on our ability to attract and retain skilled and experienced personnel. Additionally, our ability to compete may be affected because insurers and other third-party payors in some cases seek to encourage the use of cheaper, generic products, which could make our products less attractive.

Manufacturing

We currently utilize a virtual supply manufacturing and distribution chain in which we do not have our own facilities to manufacture commercial or clinical trial supplies of drugs and we do not have our own distribution facilities. Additionally, we do not intend to develop such facilities for any product in the near future. Instead, we contract with third parties for the manufacture, warehousing, order management, billing and collection and distribution of our products and product candidates.

We expect to continue to rely solely on third-party manufacturers to manufacture drug substance and final drug products for both clinical development and commercial sale. However, there are numerous factors that could cause interruptions in the supply of our products, including regulatory reviews, changes in our sources for manufacturing, disputes with a manufacturer, or financial instability of manufacturers, all of which could negatively impact our operation and our financial results.

We have agreements in place with Patheon Pharmaceuticals Inc. and Patheon Inc. (collectively, Patheon), subsidiaries of Thermo Fisher Scientific, for the manufacture of HETLIOZ® capsules and Fanapt® oral tablets.

In January 2014, we entered into a manufacturing agreement with Patheon for the manufacture of commercial supplies of HETLIOZ® 20 mg capsules at Patheon's Cincinnati, Ohio manufacturing site. Under the HETLIOZ® manufacturing agreement, we are responsible for supplying the active pharmaceutical ingredient (tasimelteon) for HETLIOZ® to Patheon and have agreed to order from Patheon at least 80% of the total expected yearly production of new units of HETLIOZ® capsules. Patheon is responsible for manufacturing the HETLIOZ® 20 mg capsules, conducting quality control and stability testing, and packaging the HETLIOZ® capsules. The HETLIOZ® manufacturing agreement had an initial term of five years and automatically renews after the initial term for successive terms of one year each, unless either party gives notice of its intention to terminate the agreement at least 12 months prior to the end of the then current term. Either party may terminate the HETLIOZ® manufacturing agreement under certain circumstances upon specified written notice to the other party.

As part of a settlement agreement in 2014, we assumed Novartis' manufacturing agreement with Patheon for the manufacture of commercial supplies of Fanapt®. In May 2016, we entered into a new manufacturing agreement with Patheon for the manufacture of commercial supplies of Fanapt® 1, 2, 4, 6, 8, 10 and 12 mg tablets at Patheon's Mississauga, Ontario, Canada manufacturing site. Under the Fanapt® manufacturing agreement, we are responsible for sourcing the supply of the active pharmaceutical ingredient (iloperidone), and have agreed to order from Patheon at least 70% of the total expected yearly production of new units of Fanapt® tablets for the U.S. and other specified countries each year for the term of the agreement. Patheon is responsible for manufacturing the Fanapt® 1, 2, 4, 6, 8, 10 and 12 mg tablets, conducting quality control and stability testing, and packaging the Fanapt® tablets. The Fanapt® manufacturing agreement has an initial term of five years and will automatically renew after the initial term for successive terms of one year each, unless either party gives notice of its intention

to terminate the agreement at least 12 months prior to the end of the then current term. Either party may terminate the Fanapt® manufacturing agreement under certain circumstances upon specified written notice to the other party.

In December 2020, we entered into a non-exclusive manufacturing agreement for the manufacture of commercial supplies of HETLIOZ LQ™. The HETLIOZ LQ™ manufacturing agreement has an initial term of five years and automatically renews after the initial term for successive terms of one year each, unless either party gives notice of its intention to terminate the agreement at least 12 months prior to the end of the then current term.

Government Regulation

Government authorities in the U.S., at the federal, state and local levels, and in other countries extensively regulate, among other things, the research, development, testing, manufacture, quality control, approval, labeling, packaging, storage, record-keeping, promotion, advertising, distribution, marketing and export and import of pharmaceutical products. A new drug must be approved by the FDA through the NDA process before it may be legally marketed in the U.S. The process of obtaining regulatory approvals and the subsequent compliance with appropriate federal, state, local and foreign statutes and regulations require the expenditure of substantial time and financial resources. Moreover, failure to comply with applicable regulatory requirements may result in, among other things, warning letters, clinical holds, civil or criminal penalties, recall or seizure of products, injunction, disbarment, partial or total suspension of production or withdrawal of the product from the market. Any agency or judicial enforcement action could have a material adverse effect on our business.

U.S. government regulation

U.S. drug development and regulation

In the U.S., the FDA regulates drugs under the federal Food, Drug, and Cosmetic Act (FDCA) and related regulations. Drugs are also subject to other federal, state and local statutes and regulations. The process of obtaining regulatory approvals and the subsequent compliance with appropriate federal, state and local statutes and regulations requires the expenditure of substantial time and financial resources. Failure to comply with the applicable U.S. requirements at any time during the product development process, approval process or after approval may subject an applicant to administrative or judicial sanctions. These sanctions could include the FDA's refusal to approve pending applications, withdrawal of an approval, a clinical hold, warning letters, product recalls, product seizures, total or partial suspension of production or distribution, injunctions, fines, refusals of government contracts, restitution, disgorgement or civil or criminal penalties. Any agency or judicial enforcement action could have a material adverse effect on our business.

Once a drug candidate is identified for development, it enters the preclinical testing stage. Preclinical tests include laboratory evaluations of product chemistry, toxicity and formulation, as well as animal studies. An IND application sponsor must submit the results of the preclinical tests, together with manufacturing information and analytical data, to the FDA as part of the IND. The sponsor must also include a protocol detailing, among other things, the objectives of the first phase of clinical trials, the parameters to be used in monitoring the safety of the trial, and the effectiveness criteria to be evaluated should the first phase lend itself to an efficacy evaluation. Some preclinical testing may continue even after the IND is submitted. The IND automatically becomes effective 30 days after receipt by FDA, unless FDA, within the 30-day time period, places the clinical trial on a clinical hold. Clinical holds also may be imposed by the FDA at any time before or during clinical trials due to safety concerns about on-going or proposed clinical trials or non-compliance with specific FDA requirements, and the trials may not begin or continue until the FDA notifies the sponsor that the hold has been lifted.

All clinical trials must be conducted under the supervision of one or more qualified investigators in accordance with FDA good clinical practice (GCP) requirements, which include a requirement that all research subjects provide their informed consent in writing for their participation in any clinical trial. Clinical trials must be conducted under protocols detailing the objectives of the trial, dosing procedures, subject selection and exclusion criteria and the safety and/or effectiveness criteria to be evaluated. Each protocol must be submitted to the FDA as part of the IND, and timely safety reports must be submitted to the FDA and the investigators for serious and unexpected adverse events. An Institutional Review Board (IRB) at each institution participating in the clinical trial must review and approve each protocol before a clinical trial may commence at the institution and must also approve the information regarding the trial as well as the consent form that must be provided to each trial subject or his or her legal representative, monitor the study until completed and otherwise comply with all applicable IRB regulations.

Human clinical trials are typically conducted in three sequential phases that may overlap or be combined in certain cases:

- Phase I: The compound is initially introduced into healthy human subjects and tested for safety, dosage tolerance, absorption, metabolism, distribution and excretion and, if possible, to gain an early indication of its effectiveness. In most cases, initial Phase I clinical trials are conducted with healthy volunteers. However, where the compound being evaluated is for the treatment of severe or life-threatening diseases, such as cancer, and especially when the product may be too toxic to ethically administer to healthy volunteers, the initial human testing may be conducted on patients with the target disease or condition. Sponsors sometimes subdivide their Phase I clinical trials into Phase Ia and Phase Ib clinical trials. Phase Ib clinical trials are typically aimed at confirming dosage, pharmacokinetics and safety in a larger number of patients. Some Phase Ib studies evaluate biomarkers or surrogate markers that may be associated with efficacy in patients with specific types of diseases or conditions.
- Phase II: This phase involves clinical trials in a limited patient population to identify possible adverse effects and safety risks, to preliminarily evaluate the efficacy of the product for specific targeted diseases or conditions and to confirm dosage tolerance and appropriate dosage.
- Phase III: Phase III clinical trials are undertaken to further evaluate dosage, clinical efficacy and safety in an expanded patient population, generally at geographically dispersed clinical study sites. These clinical trials, often referred to as "pivotal" clinical trials, are intended to establish the overall risk-benefit ratio of the compound and provide, if appropriate, an adequate basis for product labeling.

The FDA or the sponsor may suspend a clinical trial at any time on various grounds, including any finding that the research subjects or patients are being exposed to an unacceptable health risk. Similarly, an IRB can suspend or terminate approval of a clinical trial at its institution if the clinical trial is not being conducted in accordance with the IRB's requirements or if the drug has been associated with unexpected, serious harm to study subjects. In addition, clinical trials may be overseen by an independent group of qualified experts organized by the sponsor, known as a data safety monitoring board or committee. Depending on its charter, this committee may determine whether a trial may move forward at designated check points based on access to certain data from the trial.

Post-approval trials may also be conducted after a drug receives initial marketing approval. These trials, often referred to as "Phase IV" trials, are used to gain additional experience from the treatment of patients in the intended therapeutic indication. In certain instances, the FDA may mandate the performance of such clinical trials as a condition of approval of an NDA.

During the development of a new drug, sponsors are given several opportunities to meet with the FDA. These meetings can provide an opportunity for the sponsor to share information about the progress of the application or clinical trials, for the FDA to provide advice, and for the sponsor and the FDA to reach agreement on the next phase of development. These meetings may occur prior to the submission of an IND, at the end of Phase II clinical trials, or before an NDA is ultimately submitted. Sponsors typically use the meetings at the end of the Phase II trials to discuss Phase II clinical results and present plans for the pivotal Phase III clinical trials that they believe will support approval of the new drug. Meetings at other times may be made upon request.

Concurrent with clinical trials, companies typically complete additional, animal or other non-clinical studies, develop additional information about the chemistry and physical characteristics of the drug, and finalize a process for manufacturing the product in commercial quantities in accordance with the FDA's current Good Manufacturing Practices (cGMP) requirements. The manufacturing process must consistently produce quality batches of the drug and, among other things, the manufacturer must develop methods for testing the identity, strength, quality and purity of the final drug. In addition, appropriate packaging must be selected and tested, and stability studies must be conducted to demonstrate the effectiveness of the packaging and that the compound does not undergo unacceptable deterioration over its shelf life.

While the IND is active, progress reports summarizing the results of ongoing clinical trials and nonclinical studies performed since the last progress report must be submitted on at least an annual basis to the FDA, and written IND safety reports must be submitted to the FDA and investigators for serious and unexpected adverse events, findings from other studies suggesting a significant risk to humans exposed to the same or similar drugs, findings from animal or in vitro testing suggesting a significant risk to humans, and any clinically important, increased incidence of a serious adverse reaction compared to that listed in the protocol or investigator brochure.

There are also requirements governing the submission of certain clinical trials and completed trial results to public registries. Sponsors of certain clinical trials of FDA-regulated products are required to register and disclose specified clinical trial registration and results information, which is made publicly available at www.clinicaltrials.gov. Failure to properly report clinical trial results can result in civil monetary penalties. Disclosure of clinical trial results can often be delayed until the new product or new indication being studied has been approved.

U.S. review and approval process

The results of product development, preclinical and other non-clinical studies and clinical trials, along with descriptions of the manufacturing process, analytical tests conducted on the chemistry of the drug, proposed labeling and other relevant information are submitted to the FDA as part of an NDA. The submission of an NDA is subject to the payment of substantial user fees; a waiver of which may be obtained under certain limited circumstances.

The FDA reviews NDAs to determine, among other things, whether the product is safe and effective for its intended use and whether it is manufactured in a cGMP-compliant manner, which will assure and preserve the product's identity, strength, quality and purity. Under PDUFA-VI, the FDA has a goal of 10 months from the date of "filing" of a standard, completed NDA for a new molecular entity to review and act on the submission. This review typically takes 12 months from the date the NDA is submitted to the FDA because FDA has 60 days to make a "filing" decision after the application is submitted. The FDA conducts a preliminary review of all NDAs within the first 60 days after submission, before accepting them for filing, to determine whether they are sufficiently complete to permit substantive review. The FDA may request additional information rather than accept an NDA for filing. In this event, the NDA must be resubmitted with the additional information. The resubmitted application also is subject to review before the FDA accepts it for filing.

The FDA may refer an application for a new drug to an advisory committee within the FDA. An advisory committee is a panel of independent experts, including clinicians and other scientific experts, that reviews, evaluates and provides a recommendation as to whether and under what conditions the application should be approved. The FDA is not bound by the recommendations of such an advisory committee, but it considers advisory committee recommendations carefully when making decisions.

Before approving an NDA, the FDA will also inspect the facility where the product is manufactured. The FDA will not approve an application unless it determines that the manufacturing processes and facilities are in compliance with cGMP requirements and are adequate to assure consistent production of the product within required specifications. Before approving an NDA, the FDA may also inspect one or more clinical trial sites to assure compliance with GCP requirements.

After the FDA evaluates an NDA, it will issue an approval letter or a CRL. A CRL indicates that the review cycle of the application is complete, and the application will not be approved in its present form. A CRL usually describes the specific deficiencies in the NDA identified by the FDA and may require additional clinical data, such as an additional pivotal Phase III trial or other significant and time-consuming requirements related to clinical trials, nonclinical studies or manufacturing. If a CRL is issued, the sponsor must resubmit the NDA, addressing all of the deficiencies identified in the letter, or withdraw the application. Even if such data and information are submitted, the FDA may decide that the NDA does not satisfy the criteria for approval. An approval letter authorizes commercial marketing of the drug with prescribing information for specific indications.

The Pediatric Research Equity Act (PREA) requires IND sponsors to conduct pediatric clinical trials for most drugs, for a new active ingredient, new indication, new dosage form, new dosing regimen or new route of administration. Under the PREA, original NDAs and supplements must contain a pediatric assessment unless the sponsor has received a deferral or waiver. The required assessment must evaluate the safety and effectiveness of the product for the claimed indications in all relevant pediatric subpopulations and support dosing and administration for each pediatric subpopulation for which the product is safe and effective. The sponsor or the FDA may request a deferral of pediatric clinical trials for some or all of the pediatric subpopulations. A deferral may be granted for several reasons, including a finding that the drug is ready for approval for use in adults before pediatric clinical trials are complete or that additional safety or effectiveness data needs to be collected before the pediatric clinical trials begin. The FDA must send a non-compliance letter to any sponsor that fails to submit the required assessment, keep a deferral current or fails to submit a request for approval of a pediatric formulation.

If a drug receives FDA approval, the approval may be limited to specific diseases and dosages, which could restrict the commercial value of the product. In addition, the FDA may require testing and surveillance programs to monitor the safety of approved products that have been commercialized, and may require a sponsor to conduct post-marketing clinical trials, which are designed to further assess a drug's safety and effectiveness after NDA approval. The FDA may also place other conditions on approval, including a requirement for a risk evaluation and mitigation strategy (REMS) to assure the safe use of the drug. If the FDA concludes a REMS is needed, the sponsor of the NDA must submit a proposed REMS. The FDA will not approve the NDA without an approved REMS, if required. A REMS could include medication guides, physician communication plans or elements to assure safe use, such as restricted distribution methods, patient registries and other risk minimization tools. Any of these limitations on approval or marketing could restrict the commercial promotion, distribution, prescribing or dispensing of products. Marketing approval may be withdrawn for non-compliance with REMS or other regulatory requirements, or if problems occur following initial marketing.

Post-approval requirements

Once an approval is granted, the FDA may withdraw the approval if compliance with regulatory standards is not maintained or if problems occur after the drug reaches the market. Later discovery of previously unknown problems with a drug may result in restrictions on the drug or even complete withdrawal of the drug from the market. After approval, some types of changes to the approved drug, such as adding new indications, certain manufacturing changes and additional labeling claims, are subject to further FDA review and approval. Manufacturers and other entities involved in the manufacture and distribution of approved drugs are required to register their establishments with the FDA and certain state agencies and are subject to periodic unannounced inspections by the FDA and certain state agencies for compliance with cGMP regulations and other laws and regulations.

Our approved products are, and any additional product manufactured or distributed by us following FDA approval will be, subject to continuing regulation by the FDA, including, among other things, record-keeping requirements, reporting of adverse experiences with the drug, providing the FDA with updated safety and efficacy information, drug sampling and distribution requirements, complying with certain electronic records and signature requirements, and complying with FDA promotion and advertising requirements. The FDA strictly regulates labeling, advertising, promotion and other types of information regarding approved drugs that are placed on the market, and imposes requirements and restrictions on drug manufacturers, such as those related to direct-to-consumer advertising, the prohibition on promoting products for uses or in patient populations that are not described in the product's approved labeling (known as "off-label use"), industry-sponsored scientific and educational activities, and promotional activities involving the internet. Discovery of previously unknown problems or the failure to comply with the applicable regulatory requirements may result in restrictions on the marketing of a product for a certain indication or withdrawal of the product from the market as well as possible civil or criminal sanctions. Failure to comply with the applicable governmental requirements at any time during the product development process, approval process or after approval, may subject an applicant or manufacturer to administrative or judicial civil or criminal sanctions and adverse publicity. FDA sanctions could include refusal to approve pending applications, withdrawal of an approval, clinical holds on post-marketing clinical trials, enforcement letters, product recalls, product seizures, total or partial suspension of production or distribution, injunctions, fines, refusals of government contracts, mandated corrective advertising or communications with doctors, debarment, restitution, disgorgement of profits, or civil or criminal penalties, any of which could have a material adverse effect on our business.

Orphan drug designation

Under the Orphan Drug Act, the FDA may grant orphan drug designation to drugs intended to treat a rare disease or condition, generally a disease or condition that affects fewer than 200,000 individuals in the U.S or, if affects more than 200,000 individuals in the U.S., there is no reasonable expectation that sales of the drug will be sufficient to offset the cost of developing and making the drug available in the U.S.. Orphan drug designation must be requested before submitting an NDA. After the FDA grants Orphan drug designation, the generic identity of the drug and its potential orphan use are disclosed publicly by the FDA. Orphan drug designation does not convey any advantage in, or shorten the duration of, the regulatory review and approval process. The first NDA applicant to receive FDA approval for a particular active ingredient to treat a particular disease with FDA orphan drug designation is entitled to a seven-year exclusive marketing period in the U.S. for that product, for that indication. During the seven-year exclusivity period, the FDA may not approve any other applications to market the same drug for the same disease, except in limited circumstances, such as a showing of clinical superiority to the product with orphan drug exclusivity. Orphan drug exclusivity does not prevent FDA from approving a different drug for the same disease or condition, or the same drug for a different disease or condition. Among the other benefits of orphan drug designation are tax credits for certain research and development expenses and a waiver of the NDA application user fee.

Expedited development and review programs

The FDA has a fast track designation program that is intended to expedite or facilitate the process for reviewing new drug products that meet certain criteria. Specifically, new drugs are eligible for fast track designation if they are intended to treat a serious or life-threatening disease or condition and demonstrate the potential to address unmet medical needs for the disease or condition. With regard to a fast track product, the FDA may consider for review sections of the NDA on a rolling basis before the complete application is submitted, if the sponsor provides a schedule for the submission of the sections of the NDA, the FDA agrees to accept sections of the NDA and determines that the schedule is acceptable, and the sponsor pays any required user fees upon submission of the first section of the NDA.

Any product submitted to the FDA for approval, including a product with a fast track designation, may also be eligible for other types of FDA programs intended to expedite development and review, such as priority review and accelerated approval.

A product is eligible for priority review if it is intended to treat a serious condition, and if approved, would provide a significant improvement in safety or efficacy compared to currently marketed products. The FDA will attempt to direct additional resources to the evaluation of an application for a new drug designated for priority review in an effort to facilitate the review. The FDA endeavors to review applications with priority review designations within six months of the filing date, as compared to 10 months for review of NDAs under its current PDUFA-VI review goals.

In addition, a product may be eligible for accelerated approval. Drugs intended to treat serious or life-threatening diseases or conditions may be eligible for accelerated approval upon a determination that the product has an effect on a surrogate endpoint that is reasonably likely to predict a clinical benefit, or on a clinical endpoint that can be measured earlier than irreversible morbidity or mortality, that is reasonably likely to predict an effect on irreversible morbidity or mortality or other clinical benefit, taking into account the severity, rarity, or prevalence of the condition and the availability or lack of alternative treatments. As a condition of approval, the FDA may require that a sponsor of a drug receiving accelerated approval perform adequate and well-controlled post-marketing clinical trials. Drugs receiving accelerated approval may be subject to expedited withdrawal procedures if the sponsor fails to conduct the required post-marketing trials or if such trials fail to verify the predicted clinical benefit. In addition, the FDA currently requires as a condition for accelerated approval pre-approval of promotional materials, which could adversely impact the timing of the commercial launch of the product.

The Food and Drug Administration Safety and Innovation Act established a category of drugs referred to as “breakthrough therapies” that may be eligible to receive breakthrough therapy designation. A sponsor may seek FDA designation of a compound as a “breakthrough therapy” if the product is intended, alone or in combination with one or more other products, to treat a serious or life-threatening disease or condition and preliminary clinical evidence indicates that the product 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 includes all of the fast track program features, as well as more intensive FDA interaction and guidance. The breakthrough therapy designation is a distinct status from both accelerated approval and priority review, which can also be granted to the same drug if relevant criteria are met. If a product is designated as breakthrough therapy, the FDA will work to expedite the development and review of such drug.
Fast track designation, priority review and breakthrough therapy designation do not change the standards for approval but may expedite the development or approval process. However, even if a product qualifies for one or more of these programs, the FDA may later decide that the product no longer meets the conditions for qualification or decide that the time period for FDA review or approval will not be shortened.

Marketing exclusivity

The FDA provides periods of regulatory exclusivity, which provide the holder of an approved NDA limited protection from new competition in the marketplace for the innovation represented by its approved drug for a period of three or five years following the FDA’s approval of the NDA. Five years of exclusivity are available to NCEs. An NCE is a drug that contains no active moiety that has been approved by the FDA in any other NDA. An active moiety is the molecule or ion, excluding those appended portions of the molecule that cause the drug to be an ester, salt, including a salt with hydrogen or coordination bonds, or other noncovalent, or not involving the sharing of electron pairs between atoms, derivatives, such as a complex (i.e., formed by the chemical interaction of two compounds), chelate (i.e., a chemical compound), or clathrate (i.e., a polymer framework that traps molecules), of the molecule, responsible for the therapeutic activity of the drug substance. During the exclusivity period, the FDA may not accept for review or approve an abbreviated new drug application (ANDA) or a 505(b)(2) NDA submitted by another company that contains the previously approved active moiety. An ANDA or 505(b)(2) application, however, may be submitted one year before NCE exclusivity expires if it includes a certification that the new product will not infringe the already approved product’s listed patents, or that such patents are invalid. If a product is not eligible for the NCE exclusivity, it may be eligible for three years of exclusivity. Three-year exclusivity is available to the holder of an NDA, including a 505(b)(2) NDA, for a particular condition of approval, or change to a marketed product, such as a new formulation for a previously approved product, if one or more new clinical trials, other than bioavailability or bioequivalence trials, was essential to the approval of the application and was conducted or sponsored by the applicant. This three-year exclusivity period protects against FDA approval of ANDAs and 505(b)(2) NDAs for the condition of the new drug’s approval. As a general matter, three-year exclusivity does not prohibit the FDA from approving ANDAs or 505(b)(2) NDAs for generic versions of the original, unmodified drug product. Five-year and three-year exclusivity will not delay the submission or approval of a full NDA; however, an applicant submitting a full NDA would be required to conduct or obtain a right of reference to all of the preclinical studies and adequate and well-controlled clinical trials necessary to demonstrate safety and efficacy.

Pediatric exclusivity is another type of marketing exclusivity available in the U.S. Pediatric exclusivity provides for an additional six months of marketing exclusivity attached to another period of exclusivity if a sponsor conducts clinical trials in children in response to a written request from the FDA. The issuance of a written request does not require the sponsor to

undertake the described clinical trials. In addition, orphan drug designation, as described above, may offer a seven-year period of marketing exclusivity, except in certain circumstances.

Orange Book listing, the Hatch-Waxman Act

In seeking approval for a drug through an NDA, applicants are required to list with the FDA each patent with claims that cover the applicant's drug. Upon approval of a drug, each of the patents listed in the application for the drug is then published in the FDA's Orange Book. Drugs listed in the Orange Book can, in turn be cited by potential competitors in support of approval of an ANDA. An ANDA provides for marketing of a drug that has the same active ingredients in the same strengths and dosage form as the listed drug and has been shown through bioequivalence testing to be therapeutically equivalent to the listed drug. ANDA applicants are not required to conduct or submit results of preclinical or clinical tests to prove the safety or effectiveness of their drug, other than the requirement for bioequivalence testing. Drugs approved in this way are commonly referred to as "generic equivalents" to the listed drug, and can often be substituted by pharmacists under prescriptions written for the original listed drug.

The ANDA applicant is required to certify to the FDA concerning any patents listed for the approved drug in the Orange Book. Specifically, the applicant must certify that: (i) the required patent information has not been filed; (ii) the listed patent has expired; (iii) the listed patent has not expired, but will expire on a particular date and approval is sought after patent expiration; or (iv) the listed patent is invalid or will not be infringed by the new drug. A certification that the new drug will not infringe the already approved drug's listed patents or that such patents are invalid is called a Paragraph IV certification. If the applicant does not challenge the listed patents, the ANDA application will not be approved until all the listed patents claiming the referenced drug have expired.

If the ANDA applicant has provided a Paragraph IV certification to the FDA, the applicant must also send notice of the Paragraph IV certification to the NDA and patent holders once the ANDA has been accepted for filing by the FDA. The NDA and patent holders may then initiate a patent infringement lawsuit in response to the notice of the Paragraph IV certification. The filing of a patent infringement lawsuit within 45 days of the receipt of a Paragraph IV certification automatically prevents the FDA from approving the ANDA until the earlier of 30 months, expiration of the patent, settlement of the lawsuit or a decision in the infringement case that is favorable to the ANDA applicant.

The ANDA application also will not be approved until any non-patent exclusivity, such as exclusivity for obtaining approval of a NCE, listed in the Orange Book for the referenced drug has expired. The U.S. Drug Price Competition and Patent Term Restoration Act of 1984, more commonly known as the "Hatch-Waxman Act," provides a period of five years following approval of a drug containing no previously approved active ingredients, during which ANDAs for generic versions of those drugs cannot be submitted unless the submission contains a Paragraph IV challenge to a listed patent, in which case the submission may be made four years following the original drug approval. Federal law provides for a period of three years of exclusivity following approval of a listed drug that contains previously approved active ingredients but is approved in a new dosage form, route of administration or combination, or for a new use, the approval of which was required to be supported by new clinical trials conducted by or for the sponsor, during which FDA cannot grant effective approval of an ANDA based on that listed drug.

Fraud and abuse laws and other U.S. regulatory matters

Pharmaceutical companies are subject to broadly applicable fraud and abuse and other healthcare laws and regulations, in addition to the FDCA, that may constrain the business or financial arrangements and relationships through which these companies market, sell and distribute the products for which they obtain marketing approval. Some of the laws and regulations that may affect the ability of pharmaceutical companies to operate are described below.

Anti-kickback laws

The federal Anti-Kickback Statute prohibits, among other things, knowingly and willfully offering, paying, soliciting, or receiving remuneration, directly or indirectly, in cash or in kind, to induce or reward the purchasing, leasing, ordering or arranging for or recommending the purchase, lease, or order of any health care item or service reimbursable under federal healthcare programs such as Medicare and Medicaid. The term "remuneration" has been broadly interpreted to include anything of value, and the government can establish a violation of the Anti-Kickback Statute without proving that a person or entity had actual knowledge of the law or specific intent to violate it. This statute has been interpreted to apply to arrangements between pharmaceutical manufacturers on the one hand and prescribers, purchasers, patients, and formulary managers on the other. There are a number of statutory exceptions and regulatory safe harbors protecting certain common activities from prosecution or other regulatory sanctions, however, the exceptions and safe harbors are drawn narrowly. Failure to meet all of the

requirements of a particular statutory exception or regulatory safe harbor does not make the conduct per se illegal under the Anti-Kickback Statute, but the legality of the arrangement will be evaluated on a case-by-case basis based on the totality of the facts and circumstances. Violations of the Anti-Kickback Statute are punishable by imprisonment, criminal fines, civil monetary penalties and exclusion from the participation in federal healthcare programs, such as Medicare and Medicaid. A number of states also have anti-kickback laws that establish similar prohibitions that may apply to items or services reimbursed by government programs, as well as any third-party payors, including commercial payors, known as "all-payor" laws.

Prescription Drug Marketing Act

As part of the sales and marketing process, pharmaceutical companies frequently provide healthcare providers with samples of approved drugs. The Prescription Drug Marketing Act (PDMA) imposes requirements and limitations upon the distribution of drugs and drug samples, and prohibits states from licensing distributors of prescription drugs unless the state licensing program meets certain federal guidelines that include minimum standards for storage and handling, as well as record keeping and other requirements. Violations of the PDMA may result in criminal and civil penalties. In addition, the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act of 2010 (collectively known as the Affordable Care Act or ACA), discussed in more detail in "*Pharmaceutical Coverage, Pricing and Reimbursement and Healthcare Reform*" below, imposes annual reporting requirements related to sample distribution.

False Claims Act

The False Claims Act prohibits, among other things, knowingly presenting, or causing to be presented false or fraudulent claims for payment of government funds and knowingly making, or causing to be made or used, a false record or statement to get a false claim paid. Certain marketing practices may implicate the False Claims Act, including promotion of pharmaceutical products for unapproved uses, providing free product to customers with the expectation that customers would bill federal programs for the product, or inflating prices reported to private price publication services used to set drug reimbursement rates under federal healthcare programs. In addition, the ACA amended the Social Security Act to provide that a claim including items or services resulting from a violation of the Anti-Kickback Statute constitutes a false claim for purposes of the False Claims Act. Actions under the False Claims Act may be brought by the government or as a qui tam action by private individuals who may receive financial awards if their claims are successful. False Claims Act liability is potentially significant in the healthcare industry because the statute provides for treble damages and monetary penalties of $5,500 to $11,000 per false claim or statement, which increased to a range of $11,665 to $23,331 in June 2020, with respect to violations occurring after November 2, 2015. Violations of the False Claims Act are also punishable by exclusion from participation in federal healthcare programs, such as Medicare and Medicaid. Pharmaceutical and other life sciences companies often resolve allegations without admissions of liability for significant and sometimes material amounts to avoid the uncertainty of treble damages and per claim penalties that may be awarded in litigation. These companies may be required, however, to enter into corporate integrity agreements with the government, which may impose substantial costs on companies to ensure compliance.

HIPAA

The Health Insurance Portability and Accountability Act of 1996 (HIPAA), includes federal criminal statutory provisions that prohibit among other actions, knowingly and willfully executing, or attempting to execute, a scheme to defraud any healthcare benefit program, including private third-party payors, knowingly and willfully embezzling or stealing from a healthcare benefit program, willfully obstructing a criminal investigation of a healthcare offense, and knowingly and willfully falsifying, concealing or covering up a material fact or making any materially false, fictitious or fraudulent statement in connection with the delivery of or payment for healthcare benefits, items or services.

HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act (HITECH) and their implementing regulations, impose certain requirements and restrictions on certain types of individuals and entities relating to the privacy and security of individually identifiable health information. Among other things, HITECH makes HIPAA's privacy and security standards directly applicable not only to covered entities (e.g. health care providers and health plans), but also to business associates, i.e., independent contractors or agents of covered entities that create, receive, maintain or transmit protected health information in connection with providing a service for or on behalf of a covered entity. HITECH also created four 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.

Physician Payment Sunshine Act

The Physician Payment Sunshine Act requires manufacturers of drugs, devices, biologics and medical supplies for which payment is available under Medicare, Medicaid or the Children's Health Insurance Program to report annually (with certain exceptions) to Centers for Medicare & Medicaid Services (CMS) information related to payments or other "transfers of

value" made to physicians and teaching hospitals, and requires applicable manufacturers and group purchasing organizations to report annually to CMS ownership and investment interests held by physicians and their immediate family members and payments or other "transfers of value" to such physician owners. Failure to report relevant data may result in civil fines and/or penalties.

Foreign Corrupt Practices Act

The Foreign Corrupt Practices Act (FCPA), prohibits U.S. corporations and their representatives and intermediaries from offering, promising, authorizing or making payments to any foreign government official, government staff member, political party or political candidate in an attempt to obtain or retain business abroad. The scope of the FCPA includes interactions with certain healthcare professionals in many countries. Violation of the FCPA could result in substantial civil and criminal penalties and remedies, including fines, disgorgement, and/or imprisonment.

Analogous state laws

Analogous state fraud and abuse laws and regulations, such as state anti-kickback and false claims laws, can apply to the business practices of pharmaceutical companies, including but not limited to research, distribution, sales or marketing arrangements and claims involving healthcare items or services reimbursed by non-governmental third-party payors and are generally broad and are enforced by many different federal and state agencies as well as through private actions. In addition to requiring reporting transfers of value, some states have imposed price reporting requirements. These state laws apply to items and services reimbursed under Medicaid and other state programs, or, in several states, apply regardless of the payor. In addition, a number of states require pharmaceutical companies to report expenses relating to the marketing and promotion of pharmaceutical products and to report gifts and payments to individual physicians in the states. Other states restrict when pharmaceutical companies may provide meals to prescribers or engage in other marketing related activities or require pharmaceutical companies to implement compliance programs or marketing codes of conduct, and file periodic reports or disclosures with states. Compliance with these laws requires significant resources and companies that do not comply may face civil penalties or other consequences.

Many state laws govern the privacy and security of personal information in specified circumstances. For example, the California Consumer Privacy Act (CCPA), which became effective on January 1, 2020, established a new legal framework governing covered businesses' collection and use of personal information of California residents by, among other things, creating an expanded definition of covered personal information, establishing new privacy rights for California residents, imposing an opt-in standard for certain disclosures of personal information about minors, and creating a new and potentially severe statutory damages framework for businesses subject to certain data breaches resulting from the failure to implement and maintain reasonable security procedures and practices. While properly collected clinical trial data and all protected health information governed by HIPAA are exempt from the current version of the CCPA, other personal information may be applicable and possible changes to the CCPA may broaden its scope.

Foreign regulation

Foreign drug development, review and approval processes

Regardless of whether we obtain FDA approval for a product, we must obtain approval by the comparable regulatory authorities of foreign countries before we can commence clinical trials or marketing of the product in those countries. The approval process varies from country to country, and the time may be longer or shorter than that required for FDA approval. The requirements governing the conduct of clinical trials, product licensing, pricing and reimbursement also vary greatly from country to country. Although governed by the applicable country, clinical trials conducted outside of the U.S. typically are administered with the three-Phase sequential process that is discussed above under *U.S. drug development and regulation*. However, the foreign equivalent of an IND is not a prerequisite to performing pilot studies or Phase I clinical trials.

Under E.U. regulatory systems, we may submit Marketing Authorization Applications (MAAs) either under a centralized or decentralized procedure. The centralized procedure, which is available for drugs produced by biotechnology or which are highly innovative, provides for the grant of a single marketing authorization that is valid for all E.U. member states. This authorization is a marketing authorization approval. The decentralized procedure provides for mutual recognition of national approval decisions. Under this procedure, the holder of a national marketing authorization may submit an application to the remaining member states. Within 90 days of receiving the applications and assessment report, each member state must decide whether to recognize approval. This procedure is referred to as the mutual recognition procedure. In addition, regulatory approval of prices is required in most countries other than the U.S. We face the risk that the resulting prices would be insufficient to generate an acceptable return to us.

Foreign fraud and abuse laws and other regulatory matters

Outside the U.S., we are subject to similar regulations in those countries where we market and sell products, including with respect to transparency, bribery and other laws mentioned above. In some foreign countries, including major markets in the E.U. and Japan, the pricing of prescription pharmaceuticals is subject to governmental control. In these countries, pricing negotiations with governmental authorities can take nine to 12 months or longer after the receipt of regulatory marketing approval for a product. To obtain reimbursement or pricing approval in some countries, we may be required to conduct a clinical trial that compares the cost-effectiveness of our product to other available therapies, which can be costly and time-consuming.

The collection and processing of personal data in the E.U. is governed by the General Data Protection Regulation (GDPR), which became applicable in May 2018. The GDPR implements stringent operational requirements for processors and controllers of personal data, including, for example, expanded disclosure requirements about how personal information is to be used, strengthened individual data subject rights, limitations on retention of personal data, increased requirements pertaining to health data and pseudonymised (i.e., key-coded) data, shortened mandatory data breach notification timelines and higher standards for controllers to demonstrate they have obtained valid consent for certain data processing activities. The GDPR provides that E.U. member states may make their own additional laws and regulations in relation to the processing of genetic, biometric or health data, which could result in differences between member states, limit our ability to use and share personal data or cause our costs to increase, and harm our business and financial condition. Further, the U.K.'s exit from the E.U. in January 2020, with a transition period that ended on December 31, 2020, often referred to as Brexit, has created uncertainty with regard to data protection regulation in the U.K. While the transition period has now concluded, decisions are still to be made on how data transfers to and from the U.K. will be regulated. We are also subject to evolving and strict rules on the transfer of personal data out of the E.U. Failure to comply with E.U. data protection laws may result in significant fines, including GDPR fines of up to the higher of €20,000,000 or 4% of our total worldwide annual revenue of the preceding financial year, and other administrative penalties, which may be onerous and adversely affect our business, financial condition, results of operations and prospects.

Pharmaceutical Coverage, Pricing and Reimbursement and Healthcare Reform

Significant uncertainty exists as to the coverage and reimbursement status of products approved by the FDA and other government authorities. Sales of products will depend, in part, on the extent to which the costs of the products will be covered by third-party payors, including government health programs in the U.S. such as Medicare and Medicaid, commercial health insurers and managed care organizations. The process for determining whether a payor will provide coverage for a product may be separate from the process for setting the price or reimbursement rate that the payor will pay for the product once coverage is approved. Third-party payors are increasingly challenging the prices charged, examining the medical necessity, and reviewing the cost-effectiveness of medical products and services and imposing controls to manage costs. Third-party payors may also limit coverage to specific products on an approved list, or formulary, which might not include all of the approved products for a particular indication.

In order to secure coverage and reimbursement for any product that might be approved for sale, a company may need to conduct expensive pharmacoeconomic studies in order to demonstrate the medical necessity and cost-effectiveness of the product, in addition to the costs required to obtain FDA or other comparable regulatory approvals. A payor's decision to provide coverage for a drug product does not imply that an adequate reimbursement rate will be approved. Third party reimbursement may not be sufficient to maintain price levels high enough to realize an appropriate return on investment in product development.

A primary trend in the U.S. healthcare industry and elsewhere is cost containment. There have been a number of federal and state proposals during the last several years regarding the pricing of pharmaceutical and biopharmaceutical products, limiting coverage and reimbursement for drugs and other medical products, government control and other changes to the healthcare system in the U.S. By way of example, in March 2010, the ACA was passed, ushering in significant changes to the coverage and payment for products under government health care programs. Among the provisions of the ACA of importance to pharmaceutical companies are:

- an annual, nondeductible fee on any entity that manufactures or imports specified branded prescription drugs and biologic agents, apportioned among these entities according to their market share in certain government healthcare programs, although this fee does not apply to sales of certain products approved exclusively for orphan indications;

- expansion of eligibility criteria for Medicaid programs by, among other things, allowing states to offer Medicaid coverage to certain individuals with income at or below 133% of the federal poverty level, thereby potentially increasing a manufacturer's Medicaid rebate liability;
- expanded manufacturers' rebate liability under the Medicaid Drug Rebate Program by increasing the minimum rebate for both branded and generic drugs and revising the definition of "average manufacturer price," (AMP), for calculating and reporting Medicaid drug rebates on outpatient prescription drug prices and extending rebate liability to prescriptions for individuals enrolled in Medicaid managed care plans;
- addressed a new methodology by which rebates owed by manufacturers under the Medicaid Drug Rebate Program are calculated for drugs that are inhaled, infused, instilled, implanted or injected;
- expanded the types of entities eligible for the 340B drug discount program;
- established the Medicare Part D coverage gap discount program by requiring manufacturers to provide a 50% point-of-sale-discount off the negotiated price of applicable brand drugs to eligible beneficiaries during their coverage gap period as a condition for the manufacturers' outpatient drugs to be covered under Medicare Part D. The Bipartisan Budget Act of 2018 increased the manufacturer discount from 50% to 70% effective in 2019;
- established a new Patient-Centered Outcomes Research Institute to oversee, identify priorities in, and conduct comparative clinical effectiveness research, along with funding for such research;
- added a requirement to annually report product samples that manufacturers and distributors provide to physicians;
- expanded healthcare fraud and abuse laws, including the False Claims Act and the federal Anti-Kickback Statute, and enhanced penalties for noncompliance; and
- established the Center for Medicare and Medicaid Innovation within CMS to test innovative payment and service delivery models to lower Medicare and Medicaid spending, potentially including prescription drug spending.

Some of the provisions of the ACA have yet to be fully implemented, however, while others have been subject to judicial and Congressional challenges, as well as efforts by the former Trump administration to repeal or replace certain aspects of the ACA. While Congress has not passed comprehensive repeal legislation, it has enacted laws that modify certain provisions of the ACA such as removing or delaying penalties, starting January 1, 2019, for not complying with the ACA's individual mandate to carry health insurance, delaying the implementation of certain ACA-mandated fees, and increasing the point-of-sale discount that is owed by pharmaceutical manufacturers who participate in Medicare Part D. Additionally, in December 2018, a Texas District Court judge ruled that the ACA is unconstitutional in its entirety because the individual mandate was repealed by Congress. Further, in December 2019, the U.S. Court of Appeals for the 5th Circuit upheld the Texas District Court ruling that the individual mandate was unconstitutional and remanded the case back to the Texas District Court to determine whether the remaining provisions of the ACA are invalid as well. In March 2020, the U.S. Supreme Court granted the petitions for writs of certiorari and held oral arguments in November 2020. Accordingly, we continue to evaluate the effect that the ACA has on our business.

At the federal level, the former Trump administration supported legislative proposals and issued certain Executive Orders seeking to reduce drug prices, increase competition, lower out-of-pocket drug costs for patients, and increase patient access to lower-cost generic and biosimilar drugs. The Department of Health and Human Services (HHS), has solicited feedback on some of these measures and implemented others under its existing authority. The FDA also released a final rule in September 2020 providing guidance for states to build and submit importation plans for drugs from Canada. Further, in November 2020, HHS finalized a regulation removing safe harbor protection for price reductions from pharmaceutical manufacturers to plan sponsors under Medicare Part D, either directly or through pharmacy benefit managers, unless the price reduction is required by law. The rule also creates a new safe harbor for price reductions reflected at the point-of-sale, as well as a safe harbor for certain fixed fee arrangements between pharmacy benefit managers and manufacturers. Additionally, in December 2020, CMS issued a final rule that materially modifies current Medicaid Drug Rebate Program regulations by, among other things, broadening the definitions for "line extension" and "new formulation", the key term within the line extension definition. A "line extension" drug is subject to a higher Medicaid rebate, thereby reducing the amount the manufacturer is paid with respect to such product. These new definitions will become effective as of January 1, 2022.

Other legislative changes have been proposed and adopted since the ACA was enacted. These changes include the Budget Control Act of 2011, which, among other things, led to aggregate reductions to Medicare payments to providers of up to 2% per fiscal year that started in 2013 and will stay in effect through 2024 unless additional congressional action is taken, and the American Taxpayer Relief Act of 2012, which, among other things, reduced Medicare payments to several types of providers and increased the statute of limitations period for the government to recover overpayments to providers from three to five years. These new laws may result in additional reductions in Medicare and other healthcare funding and otherwise affect

the prices we may obtain for any of our product candidates for which we may obtain regulatory approval or the frequency with which any such product candidate is prescribed or used. Further, there have been several recent U.S. congressional inquiries and proposed state and federal legislation designed to, among other things, bring more transparency to drug pricing, review the relationship between pricing and manufacturer patient programs, reduce the costs of drugs under Medicare and reform government program reimbursement methodologies for drug products.

In the coming years, additional legislative and regulatory changes could be made to governmental health programs that could significantly impact pharmaceutical companies and the success of our product candidates. At the state level, legislatures have increasingly passed legislation and implemented regulations designed to control pharmaceutical and biological product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain product access and marketing cost disclosure and transparency measures, and, in some cases, designed to encourage importation from other countries and bulk purchasing. In addition, regional health care authorities and individual hospitals are increasingly using bidding procedures to determine what pharmaceutical products and which suppliers will be included in their prescription drug and other health care programs. These measures could reduce the ultimate demand for our products, once approved, or put pressure on our product pricing. The ACA, as well as other federal, state and foreign healthcare reform measures that have been and may be adopted in the future, could have a material adverse effect on our business. Further, it is also possible that additional governmental action is taken in response to the COVID-19 pandemic as it continues into 2021.

These healthcare reforms, as well as other healthcare reform measures that may be adopted in the future, may result in additional reductions in Medicare and other healthcare funding, more rigorous coverage criteria, new payment methodologies and additional downward pressure on the price for any approved product and/or the level of reimbursement physicians receive for administering any approved product. Reductions in reimbursement levels may negatively impact the prices we can charge or the frequency with which products are prescribed or administered. Any reduction in reimbursement from Medicare or other government programs may result in a similar reduction in payments from private payors.

Similarly, pricing and reimbursement and the containment of healthcare costs has become a priority in a number of foreign jurisdictions. In the E.U., pricing and reimbursement schemes vary widely from country to country. Some countries provide that drug products may be marketed only after a reimbursement price has been agreed. Some countries may require the completion of additional studies that compare the cost-effectiveness of a particular drug candidate to currently available therapies, or so-called health technology assessments, in order to obtain reimbursement or pricing approval. For example, the E.U. provides options for its member states to restrict the range of drug products for which their national health insurance systems provide reimbursement and to control the prices of medicinal products for human use. E.U. member states may approve a specific price for a drug product or may instead adopt a system of direct or indirect controls on the profitability of the company placing the drug product on the market. Other member states allow companies to fix their own prices for drug products but monitor and control company profits. The downward pressure on health care costs in general, particularly prescription drugs, has become intense. As a result, increasingly high barriers are being erected to the entry of new products. In addition, in some countries, cross-border imports from low-priced markets exert competitive pressure that may reduce pricing within a country. Any country that has price controls or reimbursement limitations for drug products may not provide favorable reimbursement and pricing arrangements.

Human Capital

We had 292 full-time employees as of December 31, 2020, compared with 284 employees as of December 31, 2019. None of our employees are represented by a labor union. We have not experienced any work stoppages and consider our employee relations to be good. Our human capital objectives include attracting, training and retaining employees in a manner that supports innovation across our business.

Corporate Information

We were incorporated in Delaware in 2002. Our principal executive offices are located at 2200 Pennsylvania Avenue NW, Suite 300E, Washington D.C. 20037, and our telephone number is (202) 734-3400. Our website address is www.vandapharma.com and the information contained in, or that can be accessed through, our website is not part of this Annual Report and should not be considered part of this Annual Report.

Available Information

We file annual, quarterly, and current reports, proxy statements, and other documents with the Securities and Exchange Commission (SEC) under the Securities Exchange Act of 1934 (Exchange Act). The SEC maintains a website at

www.sec.gov that contains reports, proxy and information statements, and other information regarding issuers, including us, that file electronically with the SEC.

We also make available free of charge on our Internet website at www.vandapharma.com our annual reports on Form 10-K, quarterly reports on Form 10-Q, current reports on Form 8-K, and, if applicable, amendments to those reports filed or furnished pursuant to Section 13(a) or 15(d) of the Exchange Act as soon as reasonably practicable after we electronically file such material with, or furnish it to, the SEC.

Our code of ethics, other corporate policies and procedures, and the charters of our Audit Committee, Compensation Committee and Nominating/Corporate Governance Committee are available through our Internet website at www.vandapharma.com.

ITEM 1A. RISK FACTORS

Our business, financial condition and operating results can be affected by a number of factors, whether currently known or unknown, including but not limited to those described below, any one or more of which could, directly or indirectly, cause our actual operating results and financial condition to vary materially from past, or anticipated future, operating results and financial condition. Any of these factors, in whole or in part, could materially and adversely affect our business, financial condition, operating results and the price of our common stock.

The following discussion of risk factors contains forward-looking statements. These risk factors may be important to understanding any statement in this Annual Report or elsewhere. The following information should be read in conjunction with the consolidated financial statements and related notes in Part II, Item 8, Financial Statements and Supplementary Data and Part II, Item 7, Management's Discussion and Analysis of Financial Condition and Results of Operations.

Because of the following factors, as well as other factors affecting our financial condition and operating results, past financial performance should not be considered to be a reliable indicator of future performance, and investors should not use historical trends to anticipate results or trends in future periods.

Risks Related to our Business and Industry

We are dependent on the commercial success of HETLIOZ® and Fanapt®.

Our future success is currently substantially dependent upon the commercial success of HETLIOZ® capsules for the treatment of Non-24-Hour Sleep-Wake Disorder (Non-24) and HETLIOZ® capsules and oral suspension (HETLIOZ LQ™) for the treatment of nighttime sleep disturbances in Smith-Magenis Syndrome and Fanapt® oral tablets for the treatment of schizophrenia.

In January 2014, the U.S. Food and Drug Administration (FDA) approved our New Drug Application (NDA) for HETLIOZ® for the treatment of Non-24 and in April 2014, we commenced the U.S. commercial launch of HETLIOZ®. In July 2015, the European Commission (EC) granted centralized marketing authorization with unified labeling for HETLIOZ® for the treatment of Non-24 in totally blind adults, and in August 2016 we commenced the commercial launch of HETLIOZ® in Germany. This authorization is valid in the 27 countries that are members of the European Union (E.U.), as well as European Economic Area members Iceland, Liechtenstein and Norway. We have applied for renewal of this marketing authorization, which expires in the ordinary course in July 2020. In December 2020, the FDA approved our NDA and supplemental New Drug Application (sNDA) for HETLIOZ® for the treatment of nighttime sleep disturbances in SMS in adults and children, respectively.

In the fourth quarter of 2014, we acquired the U.S. commercial rights to Fanapt®, and began selling, marketing and distributing Fanapt® in the U.S.

Our ability to generate significant product revenue from sales of HETLIOZ® and Fanapt®, both in the U.S. and abroad, in the near term will depend on, among other things, our ability to:

- minimize the impact of disruptions caused by the COVID-19 pandemic;
- defend our patents and intellectual property from generic competition;
- maintain commercial manufacturing arrangements with third-party manufacturers;
- produce, through a validated process, sufficiently large quantities of inventory of our products to meet demand;

- continue to maintain and grow a wide variety of internal sales, distribution and marketing capabilities sufficient to sustain growth in sales of our products;
- gain broad acceptance of our products from physicians, health care payors, patients, pharmacists and the medical community;
- properly price and obtain adequate coverage and reimbursement of these products by governmental authorities, private health insurers, managed care organizations and other third-party payors;
- maintain compliance with ongoing labeling, packaging, storage, advertising, promotion, recordkeeping, safety and other post-market requirements;
- obtain regulatory approval to expand the labeling of our approved products for additional indications;
- obtain regulatory approval for HETLIOZ® or Fanapt® in additional countries;
- renew and maintain our existing regulatory approval for HETLIOZ® in Europe;
- adequately protect against and effectively respond to any claims by holders of patents and other intellectual property rights that our products infringe their rights; and
- adequately protect against and effectively respond to any unanticipated adverse effects or unfavorable publicity that develops in respect to our products, as well as the emergence of new or existing competitive products, which may be proven to be more clinically effective and cost-effective.

We expect to continue to incur significant expenses and to utilize a substantial portion of our cash resources as we continue the commercialization of HETLIOZ® and Fanapt®, evaluate foreign market opportunities for HETLIOZ® and Fanapt® and continue to grow our operational capabilities, both domestically and abroad. This activity represents a significant investment in the commercial success of HETLIOZ® and Fanapt®, which is uncertain.

If our continued commercial efforts are not successful with respect to HETLIOZ® and Fanapt® in the U.S., Europe or other jurisdictions in which these products may be approved for sale, our ability to generate increased product sales revenue may be jeopardized.

The cost of growing and maintaining a sales, marketing and distribution organization may exceed its cost effectiveness. If we fail to continue to develop sales, marketing and distribution capabilities, if sales efforts are not effective or if costs of developing sales, marketing and distribution capabilities exceed their cost effectiveness, our business, results of operations and financial condition could be materially adversely affected.

Growth of HETLIOZ® and Fanapt® may be slow or limited for a variety of reasons including competing products or unanticipated safety issues. If either HETLIOZ® or Fanapt® is not successful in gaining broad commercial acceptance, our business would be harmed.

Any increase in sales of HETLIOZ® and Fanapt® will be dependent on several factors, including our ability to educate physicians and to increase physician awareness of the benefits of our products relative to competing products. The degree of further market acceptance of any of our products, including with respect to new indications, or market acceptance of approved product candidates among physicians, patients, health care payors and the medical community will depend on a number of factors, including but not limited to:

- acceptable evidence of safety and efficacy;
- relative convenience and ease of administration;
- the prevalence and severity of any adverse side effects;
- availability of alternative treatments;
- market awareness of the condition to be treated; and
- pricing and cost effectiveness.

In addition, HETLIOZ® and Fanapt® are subject to continual review by the FDA, and we cannot assure that newly discovered or reported safety issues will not arise. With the use of any newly marketed drug by a wider patient population, serious adverse events may occur from time to time that initially do not appear to relate to the drug itself. Any safety issues could cause us to suspend or cease marketing of our approved products, cause us to modify how we market our approved products, subject us to substantial liabilities and adversely affect our revenues and financial condition. In the event of a

withdrawal of either HETLIOZ® or Fanapt® from the market, our revenues would decline significantly and our business would be seriously harmed.

Global economic conditions may have an adverse effect on our business.

Financial instability or a general decline in economic conditions in the U.S. and other countries where we sell our product could adversely affect our operations. Economic conditions, and uncertainty as to the general direction of the macroeconomic environment, are beyond our control and may make any necessary debt or equity financing more difficult, more costly, and more dilutive. While we believe we have adequate capital resources to meet current working capital and capital expenditure requirements, an economic downturn or significant increase in our expenses could require additional financing on less than attractive rates or on terms that are excessively dilutive to existing stockholders. Failure to secure any necessary financing in a timely manner and on favorable terms could have a material adverse effect on our stock price and could require us to delay or abandon clinical development plans.

Sales of our products will be dependent, in large part, on reimbursement from government health administration authorities, private health insurers, distribution partners and other organizations. In the event of economic decline, these organizations may be unable to satisfy their reimbursement obligations or may delay payment. In addition, federal and state health authorities may reduce Medicare and Medicaid reimbursements, and private insurers may increase their scrutiny of claims. A reduction in the availability or extent of reimbursement could negatively affect our product sales and revenue.

In addition, we rely on third parties for several important aspects of our business. For example, we use third parties for sales, distribution, medical affairs and clinical research, and we rely upon several single source providers of raw materials and contract manufacturers for the manufacture of our products. During challenging and uncertain economic times and in tight credit markets, there may be a disruption or delay in the performance of our third-party contractors, suppliers or partners. If such third parties are unable to satisfy their commitments to us, our business and results of operations would be adversely affected.

Global health crises and pandemics, such as the global outbreak of COVID-19, may adversely impact our business.

The current global pandemic caused by the spread of the novel coronavirus (COVID-19) has led to the implementation of various responses, including government-imposed quarantines, travel restrictions and other public health safety measures. The extent to which the effects of shelter-in-place orders and our work-from-home policies may negatively impact productivity and disrupt our business will depend, in part, on the length and severity of the restrictions and other limitations on our ability to conduct our business in the ordinary course.

Our sales force has had physical access to healthcare providers curtailed, which may have a negative impact on our revenues. While we are implementing marketing and sales strategies aimed at overcoming the disruptions caused by the pandemic, we cannot ensure that these methods will be effective. Additionally, patients who might be currently using our products, or might otherwise be eligible to use our products, may be unable to meet with their healthcare providers, which may reduce the number of prescription refills or new patient starts, thereby adversely affecting our revenues.

The COVID-19 pandemic has impacted clinical research globally, including our previously reported clinical trials. While certain of our programs have resumed patient enrollment, other programs remain on hold. We may experience further disruptions that could adversely impact our supply chain, our ongoing and planned clinical trials, and other regulatory activities, including:

- interruption of, or delays in receiving, supplies of the active pharmaceutical ingredients that our contract manufacturing organizations use to manufacture our products and any related interruption of, or delays in receiving, supplies of our products from these organizations, due to staffing shortages, production slowdowns or stoppages and disruptions in delivery systems;
- delays or difficulties in clinical site initiation, including difficulties in recruiting clinical site investigators and clinical site staff;
- diversion of healthcare resources away from the conduct of clinical trials, including the diversion of hospitals serving as our clinical trial sites and hospital staff supporting the conduct of our clinical trials;
- delays or difficulties in enrolling patients in our clinical trials;

- interruption of key clinical trial activities, such as clinical trial site data monitoring, due to limitations on travel imposed or recommended by federal or state governments, employers and others or interruption of clinical trial subject visits and study procedures (such as procedures that are deemed non-essential), which may impact the integrity of subject data and clinical study endpoints;
- limitations on our employee resources or those of third-party clinical research organizations towards the development of our products, including because of sickness of employees or their families or the desire of employees to avoid contact with large groups of people; and
- interruption or delays in the operations of regulatory agencies, which may impact review and approval timelines.

In addition, the trading prices for our common stock and other biopharmaceutical companies have been highly volatile as a result of the COVID-19 pandemic. As a result, we may face difficulties raising capital through sales of our common stock or such sales may be on unfavorable terms.

The COVID-19 pandemic continues to rapidly evolve. The extent to which the outbreak may continue to impact our business, financial condition and results of operations will depend on future developments, which are highly uncertain and cannot be predicted with confidence, such as the duration of the outbreak, travel restrictions and social distancing practices, business closures or business disruptions and the effectiveness of actions taken in the U.S. and other countries to contain and treat the disease.

If the FDA does not accept for filing the NDAs that we may submit for tradipitant for the treatment of gastroparesis, motion sickness, atopic dermatitis and COVID-19 pneumonia, or the FDA determines that our clinical trial results for tradipitant for the treatment of gastroparesis, motion sickness, atopic dermatitis or COVID-19 pneumonia do not demonstrate adequate safety and efficacy, or the FDA does not approve an applicable PDUFA-VI date, continued development of tradipitant will be significantly delayed or terminated, our business will be significantly harmed, and the market price of our stock could decline.

In October 2019, we completed enrollment in EPIONE, a Phase III clinical study of tradipitant for the treatment of pruritus in atopic dermatitis and commenced enrollment in EPIONE 2, a second Phase III clinical study of tradipitant for the treatment of atopic dermatitis. We have also initiated Phase III clinical studies of tradipitant for the treatment of gastroparesis, motion sickness and COVID-19 pneumonia. If the results of our ongoing Phase III studies of tradipitant for the treatment of gastroparesis, motion sickness, atopic dermatitis and/or COVID-19 pneumonia are positive, we will likely submit an NDA with the FDA for these indications. Any adverse developments or results or perceived adverse developments or results with respect to our pre-NDA meeting with the FDA, our regulatory submission or the tradipitant clinical programs in any or all indications will significantly harm our business and could cause the market price of our stock to decline. Examples of such adverse developments include, but are not limited to:

- the FDA determining that additional clinical studies are required with respect to tradipitant for the treatment of atopic dermatitis and/or the treatment of gastroparesis and/or the treatment of motion sickness;
- safety, efficacy or other concerns arising from clinical or non-clinical studies in these programs; or
- the FDA determining that the tradipitant clinical trial programs raise safety concerns or do not demonstrate adequate efficacy.

We believe that tradipitant has a well-established safety profile, as demonstrated by the results of extensive testing in animals and humans. Despite these results, however, the FDA informed us in December 2018 that in order to treat patients beyond 12 weeks, we will have to conduct a 9-month non-rodent chronic toxicity study, which currently limits our ability to collect safety data in humans for more than 12 weeks. The non-rodent study required by the FDA necessitates the sacrifice of dozens of animals and we have disputed the necessity of a 9-month non-rodent chronic toxicity study. In February 2019, we filed a lawsuit in the U.S. District Court for the District of Columbia (DC District Court) challenging the FDA's position, but ultimately did not prevail. Despite our disagreement with the FDA, the preclinical package has allowed us to continue to conduct all of the efficacy studies necessary for NDA filing. Moreover, in July 2020, the FDA approved the use of tradipitant for up to six months with an option of renewal for an individual patient who requested expanded access. Since then, other patients who experienced a unique benefit in tradipitant studies have requested expanded access. The expanded access program is ongoing and a number of patients have initiated treatment. Although this expanded access program is not intended for data collection, we will collect safety data from this cohort of expanded access patients and include this data in its NDA for tradipitant for the treatment of gastroparesis; however, the FDA may disregard such safety data when reviewing the NDA. The lack of long-term (>12 weeks in humans) safety data would likely impact the FDA's willingness to approve tradipitant for a chronic indication. However, because long-term safety data is not normally a requirement for short-term indications, and with a

preclinical profile that has not precluded clinical development, we believe the package is complete for any NDA filing to treat patients for 12 weeks or less. In gastroparesis, for example, the FDA has communicated to us that it is considering an indication for the short-term relief of nausea in gastroparesis. While this short-term indication is not preferred, we would consider accepting this limited indication while continuing to pursue a chronic indication. The chronic treatment of itch in atopic dermatitis would be expected to have a similar issue in review as gastroparesis. Our business will be materially adversely impacted if we are not able to agree with the FDA on a regulatory path to approval for tradipitant, we experience any delay in filing, or the FDA delays or denies approval of NDA filings for the treatment of gastroparesis, motion sickness, atopic dermatitis, or COVID-19 pneumonia.

If the FDA does not approve our sNDA for HETLIOZ® for the treatment of jet lag disorder or continued development of tasimelteon for the treatment of jet lag disorder is significantly delayed or terminated, our business will be significantly harmed, and the market price of our stock could decline.

In December 2018, we announced that the FDA had accepted the HETLIOZ® sNDA for the treatment of jet lag disorder. We received a complete response letter in August 2019 in which the FDA asserted that the measures of the study were of unclear clinical significance and declined to approve our sNDA. We met with the FDA to discuss the complete response letter in a Post Action meeting and we are determining our next steps.

Any additional adverse developments or results or perceived adverse developments or results with respect to our regulatory submission for jet lag disorder will significantly harm our business and could cause the market price of our stock to decline. Examples of such adverse developments include, but are not limited to:

- the FDA determining that additional clinical studies are required with respect to the jet lag disorder program;
- safety, efficacy or other concerns arising from clinical or non-clinical studies in the jet lag disorder program, or the manufacturing processes or facilities used for the jet lag disorder program; or
- the FDA determining that the jet lag disorder program raises safety concerns or does not demonstrate substantial evidence of efficacy.

We may enter into third-party collaborations from time to time in order to develop and commercialize our products. If we are unable to identify or enter into an agreement with any material third-party collaborator, if our collaborations with any such third party are not commercially successful or if our agreement with any such third party is terminated or allowed to expire, we could be adversely affected financially or our business reputation could be harmed.

Our business strategy includes entering into collaborations with corporate collaborators for the commercialization of HETLIOZ®, Fanapt® and our other products. While we are not currently party to any material commercial collaborative arrangements, areas in which we may potentially enter into third-party collaboration arrangements include joint sales and marketing arrangements for sales and marketing in certain E.U. countries and elsewhere outside of the U.S., and future product development arrangements. If we are unable to identify or enter into an agreement with any material third-party collaborator, this could result in an adverse effect on our business, results of operations or financial condition. Any arrangements we do enter into may not be scientifically or commercially successful. The termination of any of these arrangements might adversely affect our ability to develop, commercialize and market our products.

The success of our collaboration arrangements will depend heavily on the efforts and activities of our collaborators. Our collaborators will have significant discretion in determining the efforts and resources that they will apply to these collaborations. We expect that the risks we face in connection with these future collaborations will include the following:

- our collaboration agreements are expected to be for fixed terms and subject to termination under various circumstances, including, in many cases, on short notice without cause;
- our collaborators may develop and commercialize, either alone or with others, products and services that are similar to or competitive with our products that are the subject of their collaboration with us; and
- our collaborators may change the focus of their commercialization efforts.

In recent years there have been a significant number of mergers and consolidations in the pharmaceutical and biotechnology industries, some of which have resulted in the participant companies reevaluating and shifting the focus of their business following the completion of these transactions. The ability of our products to reach their potential could be limited if any of our future collaborators decreases or fails to increase spending relating to such products.

Collaborations with pharmaceutical companies and other third parties often are terminated or allowed to expire by the other party. With respect to our future collaborations, any such termination or expiration could adversely affect us financially as well as harm our business reputation.

Even after we obtain regulatory approvals of a product, acceptance of the product in the marketplace is uncertain and failure to achieve commercial acceptance will prevent or delay our ability to generate significant revenue from such product.

Even after obtaining regulatory approvals for the sale of our products, the commercial success of these products will depend, among other things, on their acceptance by physicians, patients, third-party payors and other members of the medical community as therapeutic and cost-effective alternatives to competing products and treatments. The degree of market acceptance of any product will depend on a number of factors, including the demonstration of its safety and efficacy, its cost-effectiveness, its potential advantages over other therapies, the reimbursement policies of government and third-party payors with respect to such product, our ability to attract and maintain corporate partners, including pharmaceutical companies, to assist in commercializing our products, receipt of regulatory clearance of marketing claims for the uses that we are developing and the effectiveness of our marketing and distribution capabilities. If our approved products fail to gain market acceptance or do not become widely accepted by physicians, patients, third-party payors and other members of the medical community, it is unlikely that we will ever become profitable on a sustained basis or achieve significant revenues.

We rely and will continue to rely on outsourcing arrangements for many of our activities, including preclinical and clinical development and supply of HETLIOZ®, HETLIOZ LQ™, Fanapt® and our other products.

As of December 31, 2020, we had 292 full-time employees. We rely on outsourcing arrangements for a significant portion of our activities, including distribution, preclinical and clinical research and development, data collection and analysis and manufacturing, as well as for certain functions as a public company. We have limited control over these third parties and we cannot guarantee that they will perform their obligations in an effective and timely manner.

Disruptions to our HETLIOZ®, HETLIOZ LQ™ or Fanapt® supply chains could materially affect our level of success in commercializing HETLIOZ® or Fanapt®, thereby reducing our future earnings and prospects.

A loss or disruption with any one of our manufacturers or suppliers could disrupt the supply of HETLIOZ®, HETLIOZ LQ™ or Fanapt®, possibly for a significant time period, and we may not have sufficient inventories to maintain supply before the manufacturer or supplier could be replaced or the disruption is resolved. In addition, marketed drugs and their contract manufacturing organizations are subject to continual review, including review and approval by regulatory authorities of their manufacturing facilities and the manufacturing processes, which can result in delays in the regulatory approval process and/or commercialization. Introducing a replacement or backup manufacturer or supplier for HETLIOZ®, HETLIOZ LQ™ or Fanapt® requires a lengthy regulatory and commercial process and there can be no guarantee that we could obtain necessary regulatory approvals in a timely fashion or at all. In addition, it is difficult to identify and select qualified suppliers and manufacturers with the necessary technical capabilities, and establishing new supply and manufacturing sources involves a lengthy and technical engineering process.

Failure to comply with government regulations regarding the sale and marketing of our products could harm our business.

In U.S. markets, our ability to commercialize our products successfully, and to attract commercialization partners for our products, should we choose to do so, depends in significant part on the availability of adequate financial coverage and reimbursement from third-party payors, including, in the U.S., governmental payors such as the Medicare and Medicaid programs, managed care organizations, and private health insurers.

We participate in the Medicaid Drug Rebate Program for both HETLIOZ® and Fanapt®. Under the Medicaid Drug Rebate Program, we are required to pay a rebate to each state Medicaid program for our covered outpatient drugs that are dispensed to Medicaid beneficiaries and paid for by a state Medicaid program as a condition of having our drugs eligible for coverage under Medicaid and Medicare Part B. Those rebates are based on pricing data that are reported by us on a monthly and quarterly basis to the Centers for Medicare & Medicaid Services (CMS). Federal law requires that any company that participates in the Medicaid Drug Rebate Program also participate in the Public Health Service Act's 340B drug pricing discount program (340B program), in order for the manufacturer's drugs to be eligible for coverage under Medicaid and Medicare Part B. The 340B program requires participating manufacturers to agree to charge statutorily defined covered entities no more than the 340B "ceiling price" for the manufacturer's covered outpatient drugs. The ceiling price can represent a significant discount and is based on the pricing data reporting to the Medicaid Drug Rebate Program.

The ACA expanded the 340B program to include additional entity types: certain free-standing cancer hospitals, critical access hospitals, rural referral centers and sole community hospitals, each as defined by ACA. The ACA exempts drugs designated under section 526 of the FDC Act as "orphan drugs" from the ceiling price requirements for these newly eligible entities. The ACA also obligates the Health Resources and Services Administration to create regulations and processes to improve the integrity of the 340B program and to update the agreement that manufacturers must sign to participate in the 340B program. A final regulation regarding the calculation of the 340B ceiling price and the imposition of civil monetary penalties on manufacturers that knowingly and intentionally overcharge covered entities became effective on January 1, 2019. Implementation of this final regulation and the issuance of any other final regulations and guidance could affect our obligations under the 340B program in ways we cannot anticipate. In addition, legislation may be introduced that, if passed, would further expand the 340B program to additional covered entities or would require participating manufacturers to agree to provide 340B discounted pricing on drugs used in the inpatient setting.

Federal law also requires that for a drug manufacturer's products to be eligible for coverage under the Medicaid and Medicare Part B programs and to be purchased by certain federal agencies and grantees, the manufacturer must participate in the Department of Veterans Affairs Federal Supply Schedule (FSS), pricing program, established by Section 603 of the Veterans Health Care Act of 1992. Manufacturers that participate in the FSS pricing program must list their covered (innovator and authorized generic) drugs on an FSS contract and charge no more than Federal Ceiling Price (FCP), to the Department of Veterans Affairs, Department of Defense, Public Health Service, and Coast Guard when those agencies purchase from the FSS contract or a depot contract. FCP is calculated based on non-federal average manufacturer price data, which manufacturers must submit quarterly and annually. In addition, because our products are available in the retail and specialty pharmacy setting, we are required to provide rebates to the Department of Defense for prescriptions dispensed to Tricare beneficiaries from Tricare retail network pharmacies under the Tricare Retail Refund Program. To the extent we choose to participate in these government healthcare programs for our current and future products, these and other requirements may affect our ability to profitably sell any product for which we obtain marketing approval.

Pricing and rebate calculations vary among products and programs. The calculations are complex and will often be subject to interpretation by us, governmental or regulatory agencies and the courts. If we become aware that our reporting of pricing data for a prior quarter was incorrect, we will be obligated to resubmit the corrected data. For the Medicaid Drug Rebate Program, corrected data must be submitted for a period not to exceed 12 quarters from the quarter in which the data originally were due. Such restatements and recalculations increase our costs for complying with the laws and regulations governing the Medicaid Drug Rebate Program and other governmental pricing programs. We may be liable for errors associated with our submission of pricing data. If we are found to have knowingly submitted false pricing data to the Medicaid program or the FSS pricing program, we may be liable for civil monetary penalties in the amount of up to $100,000 per item of false information, adjusted for inflation as applicable. Our failure to submit pricing data to the Medicaid program or the FSS pricing program on a timely basis could result in a civil monetary penalty of $10,000 per day for each day the information is late, adjusted for inflation as applicable. Such failure also could be grounds for CMS to terminate our Medicaid drug rebate agreement, which is the agreement under which we would participate in the Medicaid Drug Rebate Program. In the event that CMS terminates our rebate agreement, our products may no longer be eligible for coverage under Medicaid or Medicare Part B. There can be no assurance that our submissions will not be found to be incomplete or incorrect.

Third-party payors decide which drugs they will cover and establish reimbursement and co-pay levels. Third-party payors are increasingly challenging the prices charged for medical products and services and examining their cost effectiveness, in addition to their safety and efficacy. We may need to conduct expensive pharmacoeconomic studies in order to demonstrate the cost effectiveness of our products. Even with such studies, any of our products that are commercialized may be considered less cost-effective than other products, and third-party payors may not provide coverage and reimbursement, in whole or in part, for our products. Third-party payors also are increasingly considering new metrics as the basis for reimbursement rates. It is difficult to project the impact of these evolving reimbursement mechanics on the willingness of payors to cover any of our commercialized products. In addition, we anticipate that a significant portion of our revenue from sales of commercialized products will be obtained through government payors, including Medicare and Medicaid. Any failure to obtain eligibility for coverage under those programs for products we are able to commercialize would have a material adverse effect on revenues and royalties from sales of such products.

Efforts to ensure that our business arrangements with third parties, and our business generally, will comply with applicable healthcare laws and regulations may involve substantial costs. 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, imprisonment, exclusion from government funded healthcare programs, such as Medicare and Medicaid, and the curtailment or restructuring of our operations.

We are subject to ongoing regulatory obligations and oversight of our products, and any failure by us to maintain compliance with applicable regulations may result in adverse consequences including the suspension of the manufacturing, marketing and sale of our respective products, the incurrence of significant additional expense and other limitations on our ability to commercialize our respective products.

We are subject to ongoing regulatory requirements and review, including periodic audits pertaining to the development, manufacture, labeling, packaging, adverse event reporting, distribution, storage, marketing, promotion, record keeping and export of our respective products. Failure to comply with such regulatory requirements or the later discovery of previously unknown problems with the manufacture, distributions and storage of our products, or our third-party contract manufacturing facilities or processes by which we manufacture our products may result in restrictions on our ability to develop, manufacture, market, distribute or sell our products, including potential withdrawal of our products from the market. Any such restrictions could slow or stop production development or result in decreased sales, damage to our reputation or the initiation of lawsuits against us and/or our third-party contract manufacturers. We may also be subject to additional sanctions, including, but not limited, to the following:

- Warning letters, public warnings and untitled letters;
- Court-ordered seizures or injunctions;
- Civil or criminal penalties, or criminal prosecutions;
- Variation, suspension or withdrawal of regulatory approvals for our products;
- Changes to the package insert of our products, such as additional warnings regarding potential side effects or potential limitations on the current dosage or administration;
- Requirements to communicate with physicians and other customers about concerns related to actual or potential safety, efficacy, or other issues involving our products;
- Implementation of risk mitigation programs and post-approval obligations;
- Restrictions on our continued manufacturing, marketing, distribution or sale of our products;
- Temporary or permanent closing of the facilities of our third-party contract manufacturers;
- Interruption or suspension of clinical trials; and
- Refusal by regulators to consider or approve applications for additional indications.

Any of the above sanctions could have a material adverse impact on our revenues or our reputation, and cause us to incur significant additional expenses.

In addition, if our products face any safety or efficacy issues, including drug interaction problems, under the federal Food, Drug & Cosmetic Act, the FDA has broad authority to force us to take any number of actions, including, but not limited to, the following:

- Requiring us to conduct post-approval clinical studies to assess product efficacy or known risks or new signals of serious risks, or to evaluate unexpected serious risks;
- Mandating changes to a product's label;
- Requiring us to implement a risk evaluation and mitigation strategy where necessary to assure safe use of the drug; or
- Removing an already approved product from the market.

Further, our partners, including our licensors, are subject to similar requirements and obligations as well as the attendant risks and uncertainties. If our partners, including our licensors, suffer material and adverse effects from such risks and uncertainties, our rights and benefits for our licensed products could be negatively impacted, which could have a material adverse effect on our business.

If our products are marketed or distributed in a manner that violates federal or state healthcare fraud and abuse laws, marketing disclosure laws or other federal or state laws and regulations, we may be subject to civil or criminal penalties.

In addition to FDA and related regulatory requirements, our general operations, and the research, development, manufacture, sale and marketing of our products, are subject to extensive additional federal and state healthcare regulation, including the federal Anti-Kickback Statute, the Prescription Drug Marketing Act, and the federal False Claims Act (FCA), the

federal Health Insurance Portability and Accountability Act of 1996, the federal Physician Payment Sunshine Act and the Foreign Corrupt Practices Act (and their state analogues), as discussed above in Part I, Item 1 under the heading *Government Regulation - Fraud and abuse laws and other U.S. regulatory matters*. If we or our partners, such as licensors, fail to comply with any federal and state laws or regulations governing our industry, we could be subject to administrative, criminal and civil penalties and a range of regulatory actions that could adversely affect our ability to commercialize our products, harm or prevent sales of our products, or substantially increase the costs and expenses of commercializing and marketing our products, all of which could have a material adverse effect on our business, financial condition and results of operations. In recent years, CMS has been actively proposing and implementing changes to the list of business practices that are protected by safe harbors. There is inherent risk and uncertainty in any changing regulatory environment as companies work to transition business practices to conform with new regulations.

Our activities relating to the sale and marketing of our products may be subject to scrutiny under these laws, and private individuals have been active in bringing so-called "whistleblower" lawsuits on behalf of the government (as Relators) under the FCA and similar regulations in other countries. In addition, incentives exist under applicable U.S. law that encourage employees and physicians to report violations of rules governing promotional activities for pharmaceutical products. These incentives have led to, and could continue to lead to, FCA lawsuits, which attempt to recoup moneys paid by government agencies and extract penalties from manufacturers. For example, federal enforcement agencies have recently pursued enforcement actions against pharmaceutical companies' product and patient assistance programs, including relationships with specialty pharmacies, and support for charitable foundations providing patients with co-pay assistance. In addition, Relators have filed lawsuits involving manufacturer reimbursement support services as well as promotion of pharmaceutical products beyond labeled claims. Some FCA lawsuits have resulted in government enforcement authorities obtaining significant civil and criminal settlements. Such lawsuits, whether with or without merit, are typically time-consuming and costly to defend. Such suits may also result in related shareholder lawsuits, which are also costly to defend. (See Note 17, *Legal Matters*, to the consolidated financial statements in Part II, Item 8 of this Annual Report, which is incorporated herein by reference, for information regarding ongoing litigation related to similar matters.)

Further, the FDA and other regulatory agencies strictly regulate the promotional claims that may be made about prescription products. A product may not be promoted for uses that are not approved by the FDA as reflected in the product's approved labeling. The FDA also regulates the content of promotional material, including, among other things, the presentation of efficacy information, the types of comparative claims that can be made to distinguish products from those with similar indications, and the balance of risk information provided. For drug products that are approved by the FDA under the FDA's accelerated approval regulations, unless otherwise informed by the FDA, the sponsor must submit promotional materials at least 30 days prior to the intended time of initial dissemination of the promotional materials, which delays and may negatively impact a company's ability to implement changes to its marketing materials, thereby negatively impacting revenues. For other products, the FDA does not review promotional materials prior to dissemination but does issue "Untitled Letters" or "Warning Letters" if it objects to content that has been used promotionally. The FDA may also withdraw approval of drug products under certain conditions. In particular, the FDA may withdraw approval of a drug if, among other things, the promotional materials are false or misleading, or other evidence demonstrates that the drug is not shown to be safe or effective under its conditions of use.

In recent years, in addition to federal legislation related to transparency reporting of transfers of value to healthcare providers and healthcare organizations, several states have enacted legislation requiring pharmaceutical companies to file periodic reports. Several states have adopted legislation to require pharmaceutical companies to establish marketing and promotional compliance programs or codes of conduct and/or to file periodic reports with the state or make periodic public disclosures on sales, marketing, pricing, clinical trials, and other activities. Several states have also adopted laws that prohibit certain marketing-related activities, including the provision of gifts, meals or other items to certain healthcare providers.

We have developed and implemented a corporate compliance program based on what we believe are current best practices in the pharmaceutical industry; however, relevant compliance laws are broad in scope and there may not be regulations, guidance or court decisions that definitively interpret these laws in the context of particular industry practices. We cannot guarantee that we, our employees, our partners, our consultants or our contractors are or will be in compliance with all federal and state regulations. If we, our partners, or our representatives fail to comply with any of these laws or regulations, a range of fines, penalties and/or other sanctions and regulatory actions could be imposed on us, including, but not limited to, restrictions on how we market and sell our products, significant fines, exclusions from government healthcare programs, including Medicare and Medicaid, litigation, or other sanctions. Even if we are not determined to have violated these laws, government investigations into these issues typically require the expenditure of significant resources and generate negative publicity, which could also have a material adverse effect on our business, financial condition and results of operations. Such investigations or suits have resulted in, and may continue to result in, related shareholder lawsuits, which can also have a material adverse effect on our business.

Our partners, including our licensors, are subject to similar requirements and obligations as well as the attendant risks and uncertainties. If our partners, including our licensors, suffer material and adverse effects from such risks and uncertainties, our rights and benefits for our licensed products could be negatively impacted, which could have a material adverse effect on our business.

We rely on a limited number of specialty pharmacies for distribution of HETLIOZ® in the U.S., and the loss of one or more of these specialty pharmacies or their failure to distribute HETLIOZ® effectively would materially harm our business.

HETLIOZ® is available for distribution through a limited number of specialty pharmacies in the U.S. A specialty pharmacy is a pharmacy that specializes in the dispensing of medications for complex or chronic conditions, which often require a high level of patient education and ongoing management. The use of specialty pharmacies involves certain risks, including, but not limited to, risks that these specialty pharmacies will:

- not provide us accurate or timely information regarding their inventories, the number of patients who are using HETLIOZ® or complaints about HETLIOZ®;
- reduce their efforts or discontinue to sell or support or otherwise not effectively sell or support HETLIOZ®;
- not devote the resources necessary to sell HETLIOZ® in the volumes and within the time frames that we expect;
- be unable to satisfy financial obligations to us or others; or
- cease operations.

In addition, if one or more of our specialty pharmacies do not fulfill their contractual obligations to us, or refuse or fail to adequately serve patients, or their agreements are terminated without adequate notice, shipments of HETLIOZ®, and associated revenues, would be adversely affected. We expect that it would take a significant amount of time if we were required to replace one or more of our specialty pharmacies.

Our revenues from Fanapt® are substantially dependent on sales through a limited number of wholesalers, and such revenues may fluctuate from quarter to quarter.

We sell Fanapt® primarily through a limited number of pharmaceutical wholesalers in the U.S. The use of pharmaceutical wholesalers involves certain risks, including, but not limited to, risks that these pharmaceutical wholesalers will:

- not provide us accurate or timely information regarding their inventories, demand from wholesaler customers buying Fanapt® or complaints about Fanapt®;
- reduce their efforts or discontinue to sell or support or otherwise not effectively sell or support Fanapt®;
- not devote the resources necessary to sell Fanapt® in the volumes and within the time frames that we expect;
- be unable to satisfy financial obligations to us or others; or
- cease operations.

Additionally, our reliance on a small number of wholesalers could cause revenues to fluctuate from quarter to quarter based on the buying patterns of these wholesalers. In addition, if any of these wholesalers fails to pay on a timely basis or at all, our business, financial condition and results of operations could be materially adversely affected.

We face substantial competition, which may result in others developing or commercializing products before or more successfully than we do.

Our future success will depend on our ability to demonstrate and maintain a competitive advantage with respect to our products and our ability to identify and develop additional products. Large, fully integrated pharmaceutical companies, either alone or together with collaborative partners, have substantially greater financial resources and have significantly greater experience than we do in:

- developing products;
- undertaking preclinical testing and clinical trials;
- obtaining FDA and other regulatory approvals of products; and

- manufacturing, marketing and selling products.

These companies may invest heavily and quickly to discover and develop novel products that could make our products obsolete. Accordingly, our competitors may succeed in obtaining patent protection, receiving FDA or foreign regulatory approval or commercializing superior products or other competing products before we do. Technological developments or the FDA or foreign regulatory approval of new therapeutic indications for existing products may make our products obsolete or may make them more difficult to market successfully, any of which could have a material adverse effect on our business, results of operations and financial condition.

Our products, if successfully developed and approved for commercial sale, will compete with a number of drugs and therapies currently manufactured and marketed by major pharmaceutical and other biotechnology companies. Our products may also compete with new products currently under development by others or with products that may cost less than our products. Physicians, patients, third-party payors and the medical community may not accept or utilize any of our products that may be approved. If HETLIOZ®, Fanapt® and our other products, if and when approved, do not achieve significant market acceptance, our business, results of operations and financial condition would be materially adversely affected. (See Part I, Item 1, *Business – Competition,* for a discussion of the primary competitors for HETLIOZ® and Fanapt®.)

Additionally, we may face competition from newly developed generic products. Under the Hatch-Waxman Act, newly approved drugs and indications may benefit from a statutory period of non-patent marketing exclusivity. The Hatch-Waxman Act seeks to stimulate competition by providing incentives to generic pharmaceutical manufacturers to introduce non-infringing forms of patented pharmaceutical products and to challenge patents on branded pharmaceutical products. If we are unsuccessful at challenging an ANDA, filed pursuant to the Hatch-Waxman Act, cheaper generic versions of our products, which may be favored by insurers and third-party payors, may be launched commercially, which would significantly harm our business.

To obtain an ANDA approval for a generic drug, the generic company needs to show, among other things, that its version of the product is bioequivalent to the Reference Listed Drug (RLD). This usually requires the generic company to conduct bioequivalence studies comparing its product to the RLD, and to retain sufficient samples of the RLD used in testing after a study is complete. In recent years, the U.S. federal lawmakers and the FDA have been considering proposals to facilitate the generic drug company's access to samples and foster the generic competition. For example, in February 2019, the U.S. House and Senate lawmakers reintroduced the Creating and Restoring Equal Access to Equivalent Samples Act (CREATES Act), a bill intended to require brand drug manufacturers to provide sufficient drug samples to generic and biosimilar drug developers. The proposed legislation, if enacted, would allow a biosimilar or generic product developer to bring a civil action against a brand drug manufacturer for failing to provide samples of the brand product for comparative testing "on commercially reasonable, market-based terms." The developer could receive injunctive relief and a monetary award "sufficient to deter the license holder from failing to provide other eligible product developers with sufficient quantities of a covered product on commercially reasonable, market-based terms" in certain cases.

Certain states have also taken similar actions. In 2018, Maine passed a new law that requires brand drug manufacturers to make samples of drugs distributed in the state available for sale in Maine at a price no greater than wholesale acquisition cost and without any restriction that would block or delay a biosimilar and generic drug application in a manner inconsistent with federal law. The state may seek injunctive relief and attorney's fees from a drug manufacturer who fails to comply with this requirement.

FDA and foreign regulatory approval of our products is uncertain.

The research, testing, manufacturing and marketing of products such as those that we have developed or that we are developing are subject to extensive regulation by federal, state and local government authorities, including the FDA, as well as foreign regulatory authorities in jurisdictions in which we seek approval. To obtain regulatory approval of such products, we must demonstrate to the satisfaction of the applicable regulatory agency that, among other things, the product is safe and effective for its intended use. In addition, we must show that the manufacturing facilities used to produce such products are in compliance with cGMPs.

The process of obtaining FDA and other required regulatory approvals and clearances can take many years and will require us to expend substantial time and capital. Despite the time and expense expended, regulatory approval is never guaranteed. The number of preclinical and clinical trials that will be required for FDA or foreign regulatory approval varies depending on the product, the disease or condition that the product is in development for, and the requirements applicable to that particular product. The FDA or applicable foreign regulatory agency can delay, limit or deny approval of a product for many reasons, including that:

- a product may not be shown to be safe or effective;
- the FDA or foreign agency may interpret data from preclinical and clinical trials in different ways than we do;
- the FDA or foreign agency may not approve our or our partners' manufacturing processes or facilities;
- a product may not be approved for all the indications we request;
- the FDA or foreign agency may change its approval policies or adopt new regulations;
- the FDA or foreign agency may not meet, or may extend, the PDUFA-VI date or its foreign equivalent with respect to a particular NDA or foreign application; and
- the FDA or foreign agency may not agree with our regulatory approval strategies or components of the regulatory filings, such as clinical trial designs.

For example, if certain of our methods for analyzing trial data are not accepted by the FDA or the applicable foreign agency, we may fail to obtain regulatory approval for our products.

Additionally, the approval procedure varies among countries and jurisdictions and can involve additional trials, and the time required to obtain approval may differ from that required to obtain FDA approval. Approval by the FDA does not ensure approval by regulatory authorities in other countries or jurisdictions, and approval by one foreign regulatory authority does not ensure approval by regulatory authorities in other foreign countries or jurisdictions or by the FDA.

Any delay or failure to obtain regulatory approvals for our products will result in increased costs, could diminish competitive advantages that we may attain and would adversely affect the marketing and sale of our products. Other than HETLIOZ® in the U.S. and the countries in Europe covered by the centralized marketing authorization by the EC, and Fanapt® in the U.S., Mexico and Israel, we have not received, and may never receive, regulatory approval to market any of our products in any jurisdiction.

Even following regulatory approval of our products, the FDA or the applicable foreign agency may impose limitations on the indicated uses for which such products may be marketed, subsequently withdraw approval or take other actions against us, or such products that are adverse to our business. The FDA and foreign agencies generally approve drugs for particular indications. An approval for a more limited indication reduces the size of the potential market for the product. Product approvals, once granted, may be withdrawn or modified if problems occur after initial marketing.

We and our partners also are subject to numerous federal, state, local and foreign laws, regulations and recommendations relating to safe working conditions, laboratory and manufacturing practices, the environment and the use and disposal of hazardous substances used in connection with discovery, research and development work. In addition, we cannot predict the extent to which new governmental regulations might significantly impede the discovery, development, production and marketing of our products. We or our partners may be required to incur significant costs to comply with current or future laws or regulations, and we may be adversely affected by the cost of such compliance or the inability to comply with such laws or regulations.

Our products may cause undesirable side effects or have other properties that could delay, prevent or result in the revocation of their regulatory approval or limit their marketability.

Undesirable side effects caused by our products could interrupt, delay or halt clinical trials and could result in the denial of regulatory approval by the FDA or other regulatory authorities for any or all targeted indications, and in turn prevent us from commercializing or continuing the commercialization of such products and generating revenues from their sale. We will continue to assess the side effect profile of our products in ongoing clinical development programs. However, we cannot predict whether the commercial use of our approved products (or our products in development, if and when they are approved for commercial use) will produce undesirable or unintended side effects that have not been evident in the use of, or in clinical trials conducted for, such products to date. For example, despite the positive results of our completed trials for HETLIOZ® and Fanapt®, as well as the FDA's approval of the NDA for HETLIOZ® for the treatment of Non-24 in January 2014, the NDA for Fanapt® for the treatment of schizophrenia in May 2009, the EC's grant of the centralized marketing authorization for HETLIOZ® for the treatment of Non-24 in totally blind adults in July 2015, and the NDA and sNDA for HETLIOZ® for the treatment of nighttime sleep disturbances in SMS in December 2020, we are uncertain whether either of these products will ultimately prove to be effective and safe in humans long term and in all uses. Frequently, products that have shown promising results in clinical trials have suffered significant setbacks in later clinical trials or even long after they are approved for commercial sale. Additionally, incidents of product misuse may occur. These events, among others, could result in product

recalls, product liability actions or withdrawals or additional regulatory controls, any of which could have a material adverse effect on our business, results of operations and financial condition.

In addition, if after receiving marketing approval of a product, we or others identify undesirable side effects caused by such product, we could face one or more of the following:

- regulatory authorities may require the addition of labeling statements, such as a "black box" warning or a contraindication;
- regulatory authorities may withdraw their approval of the product;
- we may be required to change the way the product is administered, conduct additional clinical trials or change the labeling of the product; and
- our or the product's reputation may suffer.

Any of these events could prevent us from achieving or maintaining market acceptance of the affected product or could substantially increase the costs and expenses of commercializing the product, which in turn could delay or prevent us from generating significant revenues from its sale.

Clinical trials for our products are expensive and their outcomes are uncertain. Any failure or delay in completing clinical trials for our products could severely harm our business.

Preclinical studies and clinical trials required to demonstrate the safety and efficacy of our products are time-consuming and expensive and together take several years to complete. Before obtaining regulatory approvals for the commercial sale of any of our products, we must demonstrate through preclinical testing and clinical trials that such product is safe and effective for use in humans. We have incurred, and we will continue to incur, substantial expense for, and devote a significant amount of time to, preclinical testing and clinical trials.

Historically, the results from preclinical testing and early clinical trials often have not predicted results of later clinical trials. A number of new drugs have shown promising results in clinical trials, but subsequently failed to establish sufficient safety and efficacy data to obtain necessary regulatory approvals. Clinical trials conducted by us or by third parties on our behalf may not demonstrate sufficient safety and efficacy to obtain the requisite regulatory approvals for our products. Regulatory authorities may not permit us to undertake any additional clinical trials for our products, may force us to stop any ongoing clinical trials and it may be difficult to design efficacy studies for our products in new indications.

Clinical development efforts performed by us may not be successfully completed or completed in a timely manner. Completion of clinical trials may take several years or more. The length of time can vary substantially with the type, complexity, novelty and intended use of the products and the size of the prospective patient population. Our ability to enroll patients in, and the commencement and rate of completion of, clinical trials for our products may be affected by many factors, including:

- the impact of global health crises, like the COVID-19 pandemic;
- the size and nature of the patient population;
- the design of the trial protocol for our clinical trials;
- the eligibility and exclusion criteria for the trial in question;
- the availability of competing therapies and competing clinical trials, and physician and patient perception of our product candidates and our other product candidates being studied in relation to these other potential options;
- the availability of raw materials and the possibility of raw materials expiring prior to their use;
- difficulty in maintaining contact with patients after treatment, resulting in incomplete data;
- poor effectiveness of our products during clinical trials;
- unforeseen safety issues or side effects;
- the number and location of clinical sites in our clinical trials;
- the proximity and availability of clinical trial sites for prospective patients;
- the availability of time and resources at the institutions where clinical trials are and will be conducted;

- the availability of adequate financing to fund ongoing clinical trial expenses;
- the study endpoints that rely on subjective patient reported outcomes; and
- governmental or regulatory delays and changes in regulatory requirements and guidelines.

If we fail to complete successfully, or have difficulty enrolling a sufficient number of patients for, our clinical trials, we or they may not receive the regulatory approvals needed to market that product. Any such failure or difficulty could have a material adverse effect on our business.

We may not be able to achieve sustained profitability.

We have been engaged in identifying and developing drug products since March 2003, which has required, and will continue to require, significant research and development expenditures. The continued commercialization of HETLIOZ® and Fanapt® will also require substantial additional expenditures.

As of December 31, 2020, we had an accumulated deficit of $197.3 million and we cannot estimate with precision the extent of our future income or loss. We may not succeed in gaining additional market acceptance of HETLIOZ® and Fanapt® in the U.S. and we may not succeed in commercializing HETLIOZ® or Fanapt® outside of the U.S. We may be unable to fully develop, obtain regulatory approval for, commercialize, manufacture, market, sell and derive revenue from our products in the timeframes we project, if at all, and our inability to do so would materially and adversely impact the market price of our common stock and our ability to raise capital and continue operations.

There can be no assurance that we will achieve sustained profitability, which depends on many factors, including but not limited to, our ability to obtain regulatory approval for our products and achieve success in commercializing them in the U.S., Europe and our other target jurisdictions, as well as other factors described in this Annual Report.

In addition, the amount we spend on developing, obtaining and maintaining regulatory approval for and commercializing our products, among other expenditures described in this Annual Report, will impact our profitability.

Our ability to use net operating loss carryforwards and tax credit carryforwards to offset future taxable income is dependent on generating future taxable income and may be limited, including as a result of transactions involving our common stock.

We have recorded deferred tax assets based on our assessment that we will be able to realize the benefits of our net operating losses and other favorable tax attributes. Realization of deferred tax assets involve significant judgments and estimates, which are subject to change and ultimately depends on generating sufficient taxable income of the appropriate character during the appropriate periods. Changes in circumstances may affect the likelihood of such realization, which in turn may trigger the need for additional valuation allowance against our deferred tax assets and adversely affect our net income and financial condition. In addition, we are potentially subject to ongoing and periodic tax examinations and audits in various jurisdictions, including with respect to the amount of our net operating losses and any limitation thereon. An adjustment to such net operating loss carryforwards, including an adjustment from a taxing authority, could result in higher tax costs, penalties and interest, thereby adversely impacting our financial condition.

In general, under Section 382 of the Internal Revenue Code of 1986, as amended (IRC), a corporation that undergoes an “ownership change” is subject to limitations on its ability to utilize its pre-change net operating losses (NOLs) and certain other tax assets (tax attributes) to offset future taxable income. In general, an ownership change occurs if the aggregate stock ownership of certain stockholders increases by more than 50 percentage points over such stockholders’ lowest percentage ownership during the testing period (generally three years). Transactions involving our common stock, even those outside our control, such as purchases or sales by investors, within the testing period could result in an ownership change. A limitation on our ability to utilize some or all of our NOLs or credits could have a material adverse effect on our results of operations and cash flows. Ownership changes occurred in the years ending December 31, 2014 and 2008. We believe that the ownership changes in 2014 and 2008 will not impact our ability to utilize NOL and credit carryforwards; however, future ownership changes may cause our existing tax attributes to have additional limitations.

If we fail to adequately fund our research and development activities and commercialization efforts, we may be unable to continue operations or we may be forced to share our rights to commercialize our products with third parties on terms that may not be attractive to us.

Our activities will necessitate significant uses of working capital throughout 2021 and beyond. It is uncertain whether cash provided by our operating activities, together with our existing funds, will be sufficient to meet our operating needs. As of December 31, 2020, our total cash and cash equivalents and marketable securities were $367.7 million. Our long-term capital requirements are expected to depend on many factors, including, among others:

- our level of success in commercializing HETLIOZ® and Fanapt® globally;
- outcomes of ongoing and potential patent litigation;
- costs of developing and maintaining sales, marketing and distribution channels and our ability to sell our products;
- market acceptance of our products;
- costs involved in establishing and maintaining manufacturing capabilities for commercial quantities of our products;
- the number of potential formulations and products in development;
- progress with preclinical studies and clinical trials;
- time and costs involved in obtaining regulatory (including FDA) approval;
- costs involved in preparing, filing, prosecuting, maintaining and enforcing patent, trademark and other intellectual property claims;
- competing technological and market developments;
- costs for recruiting and retaining employees and consultants;
- costs for training physicians; and
- legal, accounting, insurance and other professional and business-related costs.

As a result, we may need to raise additional capital to fund our anticipated operating expenses and execute on our business plans. In our capital-raising efforts, we may seek to sell debt securities or additional equity securities, obtain a bank credit facility, or enter into partnerships or other collaboration agreements. The sale of additional equity or debt securities, if convertible, could result in dilution to our stockholders and may also result in a lower price for our common stock. The incurrence of indebtedness would result in increased fixed obligations and could also result in covenants that could restrict our operations. However, we may not be able to raise additional funds on acceptable terms, or at all. If additional financing is not available when required or is not available on acceptable terms, we may be unable to fund our operations and planned growth, develop or enhance our technologies or products, take advantage of business opportunities or respond to competitive market pressures, any of which would materially harm our business, financial condition and results of operations.

If our contract research organizations (CROs) do not successfully carry out their duties or if we lose our relationships with CROs, our drug development efforts could be delayed.

Our arrangements with CROs are critical to our success in bringing our products to the market. We are dependent on CROs, third-party vendors and investigators for preclinical testing and clinical trials related to our drug discovery and development efforts and we will likely continue to depend on them to assist in our future discovery and development efforts. These parties are not our employees and we cannot control the amount or timing of resources that they devote to our programs. As such, they may not complete activities on schedule or may not conduct our clinical trials in accordance with regulatory requirements or our stated protocols. The parties with which we contract for execution of our clinical trials play a significant role in the conduct of the trials and the subsequent collection and analysis of data. If they fail to devote sufficient time and resources to our drug development programs or if their performance is substandard, it will delay the development, approval and commercialization of our products. Moreover, these parties may also have relationships with other commercial entities, some of which may compete with us. If they assist our competitors, it could harm our competitive position.

Our CROs could merge with or be acquired by other companies or experience financial or other setbacks unrelated to our collaboration that could, nevertheless, materially adversely affect our business, results of operations and financial condition.

If we lose our relationship with any one or more of these parties, we could experience a significant delay in both identifying another comparable provider and then contracting for its services. We may be unable to retain an alternative provider on reasonable terms, if at all. Even if we locate an alternative provider, it is likely that this provider may need additional time to respond to our needs and may not provide the same type or level of service as the original provider. In addition, any provider that we retain will be subject to current Good Laboratory Practices as set forth in 21 Code of Federal

Regulations (C.F.R.) Part 58 and Good Clinical Practices as set forth in 21 C.F.R. Part 50, 54, and 312, and similar international standards and we do not have control over compliance with these regulations by these providers. Consequently, if these practices and standards are not adhered to by these providers, the development and commercialization of our products could be delayed.

We rely on a limited number of third-party manufacturers to formulate and manufacture our products and our business will be seriously harmed if these manufacturers are not able to satisfy our demand and alternative sources are not available.

We do not have an in-house manufacturing capability and depend completely on a small number of third-party manufacturers and active pharmaceutical ingredient formulators for the manufacture of our products. Therefore, we are dependent on third parties for our formulation development and manufacturing of our products. This may expose us to the risk of not being able to directly oversee the production and quality of the manufacturing process and provide ample commercial supplies to successfully launch and maintain the marketing of our products. Furthermore, these third-party contractors, whether foreign or domestic, may experience regulatory compliance difficulty, mechanical shut downs, employee strikes, or other unforeseeable events that may delay or limit production. Our inability to adequately establish, supervise and conduct (either ourselves or through third parties) all aspects of the formulation and manufacturing processes would have a material adverse effect on our ability to develop and commercialize our products.

We have agreements in place with Patheon Pharmaceuticals Inc. and Patheon Inc. (collectively, Patheon), subsidiaries of Thermo Fisher Scientific, for the manufacture of HETLIOZ® and Fanapt®. In January 2014, we entered into a manufacturing agreement with Patheon for the manufacture of commercial supplies of HETLIOZ® 20 mg capsules at Patheon's Cincinnati, Ohio manufacturing site. In May 2016, we entered into a manufacturing agreement with Patheon for the manufacture of commercial supplies of Fanapt® tablets at Patheon's Mississauga, Ontario, Canada manufacturing site. Additionally, in December 2020, we entered into a non-exclusive third-party manufacturing agreement for the manufacture of commercial supplies of HETLIOZ LQ™. We do not have exclusive long-term agreements with any other third-party manufacturers of our products. If our current manufacturers, or any other third-party manufacturer, is unable or unwilling to perform its obligations under our manufacturing agreements for any reason, we may not be able to locate alternative acceptable manufacturers or formulators or enter into favorable agreements with them. Any inability to acquire sufficient quantities of our products in a timely manner from these third parties could adversely affect sales of our products, delay clinical trials and prevent us from developing our products in a cost-effective manner or on a timely basis. In addition, manufacturers of our products are subject to cGMP and similar foreign standards and we do not have control over compliance with these regulations by our manufacturers. If one of our contract manufacturers fails to maintain compliance, the production of our products could be interrupted, resulting in delays and additional costs. In addition, if the facilities of such manufacturers do not pass a pre-approval or post-approval plant inspection, the FDA will not grant approval and may institute restrictions on the marketing or sale of our products.

Our manufacturing strategy presents the following additional risks:

- because most of our third-party manufacturers and formulators are located outside of the U.S., there may be difficulties in importing our products or their components into the U.S. as a result of, among other things, FDA import inspections, incomplete or inaccurate import documentation or defective packaging; and
- because of the complex nature of our products, our manufacturers may not be able to successfully manufacture our products in a cost-effective and/or timely manner.

Materials necessary to manufacture our products may not be available on commercially reasonable terms, or at all, which may delay the development, regulatory approval and commercialization of our products.

We rely on manufacturers to purchase from third-party suppliers the materials necessary to produce our products for clinical trials and commercialization. Suppliers may not sell these materials to such manufacturers at the times we need them or on commercially reasonable terms. We do not have any control over the process or timing of the acquisition of these materials by these manufacturers. Moreover, we currently do not have any agreements for the commercial production of these materials. If the manufacturers are unable to obtain these materials for our clinical trials, product testing, potential regulatory approval of our products and commercial scale manufacturing could be delayed, significantly affecting our ability to further develop and commercialize our products. If we or our manufacturers are unable to purchase these materials for our products, there would be a shortage in supply or the commercial launch of such products would be delayed, which would materially and adversely affect our ability to generate revenues from the sale of such products.

If we cannot identify, or enter into licensing arrangements for, new products, our ability to develop a diverse product portfolio will be limited.

A component of our business strategy is acquiring rights to develop and commercialize products discovered or developed by other pharmaceutical and biotechnology companies for which we may find effective uses and markets through our unique pharmacogenetics and pharmacogenomics expertise for the treatment of central nervous system disorders. Competition for the acquisition of these products is intense. If we are not able to identify opportunities to acquire rights to commercialize additional products, we may not be able to develop a diverse portfolio of products. Additionally, it may take substantial human and financial resources to secure commercial rights to promising products. Moreover, if other firms develop pharmacogenetics and pharmacogenomics capabilities, we may face increased competition in identifying and acquiring additional products.

If we lose key scientists or management personnel, or if we fail to recruit additional highly skilled personnel, our ability to identify, develop, and commercialize new products will be impaired.

We are highly dependent on principal members of our management team and scientific staff, including our Chief Executive Officer, Mihael H. Polymeropoulos, M.D. These executives each have significant pharmaceutical industry experience. The loss of any such executives, including Dr. Polymeropoulos, or any other principal member of our management team or scientific staff, would impair our ability to identify, develop and market new products. Our management and other employees may voluntarily terminate their employment with us at any time. The loss of the services of these or other key personnel, or the inability to attract and retain additional qualified personnel, could result in delays to development or approval, loss of sales and diversion of management resources. In addition, we depend on our ability to attract and retain other highly skilled personnel, including research scientists. Competition for qualified personnel is intense, and the process of hiring and integrating such qualified personnel is often lengthy. We may be unable to recruit such personnel on a timely basis, if at all, which would negatively impact our development and commercialization programs.

Additionally, we do not currently maintain “key person” life insurance on the lives of our executives or any of our employees. This lack of insurance means that we may not have adequate compensation for the loss of the services of these individuals.

Product liability lawsuits could divert our resources, result in substantial liabilities and reduce the commercial potential of our products.

The risk that we may be sued on product liability claims is inherent in the development and sale of pharmaceutical products. For example, we face a risk of product liability exposure related to the testing of our products in clinical trials and will face even greater risks upon commercialization of our products. We believe that we may be at a greater risk of product liability claims relative to other pharmaceutical companies because certain of our products are intended to treat central nervous system disorders, among others, and it is possible that we may be held liable for the behavior and actions of patients who use our products. These lawsuits may divert our management from pursuing our business strategy and may be costly to defend. In addition, if we are held liable in any of these lawsuits, we may incur substantial liabilities and we may be forced to limit or forego further commercialization of one or more of our products. Although we maintain product liability insurance, our aggregate coverage limit under this insurance is $30.0 million, and while we believe this amount of insurance is sufficient to cover our product liability exposure, these limits may not be high enough to fully cover potential liabilities. As our development activities and commercialization efforts progress and we sell our products, this coverage may be inadequate, we may be unable to obtain adequate coverage at an acceptable cost or we may be unable to get adequate coverage at all or our insurer may disclaim coverage as to a future claim. This could prevent the commercialization or limit the commercial potential of our products. Even if we are able to maintain insurance that we believe is adequate, our results of operations and financial condition may be materially adversely affected by a product liability claim. Uncertainties resulting from the initiation and continuation of products liability litigation or other proceedings could have a material adverse effect on our ability to compete in the marketplace. Product liability litigation and other related proceedings may also require significant management time.

E.U. Member States tend to impose strict price controls, which may delay or prevent the further commercial launch or impede the commercial success of HETLIOZ® in Europe and adversely affect our future results of operations.

In the E.U., prescription drug pricing and reimbursement are subject to governmental control and reimbursement mechanisms used by private and public health insurers in the E.U. vary by Member State. For the public systems, reimbursement is determined by guidelines established by the legislature or responsible national authority. As elsewhere, inclusion in reimbursement catalogues focuses on the medical usefulness, need, quality and economic benefits to patients and the health care system. Acceptance for reimbursement comes with cost, use and often volume restrictions, which can vary by

Member State. Although we have received marketing authorization for HETLIOZ® capsules from the EC, pricing negotiations with governmental authorities may take a considerable amount of time in those Member States that impose price controls. For example, we launched HETLIOZ® commercially in Germany in August 2016, and concluded our pricing negotiations with German authorities in October 2017. In addition, to obtain reimbursement or pricing approval for HETLIOZ® in some Member States, we may be required to conduct a clinical trial that compares the cost-effectiveness of HETLIOZ®, to other available therapies.

Some Member States require approval of the sale price of a drug before it can be marketed. In many countries, the pricing review period begins after marketing or product licensing approval is granted. In some Member States, prescription pharmaceutical pricing remains subject to continuing governmental control even after initial approval is granted. As a result, we may be subject to lengthy price regulations that delay or prevent the commercial launch of HETLIOZ® in a particular Member State and negatively impact the revenues that are generated from the sale of HETLIOZ® in that country. If reimbursement of HETLIOZ® is unavailable or limited in scope or amount, or if pricing for HETLIOZ® is set at unsatisfactory levels or takes too long to establish, or if there is competition from lower priced cross-border sales, our results of operations will be negatively affected.

We may not be able to effectively market and sell our future products, if approved, in the U.S.

We plan to continue to build our sales and marketing capabilities in the U.S. to commercialize future products, if approved. Our current sales and marketing capabilities in the U.S. may not be adequate to support the commercialization of future products and we would expect to build such capabilities by investing significant amounts of financial and management resources. Furthermore, the cost of establishing and maintaining marketing and sales capabilities may not be justifiable in light of the revenues generated by any future products.

If we are unable to establish and maintain adequate sales and marketing capabilities for future products or are unable to do so in a timely manner, we may not be able to generate product revenues from these products, which may prevent us from reaching or maintaining profitability.

Healthcare legislative reform measures or developments arising from changes in the political climate may have a material adverse effect on our business and results of operations.

In the U.S., there have been and continue to be a number of legislative initiatives to contain healthcare costs. For example, in March 2010, the ACA was passed, which substantially changes the way healthcare is financed by both governmental and private insurers, and significantly impacts the U.S. pharmaceutical industry. The ACA, among other things, increases the minimum Medicaid rebates owed by manufacturers under the Medicaid Drug Rebate Program and extends the rebate program to individuals enrolled in Medicaid managed care organizations, establishes annual fees and taxes on manufacturers of certain branded prescription drugs, and creates a new Medicare Part D coverage gap discount program, in which manufacturers must agree to offer 70% point-of-sale discounts off negotiated prices of applicable brand drugs to eligible beneficiaries during their coverage gap period, as a condition for the manufacturer's outpatient drugs to be covered under Medicare Part D.

Some of the provisions of the ACA have yet to be fully implemented, while certain provisions have been subject to judicial and Congressional challenges, as well as efforts by the former Trump administration to repeal or replace certain aspects of the ACA. While Congress has not passed comprehensive repeal legislation, it has enacted laws that modify certain provisions of the ACA such as removing or delaying penalties, starting January 1, 2019, for not complying with the ACA's individual mandate to carry health insurance, delaying the implementation of certain ACA-mandated fees, and increasing the point-of-sale discount that is owed by pharmaceutical manufacturers who participate in Medicare Part D. Further, in December 2018, a Texas District Court judge ruled that the ACA is unconstitutional in its entirety because the individual mandate was repealed by Congress. Further, in December 2019, the U.S. Court of Appeals for the 5th Circuit upheld the Texas District Court ruling that the individual mandate was unconstitutional and remanded the case back to the Texas District Court to determine whether the remaining provisions of the ACA are invalid as well. In March 2020, the U.S. Supreme Court granted the petitions for writs of certiorari and held oral arguments in November 2020. Accordingly, we continue to evaluate the effect that the ACA has on our business. At the federal level, the former Trump administration supported legislative proposals and issued certain Executive Orders seeking to reduce drug prices, increase competition, lower out-of-pocket drug costs for patients, and increase patient access to lower-cost generic and biosimilar drugs. The Department of Health and Human Services (HHS), has solicited feedback on some of these measures and implemented others under its existing authority. The FDA also released a final rule in September 2020 providing guidance for states to build and submit importation plans for drugs from Canada. Further, in November 2020, HHS finalized a regulation removing safe harbor protection for price reductions from pharmaceutical manufacturers to plan sponsors under Medicare Part D, either directly or through pharmacy benefit managers, unless the price

reduction is required by law. The rule also creates a new safe harbor for price reductions reflected at the point-of-sale, as well as a safe harbor for certain fixed fee arrangements between pharmacy benefit managers and manufacturers. Additionally, in December 2020, CMS issued a final rule that materially modifies current Medicaid Drug Rebate Program regulations by, among other things, broadening the definitions for "line extension" and "new formulation", the key term within the line extension definition. A "line extension" drug is subject to a higher Medicaid rebate, thereby reducing the amount the manufacturer is paid with respect to such product. These new definitions will become effective as of January 1, 2022.

Other legislative changes have been proposed and adopted since the ACA was enacted. These changes include the Budget Control Act of 2011, which, among other things, led to aggregate reductions to Medicare payments to providers of up to 2% per fiscal year that started in 2013 and will stay in effect through 2024 unless additional congressional action is taken, and the American Taxpayer Relief Act of 2012, which, among other things, reduced Medicare payments to several types of providers and increased the statute of limitations period for the government to recover overpayments to providers from three to five years. These new laws may result in additional reductions in Medicare and other healthcare funding and otherwise affect the prices we may obtain for any of our product candidates for which we may obtain regulatory approval or the frequency with which any such product candidate is prescribed or used. Further, there have been several recent U.S. congressional inquiries and proposed state and federal legislation designed to, among other things, bring more transparency to drug pricing, review the relationship between pricing and manufacturer patient programs, reduce the costs of drugs under Medicare and reform government program reimbursement methodologies for drug products.

Additionally, there has been increasing legislative and enforcement interest in the U.S. with respect to specialty drug pricing practices. Specifically, there have been several recent U.S. Congressional inquiries and proposed and enacted federal and state legislation designed to, among other things, bring more transparency to drug pricing, reduce the cost of prescription drugs under Medicare, review the relationship between pricing and manufacturer patient programs, and reform government program reimbursement methodologies for drugs. We expect that additional state and federal healthcare reform measures will be adopted in the future, any of which could result in more rigorous coverage criteria and/or limit the amounts that federal and state governments will pay for healthcare products and services, which could result in reduced demand for our products and additional downward pricing pressures. Any reduction in reimbursement from Medicare or other government programs may result in a similar reduction in payments from private third-party payors.

These healthcare reforms, as well as other healthcare reform measures that may be adopted in the future, may result in additional reductions in Medicare and other healthcare funding, more rigorous coverage criteria, new payment methodologies and additional downward pressure on the price for any approved product and/or the level of reimbursement physicians receive for administering any approved product. Reductions in reimbursement levels may negatively impact the prices we can charge or the frequency with which products are prescribed or administered. Any reduction in reimbursement from Medicare or other government programs may result in a similar reduction in payments from private payors.

Changes in U.S. social, political, regulatory and economic conditions or in laws and policies governing foreign trade, manufacturing, development and investment, and any negative sentiments towards the U.S. as a result of such changes, could also adversely affect our business.

In addition, the U.K.'s exit from the E.U. in January 2020, with a transition period that ended on December 31, 2020, often referred to as Brexit, has created uncertainty with regard to data protection regulation in the U.K. While the transition period has now concluded, decisions are still to be made on how data transfers to and from the U.K. will be regulated. Since the regulatory framework for pharmaceutical products in the U.K. covering quality, safety and efficacy of pharmaceutical products, clinical trials, marketing authorization, commercial sales and distribution of pharmaceutical products is derived from E.U. directives and regulations, Brexit could materially impact the future regulatory regime that applies to products and the approval of product candidates in the U.K. It remains to be seen how, if at all, Brexit will impact regulatory requirements for product candidates and products in the U.K. These possible negative impacts, and others resulting from the U.K.'s withdrawal from the E.U., may adversely affect our operating results and growth prospects as well as the manner in which we conduct our business operations in Europe.

Risks related to intellectual property and other legal matters

Our rights to develop and commercialize our products are subject in part to the terms and conditions of licenses or sublicenses granted to us by other pharmaceutical companies.

Our rights to our product portfolio are based in part on patents and other intellectual property licensed from third parties. These third parties may generally terminate the license agreements under certain circumstances, including a material breach of the agreement by the other. In the event we terminate our license, or if the third party terminates our license due to

our breach, rights to the intellectual property revert back to the licensor. Any termination or reversion of our rights to develop or commercialize our products would have a material adverse effect on our business.

If our efforts to protect the proprietary nature of the intellectual property related to our products are not adequate, we may not be able to compete effectively in our markets.

Method of treatment patents protect the use of a product for the method specified in the patent claims. This type of patent does not prevent a competitor from making and marketing a product that is identical to our product for a use that is outside the scope of the patented method. Moreover, even if competitors do not actively promote their product for our patented methods, physicians may prescribe these products "off-label." Although off-label prescriptions may infringe or contribute to the infringement of method of treatment patents, such infringement may be difficult to prevent.

Our patents and patent applications may be challenged or fail to result in issued patents and our existing or future patents may be too narrow to prevent third parties from developing or designing around these patents. In addition, we generally rely on trade secret protection and confidentiality agreements to protect certain proprietary know-how that is not patentable, for processes for which patents are difficult to enforce and for any other elements of our drug development processes that involve proprietary know-how, information and technology that is not covered by patent applications. While we require all of our employees, consultants, advisors and any third parties who have access to our proprietary know-how, information and technology to enter into confidentiality agreements, we cannot be certain that this know-how, information and technology will not be disclosed or that competitors will not otherwise gain access to our trade secrets or independently develop substantially equivalent information and techniques. Further, the laws of some foreign countries do not protect proprietary rights to the same extent as the laws of the U.S. As a result, we may encounter significant problems in protecting and defending our intellectual property both in the U.S. and abroad. If we are unable to protect or defend the intellectual property related to our technologies, we will not be able to establish or maintain a competitive advantage in our market.

Even if our patent applications issue as patents, they may not issue in a form that will provide us with any meaningful protection, prevent competitors from competing with us or otherwise provide us with any competitive advantage. Our competitors may be able to circumvent our owned or licensed patents by developing similar or alternative technologies or products in a non-infringing manner. Our competitors may seek to market generic versions of any approved products by submitting ANDAs to the FDA in which they claim that patents owned or licensed by us are invalid, unenforceable and/or not infringed. Alternatively, our competitors may seek approval to market their own products similar to or otherwise competitive with our products. In these circumstances, we may need to defend and/or assert our patents, including by filing lawsuits alleging patent infringement. In any of these types of proceedings, a court or other agency with jurisdiction may find our patents invalid and/or unenforceable. Even if we have valid and enforceable patents, these patents still may not provide protection against competing products or processes sufficient to achieve our business objectives.

The issuance of a patent is not conclusive as to its inventorship, scope, validity or enforceability, and our owned and licensed patents may be challenged in the courts or patent offices in the U.S. and abroad. Such challenges may result in loss of exclusivity or freedom to operate or in patent claims being narrowed, invalidated or held unenforceable, in whole or in part, which could limit our ability to stop others from using or commercializing similar or identical technology and products, or limit the duration of the patent protection of our technology and products. In addition, given the amount of time required for the development, testing and regulatory review of new product candidates, patents protecting such candidates might expire before or shortly after such candidates are commercialized.

We are, have been, and may continue to be, involved in lawsuits to protect or enforce our patents, which could be expensive, time-consuming and unsuccessful, and third parties may challenge the validity or enforceability of our patents and they may be successful.

Even where laws provide protection or we are able to obtain patents, costly and time-consuming litigation may be necessary to enforce and determine the scope of our proprietary rights, and the outcome of such litigation would be uncertain. Moreover, any actions we may bring to enforce our intellectual property against our competitors could provoke them to bring counterclaims against us, and some of our competitors have substantially greater intellectual property portfolios than we have. To counter infringement or unauthorized use of any patents we may obtain, we may be required to file infringement claims, which can be expensive and time-consuming to litigate. In addition, if we or one of our future collaborators were to initiate legal proceedings against a third party to enforce a patent covering one of our products, current product candidates, or one of our future products, the defendant could counterclaim that the patent is invalid or unenforceable. In patent litigation in the U.S., defendant counterclaims alleging invalidity or unenforceability are commonplace and challenges to validity of patents in certain foreign jurisdictions are common as well. Grounds for a validity challenge could be an alleged failure to meet any of several statutory requirements, including lack of novelty, obviousness, non-enablement or lack of statutory subject matter. Grounds for

an unenforceability assertion could be an allegation that someone connected with prosecution of the patent withheld relevant material information from the U.S. Patent and Trademark Office, or made a materially misleading statement, during prosecution. We may assert the patents in Hatch-Waxman litigation against the party filing the ANDA to keep the competing product off of the market until the patents expire but there is a risk that we will not succeed. The party filing the ANDA may also counterclaim in the litigation that our patents are not valid or unenforceable, and the court may find one or more claims of our patents invalid or unenforceable. If this occurs, a competing generic product could be marketed prior to expiration of our patents listed in the FDA's *Approved Drug Products with Therapeutic Equivalence Evaluations*, commonly known as the "Orange Book," which would harm our business.

We have been and continue to be involved in number of lawsuits with a variety of generic drug manufacturers who have filed ANDAs relating to certain of our patents. We have been successful in asserting that these third parties have infringed certain of our patents, but we may not be successful in such lawsuits in the future. Please see Note 17, *Legal Matters,* to the consolidated financial statements in Part II, Item 8 of this Annual Report, which is incorporated herein by reference, for additional information.

If we do not obtain protection under the Hatch-Waxman Act and similar foreign legislation to extend our patents and to obtain market exclusivity for our products, our business will be harmed.

The Hatch-Waxman Act provides for an extension of patent term for drugs for a period of up to five years to compensate for time spent in development. The HETLIOZ® U.S. new chemical entity (NCE) patent (the primary patent covering the product as a new composition of matter) received the full five-year patent term extension under the Hatch-Waxman Act and so, assuming that we continue to have rights under our license agreement with respect to this product, this patent in the U.S. expires in December 2022. We also own HETLIOZ® U.S. method of treatment patents (directed to the approved method of treatment as described in the HETLIOZ® label approved by the FDA), which expire normally between 2033 and 2035, and two drug substance patents that expire in 2035. The Fanapt® U.S. NCE patent received the full five-year patent term extension under the Hatch-Waxman Act and so this patent in the U.S. expired in November 2016. In November 2013, a patent directed to a method of treating patients with Fanapt® based on genotype was issued to us by the U.S. Patent and Trademark Office. This patent, which was listed in the Orange Book in January 2015, is set to expire in 2027. Please see the risk factor entitled "We are, have been, and may continue to be, involved in lawsuits to protect or enforce our patents, which could be expensive, time-consuming and unsuccessful, and third parties may challenge the validity or enforceability of our patents and they may be successful," and Note 17, *Legal Matters,* to the consolidated financial statements in Part II, Item 8 of this Annual Report, which is incorporated herein by reference, for additional information. Eight additional U.S. patents directed to methods of treating patients with Fanapt®, which are set to expire between 2025 and 2031, were issued to us in 2015.

A directive in the E.U. provides that companies that receive regulatory approval for a new medicinal product will have a 10-year period of market exclusivity for that product (with the possibility of a further one-year extension), beginning on the date of such European regulatory approval, regardless of when the European NCE patent covering such product expires. A generic version of the approved drug may not be marketed or sold in Europe during such market exclusivity period. This directive is of material importance with respect to Fanapt®, since the European NCE patent for Fanapt® has expired.

Assuming we gain a five-year patent term restoration for tradipitant, and that we continue to have rights under our license agreement with respect to this product, we would have exclusive rights to tradipitant's U.S. NCE patent until 2029. Assuming we gain a five-year patent term restoration for VQW-765, and that we continue to have rights under our license agreement with respect to this product, we would have exclusive rights to VQW-765's U.S. NCE patent until 2028.

However, there is no assurance that we will receive the extensions of our patents or other exclusive rights available under the Hatch-Waxman Act or similar foreign legislation. If we fail to receive such extensions or exclusive rights, our ability to prevent competitors from manufacturing, marketing and selling generic versions of our products will be materially impaired.

We may not be successful in the development of products for our own account.

In addition to our business strategy of acquiring rights to develop and commercialize products, we may develop products for our own account by applying our technologies to off-patent drugs as well as developing our own proprietary molecules. Because we will be funding the development of such programs, there is a risk that we may not be able to continue to fund all such programs to completion or to provide the support necessary to perform the clinical trials, obtain regulatory approvals or market any approved products. We expect the development of products for our own account to consume substantial resources. If we are able to develop commercial products on our own, the risks associated with these programs may be greater than those associated with our programs with collaborative partners.

Litigation or third-party claims of intellectual property infringement could require us to divert resources and may prevent or delay our drug discovery and development efforts.

Our commercial success depends in part on our not infringing the patents and proprietary rights of third parties. Third parties may assert that we are employing their proprietary technology without authorization. In addition, third parties may obtain patents in the future and claim that use of our technologies infringes upon these patents.

Furthermore, parties making claims against us may obtain injunctive or other equitable relief, which could effectively block our ability to develop and commercialize one or more of our products. Defense of these claims, regardless of their merit, would divert substantial financial and employee resources from our business. In the event of a successful claim of infringement against us, we may have to pay substantial damages, obtain one or more licenses from third parties or pay royalties. In addition, even in the absence of litigation, we may need to obtain additional licenses from third parties to advance our research or allow commercialization of our products. We may fail to obtain any of these licenses at a reasonable cost or on reasonable terms, if at all. In that event, we would be unable to develop and commercialize further one or more of our products.

In addition, in the future we could be required to initiate litigation to enforce our proprietary rights against infringement by third parties. Prosecution of these claims to enforce our rights against others could divert substantial financial and employee resources from our business. If we fail to enforce our proprietary rights against others, our business will be harmed.

As described elsewhere in these risk factors and in Note 17, *Legal Matters*, to the consolidated financial statements in Part II, Item 8 of this Annual Report, incorporated herein by reference, we have initiated lawsuits to enforce our patent rights against certain generic pharmaceutical companies.

General Risk Factors

Our stock price has been highly volatile and may be volatile in the future, and purchasers of our common stock could incur substantial losses.

The realization of any of the risks described in these risk factors or other unforeseen risks could have a dramatic and adverse effect on the market price of our common stock. Between January 1, 2020 and December 31, 2020, the high and low sale prices of our common stock as reported on The Nasdaq Global Market varied between $7.12 and $16.96. Additionally, market prices for securities of biotechnology and pharmaceutical companies, including ours, have historically been very volatile. The market for these securities has from time to time experienced significant price and volume fluctuations for reasons that were unrelated to the operating performance of any one company.

The following factors, in addition to the other risk factors described in this section, may also have a significant impact on the market price of our common stock:

- our level of success in commercializing our products;
- our level of success in executing our commercialization strategies;
- publicity regarding actual or potential testing or trial results relating to products under development by us or our competitors;
- the outcome of regulatory review relating to products under development by us or our competitors;
- regulatory developments in the U.S. and foreign countries;
- developments concerning any collaboration or other strategic transaction we may undertake;
- publicity regarding actual or potential litigation involving us;
- announcements of patent issuances or denials, technological innovations or new commercial products by us or our competitors;
- safety issues with our products or those of our competitors;
- announcements of technological innovations or new therapeutic products or methods by us or others;
- actual or anticipated variations in our quarterly operating results;
- changes in estimates of our financial results or recommendations by securities analysts or failure to meet such financial expectations;

- changes in government regulations or policies;
- changes in patent legislation or patent decisions or adverse changes to patent law;
- additions or departures of key personnel or members of our board of directors;
- the publication of negative research or articles about our company, our business or our products by industry analysts or others;
- market rumors or press reports;
- publicity regarding actual or potential transactions involving us; and
- economic, political and other external factors beyond our control.

We have been and may in the future be subject to litigation, which could harm our stock price, business, results of operations and financial condition.

We have been the subject of litigation in the past and may be subject to litigation in the future. In the past, following periods of volatility in the market price of their stock, many companies, including us, have been the subjects of securities class action litigation. Any such litigation can result in substantial costs and diversion of management's attention and resources and could harm our stock price, business results of operations and financial condition. As a result of these factors, holders of our common stock might be unable to sell their shares at or above the price they paid for such shares.

If there are substantial sales of our common stock, our stock price could decline.

A small number of institutional investors and private equity funds hold a significant number of shares of our common stock. Sales by these stockholders of a substantial number of shares, or the expectation of such sales, could cause a significant reduction in the market price of our common stock.

In addition to our outstanding common stock, as of December 31, 2020, there were a total of 5,246,381 shares of our common stock that we have registered and that we are obligated to issue upon the exercise of currently outstanding options and settlement of restricted stock unit awards granted under our 2006 and 2016 Equity Incentive Plans. Upon the exercise of these options or settlement of the shares underlying these restricted stock units, as the case may be, in accordance with their respective terms, these shares may be resold freely, subject to restrictions imposed on our affiliates under Rule 144. If significant sales of these shares occur in short periods of time, these sales could reduce the market price of our common stock. Any reduction in the trading price of our common stock could impede our ability to raise capital on attractive terms, if at all.

If securities or industry analysts do not publish research or reports or publish unfavorable research about our business, our stock price and trading volume could decline.

The trading market for our common stock will depend in part on the research and reports that securities or industry analysts publish about us or our business. We currently have research coverage by securities and industry analysts. If one or more of the analysts who covers us downgrades our stock, our stock price would likely decline. If one or more of these analysts ceases coverage of our company or fails to regularly publish reports on us, interest in the purchase of our stock could decrease, which could cause our stock price or trading volume to decline.

Our common stock may experience future dilution as a result of future equity offerings.

In order to raise additional capital, we may in the future offer additional shares of our common stock or other securities convertible into or exchangeable for our common stock at prices that may not be the same as the price per share in previous offerings. We may sell shares or other securities in any other offering at a price per share that is less than the price per share paid by investors in previous offerings, and investors purchasing shares or other securities in the future could have rights superior to existing stockholders. The price per share at which we sell additional shares of our common stock, or securities convertible or exchangeable into common stock, in future transactions may be higher or lower than the price per share paid by investors.

Our business could be negatively affected as a result of the actions of activist stockholders.

Proxy contests have been waged against many companies in the biopharmaceutical industry, including us, over the last several years. If faced with a proxy contest or other type of shareholder activism, we may not be able to respond successfully to

the contest or dispute, which would be disruptive to our business. Even if we are successful, our business could be adversely affected by a proxy contest or shareholder dispute involving us because:

- responding to proxy contests and other actions by activist stockholders can be costly and time-consuming, disrupting operations and diverting the attention of management and employees;
- perceived uncertainties as to future direction may result in the loss of potential acquisitions, collaborations or in-licensing opportunities, and may make it more difficult to attract and retain qualified personnel and business partners; and
- if individuals are elected to a board of directors with a specific agenda, it may adversely affect our ability to effectively and timely implement our strategic plan and create additional value for our stockholders.

These actions could cause our stock price to experience periods of volatility.

Anti-takeover provisions in our charter and bylaws and under Delaware law, and the adoption of a rights plan, could prevent or delay a change in control of our company.

We are a Delaware corporation and the anti-takeover provisions of Section 203 of the Delaware General Corporation Law may discourage, delay or prevent a change in control by prohibiting us from engaging in a business combination with an interested stockholder for a period of three years after the person becomes an interested stockholder, even if a change of control would be beneficial to our existing stockholders. In addition, our amended and restated certificate of incorporation and bylaws may discourage, delay or prevent a change in our management or control over us that stockholders may consider favorable. Our amended and restated certificate of incorporation and bylaws:

- authorize the issuance of "blank check" preferred stock that could be issued by our board of directors to thwart a takeover attempt;
- do not provide for cumulative voting in the election of directors, which would allow holders of less than a majority of the stock to elect some directors;
- establish a classified board of directors, as a result of which the successors to the directors whose terms have expired will be elected to serve from the time of election and qualification until the third annual meeting following their election;
- require that directors only be removed from office for cause;
- provide that vacancies on the board of directors, including newly created directorships, may be filled only by a majority vote of directors then in office;
- limit who may call special meetings of stockholders;
- prohibit stockholder action by written consent, requiring all actions to be taken at a meeting of the stockholders; and
- establish advance notice requirements for nominating candidates for election to the board of directors or for proposing matters that can be acted upon by stockholders at stockholder meetings.

Our board of directors previously adopted a rights agreement, the provisions of which could have had the effect of discouraging, delaying or preventing a change in or management or control over us. While there is no plan to do so at this time, our board of directors may choose to adopt a new rights plan in the future.

Changes to tax regulations to which we are subject could adversely affect us.

We are subject to tax laws, treaties and regulations in the countries in which we operate, and these laws and treaties are subject to interpretation. New legislation or regulation that could affect our tax burden could be enacted by any governmental authority. We cannot predict the timing or extent of such tax-related developments which could have a negative impact on our financial results. We have taken, and will continue to take, tax positions based on our interpretation of such tax laws. However, a challenge by a taxing authority, our ability to utilize tax benefits such as carryforwards or tax credits, or a deviation from other tax-related assumptions may cause our actual financial results to deviate from previous estimates.

Future transactions may harm our business or the market price of our stock.

We regularly review potential transactions related to technologies, products or product rights and businesses complementary to our business. These transactions could include:

- mergers;
- acquisitions;
- strategic alliances;
- licensing agreements; and
- co-promotion and similar agreements.

We may choose to enter into one or more of these transactions at any time, which may cause substantial fluctuations in the market price of our stock. Moreover, depending upon the nature of any transaction, we may experience a charge to earnings, which could also materially adversely affect our results of operations and could harm the market price of our stock.

We may undertake strategic acquisitions in the future, and difficulties integrating such acquisitions could damage our ability to achieve or sustain profitability.

Although we have no experience in acquiring businesses, we may acquire businesses or assets that complement or augment our existing business. If we acquire businesses with promising products or technologies, we may not be able to realize the benefit of acquiring such businesses if we are unable to move one or more products through preclinical and/or clinical development to regulatory approval and commercialization. Integrating any newly acquired businesses or technologies could be expensive and time-consuming, resulting in the diversion of resources from our current business. We may not be able to integrate any acquired business successfully. We cannot assure that, following an acquisition, we will achieve revenues, specific net income or loss levels that justify the acquisition or that the acquisition will result in increased earnings, or reduced losses, for the combined company in any future period. Moreover, we may need to raise additional funds through public or private debt or equity financing to acquire any businesses, which would result in dilution for stockholders or the incurrence of indebtedness and may not be available on terms which would otherwise be acceptable to us. We may not be able to operate acquired businesses profitably or otherwise implement our growth strategy successfully.

Our operating results may fluctuate significantly due to a number of factors which make our future results difficult to predict and could cause our operating results to fall below expectations or our guidance.

Our operating results will continue to be subject to fluctuations and are affected by numerous factors, including:

- product sales;
- cost of product sales;
- marketing and other expenses;
- manufacturing or supply issues;
- the timing and amount of royalties or milestone payments;
- our addition or termination of development programs;
- variations in the level of expenses related to our products or future development programs;
- regulatory developments affecting our products or those of our competitors;
- our execution of collaborative, licensing or other arrangements, and the timing of payments we may make or receive under these arrangements;
- any intellectual property infringement or other lawsuit in which we may become involved; and
- the timing and recognition of stock-based compensation expense.

If our operating results fall below the expectations of investors or securities analysts or below any guidance we may provide, the price of our common stock could decline substantially. Furthermore, any fluctuations in our operating results may, in turn, cause the price of our stock to fluctuate substantially. We believe that comparisons of our financial results are not necessarily meaningful and should not be relied upon as an indication of our future performance.

We are increasingly dependent on information technology systems, infrastructure and data. Cybersecurity breaches could expose us to liability, damage our reputation, compromise our confidential information or otherwise adversely affect our business.

We are increasingly dependent upon information technology systems, infrastructure and data. Our computer systems may be vulnerable to service interruption or destruction, malicious intrusion and random attack. Security breaches pose a risk that sensitive data, including intellectual property, trade secrets or personal information may be exposed to unauthorized persons or to the public. Cyber-attacks are increasing in their frequency, sophistication and intensity, and have become increasingly difficult to detect. Cyber-attacks could include the deployment of harmful malware, denial-of service, social engineering and other means to affect service reliability and threaten data confidentiality, integrity and availability. Our key business partners face similar risks, and a security breach of their systems could adversely affect our security posture. While we continue to invest in data protection and information technology, there can be no assurance that our efforts will prevent service interruptions, or identify breaches in our systems, that could adversely affect our business and operations and/or result in the loss of critical or sensitive information, which could result in financial, legal, business or reputational harm.

Our internal computer systems, or those of our collaborator, CROs or other contractors or consultants, may fail or suffer security breaches, which could result in a material disruption of development programs for our product candidates.

Despite the implementation of security measures, our internal computer systems and those of our collaborators, CROs, and other contractors and consultants are vulnerable to damage from computer viruses, unauthorized access, natural disasters, terrorism, war and telecommunication and electrical failures. Information security risks have significantly increased in recent years in part due to the proliferation of new technologies and the increased sophistication and activities of organized crime, hackers, terrorists and other external parties, including foreign state actors. As cyber threats continue to evolve, we may be required to expend significant additional resources to continue to modify or enhance our protective measures or to investigate and remediate any information security breaches.

While we have not experienced any such system failure, accident or security breach to date, if such an event were to occur and cause interruptions in our operations, it could result in a material disruption of our independent drug development programs. For example, the loss of clinical trial data from ongoing or future clinical trials for any of our product candidates could result in delays in regulatory approval efforts and significantly increase costs to recover or reproduce the data. Our information security systems are also subject to laws and regulations requiring that we take measures to protect the privacy and security of certain information we gather and use in our business. For example, HIPAA and its implementing regulations impose, among other requirements, certain regulatory and contractual requirements regarding the privacy and security of personal health information. In addition to HIPAA, numerous other federal and state laws, including, without limitation, state security breach notification laws, state health information privacy laws and federal and state consumer protection laws, govern the collection, use, disclosure and storage of personal information. To the extent that any disruption or security breach were to result in a loss of or damage to data or applications, or inappropriate disclosure of confidential or proprietary information or personal health information, we could incur substantial liability, our reputation would be damaged, and the further development of our product candidates could be delayed.

ITEM 1B. UNRESOLVED STAFF COMMENTS

Not applicable.

ITEM 2. PROPERTIES

Our headquarters office consists of a total of 43,462 square feet of office space located at 2200 Pennsylvania Avenue, N.W. in Washington, D.C. under operating leases and subleases that expire between 2026 and 2028 and are subject to renewal options. In addition, we have 2,880 square feet of office space in London, England under an operating lease that has a lease term ending in 2023 and is subject to a renewal option, and other short-term leases. We believe that these facilities are suitable and adequate to meet our anticipated near-term needs. We anticipate that following the expiration of the leases, additional or alternative space will be available at commercially reasonable terms.

ITEM 3. LEGAL PROCEEDINGS

Information with respect is item may be found in Note 17, *Legal Matters,* to the consolidated financial statements in Part II, Item 8 of this Annual Report, which is incorporated herein by reference.

ITEM 4. MINE SAFETY DISCLOSURES

Not applicable.

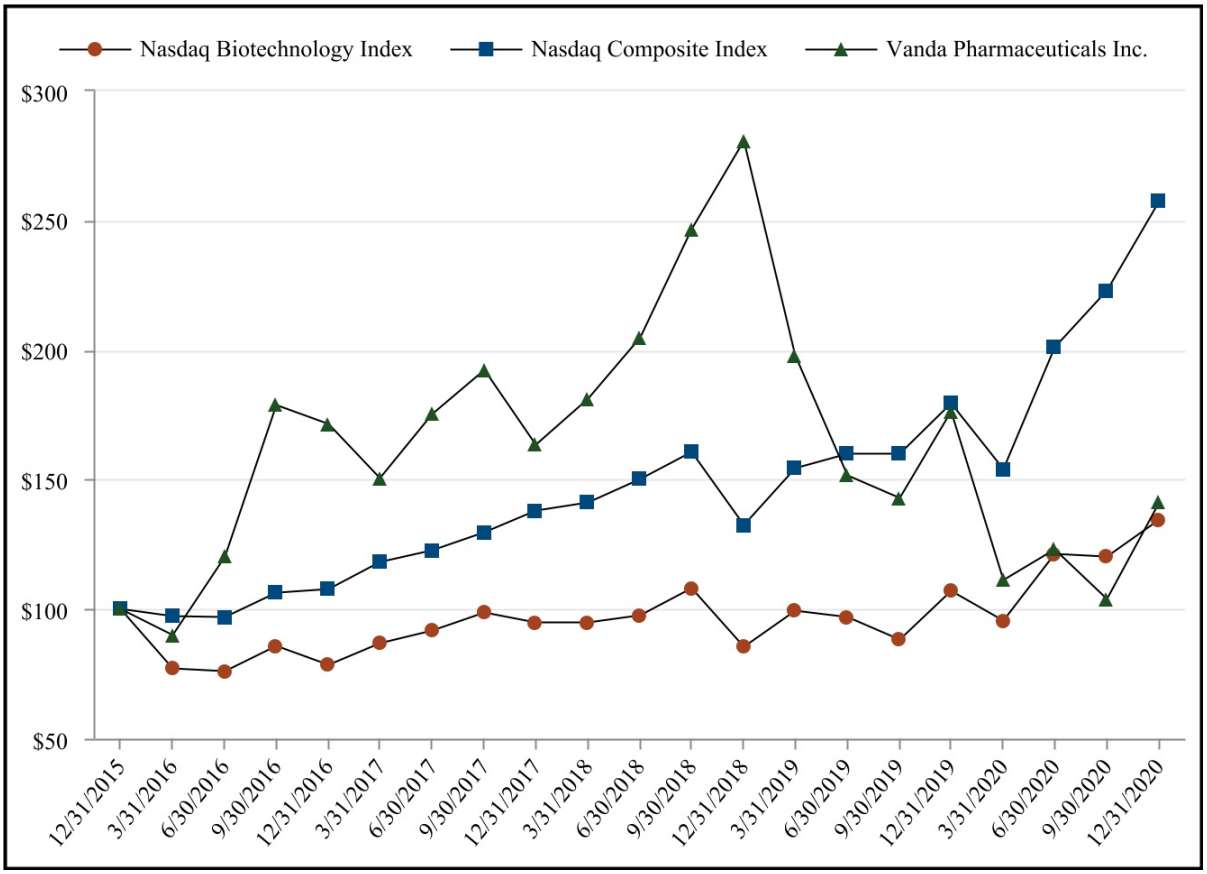
PART II

ITEM 5. MARKET FOR REGISTRANT'S COMMON EQUITY, RELATED STOCKHOLDER MATTERS AND ISSUER PURCHASES OF EQUITY SECURITIES

Our common stock is quoted on The Nasdaq Global Market under the symbol "VNDA." As of February 4, 2021, there were seven holders of record of our common stock. The number of holders of record of our common stock does not reflect the number of beneficial holders whose shares are held by depositors, brokers or other nominees.

Market Price of and Dividends on the Registrant's Common Equity and Related Stockholder Matters

The following graph shows the cumulative five-year total return on our common stock relative to the cumulative total returns of the Nasdaq Composite Index and the Nasdaq Biotechnology Index. An investment of $100 (with reinvestment of dividends) is assumed to have been made in our common stock and in each of the indexes on December 31, 2015 and its relative performance is tracked through December 31, 2020. The comparisons in the table are required by the Securities and Exchange Commission (SEC) and are not intended to forecast or be indicative of possible future performance of our common stock. We have never paid cash dividends to our stockholders and do not plan to pay dividends in the foreseeable future. The following graph and related information is being furnished solely to accompany this Annual Report pursuant to Item 201(e) of Regulation S-K and shall not be deemed "soliciting materials" or to be "filed" with the SEC (other than as provided in Item 201), nor shall such information be incorporated by reference into any of our filings under the Securities Act of 1933, as amended, or the Securities Exchange Act of 1934, as amended, whether made before or after the date hereof, and irrespective of any general incorporation language in any such filing.



Securities Authorized for Issuance under Equity Incentive Plans

Information regarding securities authorized for issuance under equity incentive plans will be contained in our Proxy Statement for the 2021 Annual Meeting of Stockholders to be filed with the SEC within 120 days after the end of the fiscal year ended December 31, 2020 and is incorporated herein by reference pursuant to General Instruction G(3) to Form 10-K.

ITEM 6. SELECTED CONSOLIDATED FINANCIAL DATA

The Consolidated Statements of Operations data for the years ended December 31, 2020, 2019 and 2018 and the Consolidated Balance Sheet data as of December 31, 2020 and 2019 are each derived from our audited consolidated financial statements included in this Annual Report. The Consolidated Statements of Operations data for the years ended December 31, 2017 and 2016, and the Consolidated Balance Sheet data as of December 31, 2018, 2017 and 2016 are each derived from our audited consolidated financial statements not included herein. Our historical results for any prior period are not necessarily indicative of results to be expected in any future period.

The following data should be read together with our consolidated financial statements and accompanying notes and Part II, Item 7, *Management's Discussion and Analysis of Financial Condition and Results of Operations,* included in this Annual Report.

	Year Ended December 31,				
(in thousands, except for share and per share amounts)	2020	2019 (1)	2018 (1)(2)	2017 (1)(2)	2016 (1)(2)
Statements of Operations Data					
Total revenues	$ 248,168	$ 227,188	$ 193,118	$ 165,083	$ 146,017
Operating expenses:					
Cost of goods sold excluding amortization	23,364	24,488	20,508	17,848	24,712
Research and development	55,577	48,649	43,594	38,547	29,156
Selling, general and administrative	140,510	129,736	105,751	123,841	99,787
Intangible asset amortization	1,478	1,505	1,527	1,750	10,933
Total operating expenses	220,929	204,378	171,380	181,986	164,588
Income (loss) from operations	27,239	22,810	21,738	(16,903)	(18,571)
Other income	4,416	6,218	3,608	1,472	665
Income (loss) before income taxes	31,655	29,028	25,346	(15,431)	(17,906)
Provision (benefit) for income taxes	8,318	(86,525)	138	136	104
Net income (loss)	$ 23,337	$ 115,553	$ 25,208	$ (15,567)	$ (18,010)
Net income (loss) per share:					
Basic	$ 0.43	$ 2.17	$ 0.50	$ (0.35)	$ (0.41)
Diluted	$ 0.42	$ 2.11	$ 0.48	$ (0.35)	$ (0.41)
Weighted average shares outstanding:					
Basic	54,427,683	53,137,562	50,859,947	44,735,146	43,449,441
Diluted	55,190,802	54,847,060	53,045,257	44,735,146	43,449,441

	December 31,				
(in thousands)	2020	2019 (1)	2018 (1)	2017 (1)	2016 (1)
Balance Sheet Data					
Cash and cash equivalents	$ 61,031	$ 45,072	$ 61,005	$ 33,627	$ 40,426
Marketable securities	306,709	267,057	196,355	109,786	100,914
Working capital	343,209	294,631	246,117	99,494	123,855
Total assets	533,456	483,748	332,130	205,425	210,374
Long-term liabilities	14,254	13,298	3,693	3,675	28,724
Total liabilities	80,190	72,803	56,708	74,038	79,044
Accumulated deficit	(197,328)	(220,665)	(336,218)	(361,426)	(345,859)
Total stockholders' equity	453,266	410,945	275,422	131,387	131,330

(1) We adopted Accounting Standards Codification (ASC) 842 *Leases* (ASC 842), effective January 1, 2019, using a modified retrospective transition. Results for the years ended prior to December 31, 2019 are accounted for in accordance with ASC 840.

(2) We adopted ASC 606 *Revenue from Contracts with Customers* (ASC 606), effective January 1, 2018, using the modified retrospective method to those contracts that were not completed as of January 1, 2018. Results for the years ended prior to December 31, 2018 are accounted for in accordance with ASC 605.

ITEM 7. MANAGEMENT'S DISCUSSION AND ANALYSIS OF FINANCIAL CONDITION AND RESULTS OF OPERATIONS

You should read the following discussion and analysis of our financial condition and results of operations together with Part II, Item 6, Selected Consolidated Financial Data, and our consolidated financial statements and related notes appearing in this annual report on Form 10-K (Annual Report). This discussion and analysis generally addresses 2020 and 2019 items and year-to-year comparisons between 2020 and 2019. Discussions of 2018 items and year-to-year comparisons between 2019 and 2018 that are not included in this Annual Report can be found in Part II, Item 7, Management's Discussion and Analysis of Financial Condition and Results of Operations, in our Annual Report on Form 10-K for the fiscal year ended December 31, 2019. Some of the information contained in this discussion and analysis or set forth elsewhere in this Annual Report include historical information and other information with respect to our plans and strategy for our business and contain forward-looking statements that involve risks, uncertainties and assumptions. Our actual results may differ materially from those anticipated in these forward-looking statements as a result of certain factors, including but not limited to those set forth under Part I, Item 1A, Risk Factors, and elsewhere in this Annual Report.

Overview

Vanda Pharmaceuticals Inc. (we, our or Vanda) is a leading global biopharmaceutical company focused on the development and commercialization of innovative therapies to address high unmet medical needs and improve the lives of patients.

We strive to advance novel approaches to bring important, new medicines to market through responsible innovation. We are committed to the use of technologies that support sound science, including genetics and genomics, in drug discovery, clinical trials and the commercial positioning of our products.

Our commercial portfolio is currently comprised of two products, HETLIOZ® for the treatment of Non-24-Hour Sleep-Wake Disorder (Non-24) and nighttime sleep disturbances in Smith-Magenis Syndrome (SMS) and Fanapt® for the treatment of schizophrenia. HETLIOZ® is the first treatment for patients with Non-24 and SMS approved by the U.S. Food and Drug Administration (FDA). In addition, we have a number of drugs in development, including:

- HETLIOZ® (tasimelteon) for the treatment of jet lag disorder, pediatric Non-24, delayed sleep phase disorder (DSPD) and autism spectrum disorder (ASD);
- Fanapt® (iloperidone) for the treatment of bipolar disorder and Parkinson's disease psychosis (PDP) and a long acting injectable (LAI) formulation for the treatment of schizophrenia;
- Tradipitant (VLY-686), a small molecule neurokinin-1 receptor (NK-1R) antagonist, for the treatment of gastroparesis, motion sickness, atopic dermatitis, and COVID-19 pneumonia;
- VTR-297, a small molecule histone deacetylase (HDAC) inhibitor for the treatment of hematologic malignancies and with potential use as a treatment for several oncology indications;
- Portfolio of Cystic Fibrosis Transmembrane Conductance Regulator (CFTR) activators and inhibitors, including VSJ-110 for the treatment of dry eye and ocular inflammation and BPO-27 for the treatment of secretory diarrhea disorders, including cholera; and
- VQW-765, a small molecule nicotinic acetylcholine receptor partial agonist, with potential use for the treatment of psychiatric disorders.

Operational Highlights

Products

Vanda is encouraged by the strength of its commercial performance during the fourth quarter of 2020. Vanda continues to implement marketing and sales strategies aimed at supporting growth and minimizing the impact of disruptions caused by the COVID-19 pandemic, including the Fanapt® for schizophrenia direct-to-consumer campaign, which was launched in 2020. Vanda is continuing its activities to support and facilitate the treatment of individuals in the U.S. living with SMS, and is committed to its awareness campaign and the support of patients suffering with Non-24.

Pipeline

Tradipitant

- The gastroparesis Phase III clinical study (VP-VLY-686-3301) is ongoing. The study has a target enrollment of 200 randomized patients and is expected to complete enrollment in the first half of 2021, with a New Drug Application (NDA) filing projected in the second half of 2021.
- The COVID-19 pneumonia Phase III clinical study (ODYSSEY VLY-686-3501) is ongoing.

HETLIOZ® (tasimelteon)

- In December 2020, the FDA approved HETLIOZ® capsule and liquid formulations for the treatment of adults and children, respectively, with nighttime sleep disturbances in SMS. HETLIOZ® capsules, for adults with SMS, were immediately available after approval and HETLIOZ LQ™ oral suspension, for children with SMS, is expected to be available in the first quarter of 2021. SMS is estimated to affect 1/15,000-25,000 births in the U.S. HETLIOZ® is the first and only FDA approved medication for patients with SMS.
- A Phase III clinical study for HETLIOZ® in DSPD is expected to be initiated in the first quarter of 2021.
- A clinical development program for HETLIOZ® in ASD is expected to be initiated in the first quarter of 2021.

Fanapt® (iloperidone)

- Development of the LAI formulation of Fanapt® is ongoing.
- A clinical program for Fanapt® in PDP is expected to begin in the first quarter of 2021.

Since we began operations, we have devoted substantially all of our resources to the in-licensing, clinical development and commercialization of our products. Our ability to generate meaningful product sales and achieve profitability largely depends on our level of success in commercializing HETLIOZ® and Fanapt® in the U.S. and Europe, on our ability, alone or with others, to complete the development of our products, and to obtain the regulatory approvals for and to manufacture, market and sell our products. The results of our operations will vary significantly from year-to-year and quarter-to-quarter and depend on a number of factors, including risks related to our business, risks related to our industry, and other risks that are detailed in Part I, Item 1A, *Risk Factors,* of this Annual Report.

Critical Accounting Policies

The preparation of our consolidated financial statements requires us to make estimates and assumptions that affect the reported amounts of assets and liabilities and the disclosure of contingent assets and liabilities at the date of our financial statements, as well as the reported revenues and expenses during the reported periods. We base our estimates on historical experience and on various other factors that we believe are reasonable under the circumstances, the results of which form the basis for making judgments about the carrying value of assets and liabilities that are not apparent from other sources. Actual results may differ from these estimates under different assumptions or conditions.

A summary of our significant accounting policies appears in the notes to our audited consolidated financial statements for the year ended December 31, 2020 included in this Annual Report. However, we believe that the following accounting policies are important to understanding and evaluating our reported financial results, and we have accordingly included them in this discussion.

Revenue from net product sales. Our net product sales consist of sales of HETLIOZ® and sales of Fanapt®. In accordance with ASC 606 *Revenue from Contracts with Customers* (ASC 606), we account for a contract when it has approval and commitment from both parties, the rights of the parties are identified, payment terms are identified, the contract has commercial substance and collectability of consideration is probable. We recognize revenue when control of the product is transferred to the customer in an amount that reflects the consideration we expect to be entitled to in exchange for those product sales, which is typically once the product physically arrives at the customer.

HETLIOZ® is available in the U.S. for distribution through a limited number of specialty pharmacies, and is not available in retail pharmacies. Fanapt® is available in the U.S. for distribution through a limited number of wholesalers and is available in retail pharmacies. We invoice and record revenue when customers, specialty pharmacies and wholesalers, receive product from the third-party logistics warehouse, which is the point at which control is transferred to the customer. Revenues and accounts receivable are concentrated with these customers. Outside the U.S., we sell HETLIOZ® in Germany and have a distribution agreement with Megapharm Ltd. for the commercialization of Fanapt® in Israel. Receivables are carried at

transaction price net of allowance for credit losses. Allowance for credit losses is measured using historical loss rates based on the aging of receivables and incorporating current conditions and forward-looking estimates.

The transaction price is determined based upon the consideration to which we will be entitled in exchange for transferring product to the customer. Our product sales are recorded net of applicable product revenue allowances for which reserves are established and include discounts, rebates, chargebacks, service fees, co-pay assistance and product returns that are applicable for various government and commercial payors. We estimate the amount of variable consideration that should be included in the transaction price utilizing the most likely amount method and update our estimate at each reporting date. Variable consideration is included in the transaction price if, in our judgment, it is probable that a significant future reversal of cumulative revenue under the contract will not occur. Allowances for rebates, chargebacks and co-pay assistance are based upon the insurance benefits of the end customer, which are estimated using historical activity and, where available, actual and pending prescriptions for which we have validated the insurance benefits. Reserves for variable consideration are classified as product revenue allowances on the Consolidated Balance Sheets, with the exception of prompt-pay discounts which are classified as reductions of accounts receivable. The reserve for product returns for which the product may not be returned for a period of greater than one year from the balance sheet date is included as a component of other non-current liabilities in the Consolidated Balance Sheets. Uncertainties related to variable consideration are generally resolved in the quarter subsequent to period end, with the exception of Medicaid rebates, which are dependent upon the timing of when states submit reimbursement claims, and product returns that are resolved during the product expiry period specified in the customer contract. We currently record sales allowances for the following:

- *Prompt-pay:* Specialty pharmacies and wholesalers are offered discounts for prompt payment. We expect that the specialty pharmacies and wholesalers will earn prompt payment discounts and, therefore, deduct the full amount of these discounts from total product sales when revenues are recognized.
- *Rebates:* Allowances for rebates include mandated discounts under the Medicaid Drug Rebate Program as well as contracted rebate programs with other payors. Rebate amounts owed after the final dispensing of the product to a benefit plan participant are based upon contractual agreements or legal requirements with public sector benefit providers, such as Medicaid. The allowance for rebates is based on statutory or contracted discount rates and estimated patient utilization.
- *Chargebacks:* Chargebacks are discounts that occur when contracted indirect customers purchase directly from specialty pharmacies and wholesalers. Contracted indirect customers, which currently consist primarily of Public Health Service institutions and federal government entities purchasing via the Federal Supply Schedule, generally purchase the product at a discounted price. The specialty pharmacy or wholesaler, in turn, charges back the difference between the price initially paid by the specialty pharmacy or wholesaler and the discounted price paid to the specialty pharmacy or wholesaler by the contracted customer.
- *Medicare Part D coverage gap:* The Medicare Part D prescription drug benefit requires manufacturers to fund approximately 70% of the Medicare Part D insurance coverage gap for prescription drugs sold to eligible patients for applicable drugs. We account for the Medicare Part D coverage gap using a point of sale model. Estimates for expected Medicare Part D coverage gap are based in part on historical activity and, where available, actual and pending prescriptions when we have validated the insurance benefits.
- *Service fees:* We receive sales order management, data and distribution services from certain customers. These fees are based on contracted terms and are known amounts. We accrue service fees at the time of revenue recognition, resulting in a reduction of product sales and the recognition of an accrued liability, unless it is a payment for a distinct good or service from the customer in which case the fair value of those distinct goods or services are recorded as selling, general and administrative expense.
- *Co-payment assistance:* Patients who have commercial insurance and meet certain eligibility requirements may receive co-payment assistance. Co-pay assistance utilization is based on information provided by our third-party administrator.
- *Product returns:* We generally offer direct customers a limited right to return as contractually defined with our customers. We consider several factors in the estimation process, including expiration dates of product shipped to customers, inventory levels within the distribution channel, product shelf life, historical return activity, including activity for product sold for which the return period has past, prescription trends and other relevant factors. We do not expect returned goods to be resalable. There was no right of return asset as of December 31, 2020 or 2019.

The following table summarizes sales discounts and allowance activity as of and for the years ended December 31, 2020, 2019 and 2018:

(in thousands)	Rebates & Chargebacks	Discounts, Returns and Other	Total
Balances at December 31, 2017	20,229	$ 7,357	$ 27,586
Provision related to current period sales	59,317	23,796	83,113
Adjustments for prior period sales	811	370	1,181
Credits/payments made	(58,223)	(21,823)	(80,046)
Balances at December 31, 2018	22,134	9,700	31,834
Provision related to current period sales	59,358	26,872	86,230
Adjustments for prior period sales	(350)	(399)	(749)
Credits/payments made	(58,750)	(26,022)	(84,772)
Balances at December 31, 2019	22,392	10,151	32,543
Provision related to current period sales	70,563	27,952	98,515
Adjustments for prior period sales	(480)	1,327	847
Credits/payments made	(65,605)	(30,557)	(96,162)
Balances at December 31, 2020	$ 26,870	$ 8,873	$ 35,743

The provision for rebates and chargebacks of $70.6 million and $59.4 million for the years ended December 31, 2020 and 2019, respectively, and their ending balances at December 31, 2020 and 2019, primarily represent Medicaid rebates applicable to sales of Fanapt® and, to a lesser extent, Medicaid rebates applicable to sales of HETLIOZ®. The provision for discounts, returns and other of $28.0 million and $26.9 million for the years ended December 31, 2020 and 2019, primarily represents wholesaler distribution fees applicable to sales of Fanapt® and, to a lesser extent, estimated product returns of Fanapt®, and co-pay assistance costs and prompt pay discounts applicable to the sales of both HETLIOZ® and Fanapt®. The ending balances of discounts, returns and other as of December 31, 2020 and 2019 primarily represent estimated product returns of Fanapt® and wholesaler distribution fees applicable to sales of Fanapt®.

Stock-based compensation. Compensation costs for all stock-based awards to employees and directors are measured based on the grant date fair value of those awards and recognized over the period during which the employee or director is required to perform service in exchange for the award. We use the Black-Scholes-Merton option pricing model to determine the fair value of stock options. The determination of the fair value of stock options on the date of grant using an option pricing model is affected by our stock price as well as assumptions regarding a number of complex and subjective variables. These variables include the expected stock price volatility over the expected term of the awards, actual and projected employee stock option exercise behaviors, risk-free interest rate and expected dividends. Expected volatility rates are based on the historical volatility of our publicly traded common stock and other factors. The risk-free interest rates are based on the U.S. Treasury yield for a period consistent with the expected term of the option in effect at the time of the grant. We have never paid cash dividends to our stockholders and do not plan to pay dividends in the foreseeable future. As stock-based compensation expense recognized in the Consolidated Statements of Operations is based on awards ultimately expected to vest, it has been reduced for estimated forfeitures. Forfeitures are estimated at the time of grant and revised, if necessary, in subsequent periods if actual forfeitures differ from those estimates.

Research and development expenses. Research and development expenses consist primarily of fees for services provided by third parties in connection with the clinical trials, costs of contract manufacturing services for clinical trial use, milestone payments made under licensing agreements prior to regulatory approval, costs of materials used in clinical trials and research and development, costs for regulatory consultants and filings, depreciation of capital resources used to develop products, related facilities costs, and salaries, other employee-related costs and stock-based compensation for research and development personnel. We expense research and development costs as they are incurred for products in the development stage, including manufacturing costs and milestone payments made under license agreements prior to FDA approval. Upon and subsequent to FDA approval, manufacturing and milestone payments made under license agreements are capitalized. Milestone payments are accrued when it is deemed probable that the milestone event will be achieved. Costs related to the acquisition of intellectual property are expensed as incurred if the underlying technology is developed in connection with our research and development efforts and has no alternative future use.

Clinical trials are inherently complex, often involve multiple service providers, and can include payments made to investigator physicians at study sites. Because billing for services often lags delivery of service by a substantial amount of time, we often are required to estimate a significant portion of our accrued clinical expenses. Our assessments include, but are not limited to: (i) an evaluation by the project manager of the work that has been completed during the period, (ii) measurement of progress prepared internally and/or provided by the third-party service provider, (iii) analyses of data that justify the progress, and (iv) management's judgment. In the event that we do not identify certain costs that have begun to be incurred or we under- or over-estimate the level of services performed or the costs of such services, our reported expenses for such period would be too low or too high.

Intangible assets. Our intangible assets consist of capitalized license costs for products approved by the FDA. We amortize our intangible assets on a straight-line basis over the estimated useful economic life of the related product patents. We assess the impairment of intangible assets whenever events or changes in circumstances indicate that the carrying value may not be recoverable. Factors we consider important that could trigger an impairment review include significant underperformance relative to expected historical or projected future operating results, a significant adverse change in legal or regulatory factors that could affect the value or patent life including our ability to defend and enforce patent claims and other intellectual property rights and significant negative industry or economic trends. When we determine that the carrying value of our intangible assets may not be recoverable based upon the existence of one or more of the indicators of impairment, we measure any impairment based on the amount that carrying value exceeds fair value. No impairments have been recognized on our intangible assets.

Income taxes. We assess the need for a valuation allowance against our deferred tax asset each quarter through the review of all available positive and negative evidence. Deferred tax assets are reduced by a tax valuation allowance when, in the opinion of management, it is more likely than not that some portion of the deferred tax assets will not be realized. The analysis is highly dependent upon historical and projected taxable income. Projected taxable income includes significant assumptions related to revenue, commercial expenses and research and development activities. During 2019, after considering all available positive and negative evidence, including but not limited to cumulative income in recent periods, historical, current and future projected results and significant risks and uncertainties related to forecasts, we concluded that it was more likely than not that substantially all of our deferred tax assets in the U.S. are realizable in future periods. A valuation allowance has been retained against certain District of Columbia state deferred tax assets as of December 31, 2020 and 2019. Tax benefits are recognized from an uncertain tax position only if it is more likely than not that the tax position will be sustained on examination by the taxing authorities based on the technical merits of the position. The tax benefit recognized in the financial statements for a particular tax position is based on the largest benefit that is more likely than not to be realized upon settlement.

Recent Accounting Pronouncements

See Note 2, *Summary of Significant Accounting Policies,* to the consolidated financial statements included in Part II, Item 8 of this Annual Report for information on recent accounting pronouncements.

Results of Operations

We anticipate that our results of operations will fluctuate for the foreseeable future due to several factors, including our and our partners' ability to continue to successfully commercialize our products, any possible payments made or received pursuant to license agreements, progress of our research and development efforts, the timing and outcome of clinical trials and related possible regulatory approvals, and the impact of the COVID-19 pandemic.

Year ended December 31, 2020 compared to year ended December 31, 2019

Revenues. Total revenues increased by $21.0 million, or 9%, to $248.2 million for the year ended December 31, 2020 compared to $227.2 million for the year ended December 31, 2019. Revenues were as follows:

	Year Ended December 31,			
(in thousands)	**2020**	**2019**	**Net Change**	**Percent**
HETLIOZ® net product sales	$ 160,686	$ 142,980	$ 17,706	12 %
Fanapt® net product sales	87,482	84,208	3,274	4 %
Total net product sales	$ 248,168	$ 227,188	$ 20,980	9 %

HETLIOZ® net product sales increased by $17.7 million, or 12%, to $160.7 million for the year ended December 31, 2020 compared to $143.0 million for the year ended December 31, 2019. The increase to net product sales was attributable to an increase in volume and an increase in price net of deductions.

Fanapt® net product sales increased by $3.3 million, or 4%, to $87.5 million for the year ended December 31, 2020 compared to $84.2 million for the year ended December 31, 2019. The increase to net product sales was attributable to an increase in price net of deductions partially offset by a decrease in volume.

Cost of goods sold. Cost of goods sold decreased by $1.1 million, or 5%, to $23.4 million for the year ended December 31, 2020 compared to $24.5 million for the year ended December 31, 2019. Cost of goods sold includes third-party manufacturing costs of product sold, third-party royalty costs and distribution and other costs. Third-party royalty costs were 10% and 5% of HETLIOZ® net product sales in the U.S. and Germany, respectively. Third-party royalty costs on Fanapt® net product sales decreased from 9% to 6% beginning January 2020.

In addition to third-party royalty costs, HETLIOZ® and Fanapt® cost of goods sold as a percentage of revenue depends upon our cost to manufacture inventory at normalized production levels with our third-party manufacturers. We expect that, in the future, total HETLIOZ® manufacturing costs included in cost of goods sold will continue to be less than 2% of our HETLIOZ® net product sales. We expect that, in the future, total Fanapt® manufacturing costs included in cost of goods sold will continue to be less than 3% of our Fanapt® net product sales.

Research and development expenses. Research and development expenses increased by $6.9 million, or 14%, to $55.6 million for the year ended December 31, 2020 compared to $48.6 million for the year ended December 31, 2019. The increase was primarily due to an increase in clinical trial expenses associated with our Fanapt® and COVID-19 therapeutic development programs. The COVID-19 pandemic has impacted clinical research globally, including our previously reported clinical trials. While certain of our programs have resumed patient enrollment, other programs remain on hold.

The following table summarizes the costs of our product development initiatives for the years ended December 31, 2020 and 2019.

	Year Ended December 31,	
(in thousands)	**2020**	**2019**
Direct project costs (1)		
HETLIOZ®	$ 9,518	$ 8,672
Fanapt®	7,669	5,516
Tradipitant	23,540	21,290
VTR-297	1,487	1,609
CFTR	3,938	4,511
Other	2,211	668
Total direct project costs	48,363	42,266
Indirect project costs (1)		
Stock-based compensation	3,804	3,207
Other indirect overhead	3,410	3,176
Total indirect project costs	7,214	6,383
Total research and development expense	$ 55,577	$ 48,649

(1) We record direct costs, including personnel costs and related benefits, on a project-by-project basis. Many of our research and development costs are not attributable to any individual project because we share resources across several development projects. We record indirect costs that support a number of our research and development activities in the aggregate, including stock-based compensation.

We expect to incur significant research and development expenses as we continue to develop our products. In addition, we expect to incur licensing costs in the future that could be substantial, as we continue our efforts to expand our product pipeline.

Selling, general and administrative expenses. Selling, general and administrative expenses increased by $10.8 million, or 8%, to $140.5 million for the year ended December 31, 2020 compared to $129.7 million for the year ended December 31,

2019. The increase was primarily the result of increased spending on marketing activities for our commercial products, including the Fanapt® for schizophrenia direct-to-consumer campaign, partially offset by decreased spending on legal activities.

Intangible asset amortization. Intangible asset amortization was $1.5 million for each of the years ended December 31, 2020 and 2019.

Other income. Other income was $4.4 million for the year ended December 31, 2020 compared to $6.2 million for the year ended December 31, 2019. Other income primarily consists of investment income, which decreased in 2020 as a result of lower yields on our marketable securities.

Provision for income taxes. A provision for income taxes of $8.3 million was recorded for the year ended December 31, 2020 and an income tax benefit of $86.5 million was recorded for the year ended December 31, 2019. The income tax benefit for the year ended December 31, 2019 was primarily due to the reduction of the tax valuation allowance against substantially all of its deferred tax assets in the U.S. Tax expense associated with U.S. income before income taxes for the year ended December 31, 2019 was offset by a corresponding tax benefit for the reduction of the valuation allowance recorded against tax attributes that were utilized in those periods. Income tax expense was recorded related to certain U.S. state and foreign jurisdictions for the year ended December 31, 2019. See Note 15, *Income Taxes,* to the consolidated financial statements in Part II, Item 8 of this Annual Report for additional information.

Liquidity and Capital Resources

As of December 31, 2020, our total cash and cash equivalents and marketable securities were $367.7 million compared to $312.1 million at December 31, 2019. Our cash and cash equivalents are deposits in operating accounts and highly liquid investments with an original maturity of 90 days or less at date of purchase and consist of investments in money market funds with commercial banks and financial institutions, and commercial paper of high-quality corporate issuers. Our marketable securities consist of investments in government sponsored and corporate enterprises and commercial paper.

Our liquidity resources as of December 31, 2020 and 2019 are summarized as follows:

(in thousands)	December 31, 2020	December 31, 2019
Cash and cash equivalents	$ 61,031	$ 45,072
Marketable securities:		
U.S. Treasury and government agencies	166,092	88,601
Corporate debt	140,617	130,055
Asset-backed securities	—	48,401
Total marketable securities	306,709	267,057
Total cash, cash equivalents and marketable securities	$ 367,740	$ 312,129

As of December 31, 2020, we maintained all of our cash, cash equivalents and marketable securities in two financial institutions. Deposits held with these institutions may exceed the amount of insurance provided on such deposits, but we do not anticipate any losses with respect to such deposits.

Based on our current operating plans, which include costs and expenses in connection with our continued clinical development of tradipitant and our other products, U.S. commercial activities for HETLIOZ® and Fanapt®, pursuit of market approval of HETLIOZ® and Fanapt® in other regions, and payments due upon achievement of milestones under our license agreements, we believe that our cash, cash equivalents and marketable securities and cash received from product sales will be sufficient for at least the next 12 months. Our future capital requirements and the adequacy of our available funds will depend on many factors, primarily including our ability to generate revenue, the scope and costs of our commercial, manufacturing and process development activities, the magnitude of our discovery, preclinical and clinical development programs, and potential costs to acquire or license the rights to additional products.

We may need or desire to obtain additional capital to finance our operations through debt, equity or alternative financing arrangements. We may also seek capital through collaborations or partnerships with other companies. The issuance of debt could require us to grant liens on certain of our assets that may limit our flexibility and debt securities may be convertible into common stock. If we raise additional capital by issuing equity securities, the terms and prices for these financings may be much more favorable to the new investors than the terms obtained by our existing stockholders. These financings also may significantly dilute the ownership of our existing stockholders. If we are unable to obtain additional financing, we may be

required to reduce the scope of our future activities which could harm our business, financial condition and operating results. There can be no assurance that any additional financing required in the future will be available on acceptable terms, if at all.

Cash Flow

The following table summarizes our net cash flows from operating, investing and financing activities for the years ended December 31, 2020 and 2019:

	Year Ended December 31,		
(in thousands)	2020	2019	Net Change
Net cash provided by (used in):			
Operating activities:			
Net income	$ 23,337	$ 115,553	$ (92,216)
Non-cash charges	24,121	(72,731)	96,852
Net change in operating assets and liabilities	4,317	3,125	1,192
Operating activities	51,775	45,947	5,828
Investing activities:			
Purchases of property and equipment	(1,795)	(1,019)	(776)
Net purchases, sales and maturities of marketable securities	(39,704)	(67,290)	27,586
Investing activities	(41,499)	(68,309)	26,810
Financing activities:			
Proceeds from the exercise of stock options	5,634	6,264	(630)
Financing activities	5,634	6,264	(630)
Effect of exchange rate changes on cash, cash equivalents and restricted cash	53	(1)	54
Net change in cash, cash equivalents and restricted cash	$ 15,963	$ (16,099)	$ 32,062

Operating Activities. Cash flows provided by operating activities during the year ended December 31, 2020 were $51.8 million, an increase of $5.8 million compared to $45.9 million during the year ended December 31, 2019. The increase reflects an increase of $96.9 million in non-cash charges primarily due to the absence of the reduction of our tax valuation allowance against substantially all of our deferred tax assets in the U.S. and $1.2 million from the net change in operating assets and liabilities, partially offset by a decrease of $92.2 million in net income.

Investing Activities. Cash flows used in investing activities during the year ended December 31, 2020 were $41.5 million, an increase of $26.8 million compared to cash used in investing activities of $68.3 million during the year ended December 31, 2019. Investing activities reflect continued net reinvestment of available cash and cash equivalents in our portfolio of marketable securities.

Financing Activities. Cash flows provided by financing activities during the year ended December 31, 2020 were $5.6 million, a decrease of $0.6 million compared to $6.3 million during the year ended December 31, 2019. Financing activities include proceeds from exercises of common stock options.

Off-Balance Sheet Arrangements

We have no off-balance sheet arrangements, as defined in Item 303(a)(4) of the Securities and Exchange Commission's Regulation S-K.

Contractual Obligations and Commitments

The following is a summary of our non-cancellable long-term contractual cash obligations as of December 31, 2020:

	Cash payments due by year (4)						
(in thousands)	Total	2021	2022	2023	2024	2025	Thereafter
Operating leases (1)	$ 18,032	$ 2,290	$ 2,611	$ 2,462	$ 2,488	$ 2,557	$ 5,624
Milestone obligation (2)	350	350	—	—	—	—	—
Purchase commitments (3)	1,447	966	481	—	—	—	—
Total non-cancellable long-term contractual cash obligations	$ 19,829	$ 3,606	$ 3,092	$ 2,462	$ 2,488	$ 2,557	$ 5,624

(1) Operating leases include the minimum lease payments for our operating lease liabilities. This table does not include obligations under short-term lease agreements, variable payments for building maintenance and other services and executory costs associated with our operating lease agreements.

(2) This table includes a probable future $350,000 milestone obligation under our license agreement with University of California San Francisco due upon the conclusion of a Phase I study. This table does not include potential future milestone obligations under our license agreements for which we have not deemed it probable that the milestone event will occur as of December 31, 2020. See Part I, Item 1, *Business - License Agreements*, of this Annual Report, for a description of our licensing arrangements and remaining milestone obligations.

(3) Purchase commitments include non-cancellable purchase commitments for agreements longer than one year and primarily relate to commitments for data services. This table does not include various other long-term agreements entered into for services with other third-party vendors, such as inventory purchase commitments, due to the cancellable nature of the services or variable terms within the agreement. Additionally, this table does not include rebates, chargebacks or discounts recorded as liabilities at the time that product sales are recognized as revenue.

(4) This table does not include liabilities related to uncertain tax positions taken as of December 31, 2020. Due to the uncertainties in the timing of potential tax audits, the timing associated with the resolution of these positions is also uncertain.

ITEM 7A. QUALITATIVE AND QUANTITATIVE DISCLOSURES ABOUT MARKET RISK

Interest Rate Risks

Our exposure to market risk is currently confined to our cash and cash equivalents, marketable securities and restricted cash. We currently do not hedge interest rate exposure. We have not used derivative financial instruments for speculation or trading purposes. Because of the short-term maturities of our cash and cash equivalents and marketable securities, we do not believe that an increase in market rates would have any significant impact on the realized value of our investments.

Concentrations of Credit Risk

We deposit our cash with financial institutions that we consider to be of high credit quality and purchase marketable securities that are generally investment grade, liquid, short-term fixed income securities and money-market instruments denominated in U.S. dollars. Our marketable securities consist of commercial paper, corporate notes and U.S. government agency notes.

Revenues and accounts receivable are concentrated with specialty pharmacies and wholesalers. There were 5 major customers that each accounted for more than 10% of total revenues and, as a group, represented 95% of total revenues for the year ended December 31, 2020. There were 5 major customers that each accounted for more than 10% of accounts receivable and, as a group, represented 90% of total accounts receivable at December 31, 2020. We mitigate our credit risk relating to accounts receivable from customers by performing ongoing credit evaluations.

Foreign Currency Risk

We are exposed to risks related to changes in foreign currency exchange rates relating to our foreign operations. The functional currency of our international subsidiaries is the local currency. We are exposed to foreign currency risk to the extent

that we enter into transactions denominated in currencies other than our subsidiaries' respective functional currencies. We are also exposed to unfavorable fluctuations of the U.S. dollar, which is our reporting currency, against the currencies of our operating subsidiaries when their respective financial statements are translated into U.S. dollars for inclusion in our consolidated financial statements. We do not currently hedge our foreign currency exchange rate risk. Foreign currency has not had a material impact on our results of operations.

Effects of inflation

Inflation has not had a material impact on our results of operations.

ITEM 8. FINANCIAL STATEMENTS AND SUPPLEMENTARY DATA

The consolidated financial statements and related financial statement schedules required to be filed are listed in the Index to Consolidated Financial Statements and are incorporated in Part IV, Item 15 of this Annual Report.

ITEM 9. CHANGES IN AND DISAGREEMENTS WITH ACCOUNTANTS ON ACCOUNTING AND FINANCIAL DISCLOSURE

None.

ITEM 9A. CONTROLS AND PROCEDURES

Conclusion Regarding the Effectiveness of Disclosure Controls and Procedures

Under the supervision and with the participation of our management, including the Chief Executive Officer and Chief Financial Officer, we evaluated the effectiveness of the design and operation of our disclosure controls and procedures (as defined in Rules 13a-15(e) and 15d-15(e) under the Securities Exchange Act of 1934 (Exchange Act)) as of December 31, 2020. Based upon that evaluation, our Chief Executive Officer and Chief Financial Officer concluded that our disclosure controls and procedures are effective as of December 31, 2020, the end of the period covered by this Annual Report, to ensure that the information required to be disclosed by us in the reports that we file or submit under the Exchange Act is recorded, processed, summarized and reported within the time periods specified in the SEC's rules and forms, and that such information is accumulated and communicated to our management, including our Chief Executive Officer and Chief Financial Officer, as appropriate to allow timely decisions regarding required disclosures.

Management's Report on Internal Control over Financial Reporting

Our management is responsible for establishing and maintaining an adequate system of internal control over financial reporting, as defined in the Exchange Act Rule 13a-15(f). Management conducted an assessment of our internal control over financial reporting based on the original framework established in 2013 by the Committee of Sponsoring Organizations of the Treadway Commission in *Internal Control — Integrated Framework.* Based on the assessment, management concluded that, as of December 31, 2020, our internal control over financial reporting was effective. The effectiveness of our internal control over financial reporting as of December 31, 2020 has been audited by PricewaterhouseCoopers LLP, an independent registered public accounting firm, as stated in their report included in this Annual Report.

Changes in Internal Control over Financial Reporting

There has been no change in our internal control over financial reporting (as defined in Rules 13a-15(f) and 15d-15(f) under the Exchange Act) during the fourth quarter of 2020 that has materially affected, or is reasonably likely to materially affect, our internal control over financial reporting.

ITEM 9B. OTHER INFORMATION

None.

PART III

ITEM 10. DIRECTORS, EXECUTIVE OFFICERS AND CORPORATE GOVERNANCE

Information required under this item will be contained in our Proxy Statement for the 2021 Annual Meeting of Stockholders to be filed with the SEC within 120 days after the end of the fiscal year ended December 31, 2020 and is incorporated herein by reference pursuant to General Instruction G(3) to Form 10-K.

ITEM 11. EXECUTIVE COMPENSATION

Information required under this item will be contained in our Proxy Statement for the 2021 Annual Meeting of Stockholders to be filed with the SEC within 120 days after the end of the fiscal year ended December 31, 2020 and is incorporated herein by reference pursuant to General Instruction G(3) to Form 10-K, except that information required by Item 407(e)(5) of Regulation S-K will be deemed furnished in this Form 10-K and will not be deemed incorporated by reference into any filing under the Securities Act of 1933, as amended, or the Securities Exchange Act of 1934, as amended, except to the extent that we specifically incorporate it by reference into such filing.

ITEM 12. SECURITY OWNERSHIP OF CERTAIN BENEFICIAL OWNERS AND MANAGEMENT AND RELATED STOCKHOLDER MATTERS

Information required under this item will be contained in our Proxy Statement for the 2021 Annual Meeting of Stockholders to be filed with the SEC within 120 days after the end of the fiscal year ended December 31, 2020 and is incorporated herein by reference pursuant to General Instruction G(3) to Form 10-K.

ITEM 13. CERTAIN RELATIONSHIPS AND RELATED TRANSACTIONS, AND DIRECTOR INDEPENDENCE

Information required under this item will be contained in our Proxy Statement for the 2021 Annual Meeting of Stockholders to be filed with the SEC within 120 days after the end of the fiscal year ended December 31, 2020 and is incorporated herein by reference pursuant to General Instruction G(3) to Form 10-K.

ITEM 14. PRINCIPAL ACCOUNTANT FEES AND SERVICES

Information required under this item will be contained in our Proxy Statement for the 2021 Annual Meeting of Stockholders to be filed with the SEC within 120 days after the end of the fiscal year ended December 31, 2020 and is incorporated herein by reference pursuant to General Instruction G (3) to Form 10-K.

PART IV

ITEM 15. EXHIBITS AND FINANCIAL STATEMENTS SCHEDULES

The consolidated financial statements filed as part of this annual report on Form 10-K are listed in the Index to Consolidated Financial Statements. Certain schedules are omitted because they are not applicable, or not required, or because the required information is included in the consolidated financial statements or notes thereto. The Exhibits are listed in the Exhibit Index.

Signatures

Pursuant to the requirements of Section 13 and 15(d) of the Securities Exchange Act of 1934, as amended, the registrant has duly caused this annual report on Form 10-K to be signed on its behalf by the undersigned, thereunto duly authorized.

Vanda Pharmaceuticals Inc.

February 11, 2021

By: /s/ Mihael H. Polymeropoulos, M.D.
Mihael H. Polymeropoulos, M.D.
President and Chief Executive Officer

Pursuant to the requirements of the Securities Act of 1934, this annual report on Form 10-K has been signed below by the following persons on behalf of the registrant and in the capacities and on the dates indicated.

Name	Title	Date
/s/ Mihael H. Polymeropoulos, M.D. Mihael H. Polymeropoulos, M.D.	President and Chief Executive Officer and Director (Principal Executive Officer)	February 11, 2021
/s/ Kevin Moran Kevin Moran	Chief Financial Officer (Principal Financial Officer and Principal Accounting Officer)	February 11, 2021
/s/ H. Thomas Watkins H. Thomas Watkins	Chairman of the Board and Director	February 11, 2021
/s/ Anne Sempowski Ward Anne Sempowski Ward	Director	February 11, 2021
/s/ Phaedra Chrousos Phaedra Chrousos	Director	February 11, 2021
/s/ Richard W. Dugan Richard W. Dugan	Director	February 11, 2021
/s/ Stephen Ray Mitchell Stephen Ray Mitchell	Director	February 11, 2021

Vanda Pharmaceuticals Inc.

Index to Consolidated Financial Statements

Report of Independent Registered Public Accounting Firm

To the Board of Directors and Stockholders of Vanda Pharmaceuticals Inc.

Opinions on the Financial Statements and Internal Control over Financial Reporting

We have audited the accompanying consolidated balance sheets of Vanda Pharmaceuticals Inc. and its subsidiaries (the "Company") as of December 31, 2020 and 2019, and the related consolidated statements of operations, of comprehensive income, of changes in stockholders' equity and of cash flows for each of the three years in the period ended December 31, 2020, including the related notes (collectively referred to as the "consolidated financial statements"). We also have audited the Company's internal control over financial reporting as of December 31, 2020, based on criteria established in *Internal Control - Integrated Framework* (2013) issued by the Committee of Sponsoring Organizations of the Treadway Commission (COSO).

In our opinion, the consolidated financial statements referred to above present fairly, in all material respects, the financial position of the Company as of December 31, 2020 and 2019, and the results of its operations and its cash flows for each of the three years in the period ended December 31, 2020 in conformity with accounting principles generally accepted in the United States of America. Also in our opinion, the Company maintained, in all material respects, effective internal control over financial reporting as of December 31, 2020, based on criteria established in *Internal Control - Integrated Framework* (2013) issued by the COSO.

Change in Accounting Principle

As discussed in Note 2 to the consolidated financial statements, the Company changed the manner in which it accounts for leases in 2019.

Basis for Opinions

The Company's management is responsible for these consolidated financial statements, for maintaining effective internal control over financial reporting, and for its assessment of the effectiveness of internal control over financial reporting, included in Management's Report on Internal Control over Financial Reporting appearing under Item 9A. Our responsibility is to express opinions on the Company's consolidated financial statements and on the Company's internal control over financial reporting based on our audits. We are a public accounting firm registered with the Public Company Accounting Oversight Board (United States) (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 audits to obtain reasonable assurance about whether the consolidated financial statements are free of material misstatement, whether due to error or fraud, and whether effective internal control over financial reporting was maintained in all material respects.

Our audits of the consolidated financial statements included performing procedures to assess the risks of material misstatement of the consolidated 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 consolidated 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 consolidated financial statements. Our audit of internal control over financial reporting included obtaining an understanding of internal control over financial reporting, assessing the risk that a material weakness exists, and testing and evaluating the design and operating effectiveness of internal control based on the assessed risk. Our audits also included performing such other procedures as we considered necessary in the circumstances. We believe that our audits provide a reasonable basis for our opinions.

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 (i) pertain to the maintenance of records that, in reasonable detail, accurately and fairly reflect the transactions and dispositions of the assets of the company; (ii) 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 (iii) 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.

Critical Audit Matters

The critical audit matter communicated below is a matter arising from the current period audit of the consolidated financial statements that was communicated or required to be communicated to the audit committee and that (i) relates to accounts or disclosures that are material to the consolidated financial statements and (ii) 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 matter below, providing a separate opinion on the critical audit matter or on the accounts or disclosures to which it relates.

Medicaid Rebates for Fanapt®

As described in Note 2 to the consolidated financial statements, the allowances for rebates include mandated discounts under the Medicaid Drug Rebate Program as well as contracted rebate programs with other payors. Rebate amounts owed after the final dispensing of the product to a benefit plan participant are based upon contractual agreements or legal requirements with public sector benefit providers, such as Medicaid. The allowance for rebates is based on statutory or contracted discount rates and estimated patient utilization. The Company has recorded product revenue allowances of $34.4 million as of December 31, 2020, of which a significant amount relates to allowances for Fanapt® Medicaid rebates.

The principal considerations for our determination that performing procedures relating to the Fanapt® Medicaid rebates is a critical audit matter are the significant judgment by management due to the significant measurement uncertainty involved in developing the allowances, as these allowances are based on assumptions developed for estimated patient utilization, primarily payor mix and invoice lag; this in turn led to a high degree of auditor judgment, subjectivity and effort in performing procedures and evaluating audit evidence related to the estimated patient utilization assumption.

Addressing the matter involved performing procedures and evaluating audit evidence in connection with forming our overall opinion on the consolidated financial statements. These procedures included testing the effectiveness of controls relating to the allowances for Fanapt® Medicaid rebates, including controls over the assumptions used to estimate these rebates. These procedures also included, among others, (i) developing an independent estimate of the Fanapt® Medicaid rebates by utilizing third-party information related to patient utilization, as well as the historical trends of the invoice lag; and (ii) comparing the independent estimate to management's estimate. Developing the independent estimate involved (i) testing the completeness and accuracy of the patient utilization data from third-party reports, and (ii) testing rebate claims processed by the Company, including evaluating those claims for consistency with the contractual and mandated terms of the Medicaid Drug Rebate Program.

/s/ PricewaterhouseCoopers LLP

Baltimore, Maryland
February 11, 2021

We have served as the Company's auditor since 2003.

VANDA PHARMACEUTICALS INC.
CONSOLIDATED BALANCE SHEETS

(in thousands, except for share and per share amounts)	December 31, 2020	December 31, 2019
ASSETS		
Current assets:		
Cash and cash equivalents	$ 61,031	$ 45,072
Marketable securities	306,709	267,057
Accounts receivable, net	30,036	26,367
Inventory	1,280	1,140
Prepaid expenses and other current assets	10,089	14,500
Total current assets	409,145	354,136
Property and equipment, net	4,136	3,864
Operating lease right-of-use assets	10,459	11,180
Intangible assets, net	21,559	23,037
Deferred tax assets	81,516	87,680
Non-current inventory and other	6,641	3,851
Total assets	$ 533,456	$ 483,748
LIABILITIES AND STOCKHOLDERS' EQUITY		
Current liabilities:		
Accounts payable and accrued liabilities	$ 31,509	$ 27,590
Product revenue allowances	34,427	31,915
Total current liabilities	65,936	59,505
Operating lease non-current liabilities	11,497	12,455
Other non-current liabilities	2,757	843
Total liabilities	80,190	72,803
Commitments and contingencies (Notes 10 and 17)		
Stockholders' equity:		
Preferred stock, $0.001 par value; 20,000,000 shares authorized, and no shares issued or outstanding at December 31, 2020 and 2019, respectively	—	—
Common stock, $0.001 par value; 150,000,000 shares authorized; 54,865,092 and 53,549,612 shares issued and outstanding at December 31, 2020 and 2019, respectively	55	54
Additional paid-in capital	650,300	631,307
Accumulated other comprehensive income	239	249
Accumulated deficit	(197,328)	(220,665)
Total stockholders' equity	453,266	410,945
Total liabilities and stockholders' equity	$ 533,456	$ 483,748

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

VANDA PHARMACEUTICALS INC.
CONSOLIDATED STATEMENTS OF OPERATIONS

(in thousands, except for share and per share amounts)	Year Ended December 31, 2020	2019	2018
Revenues:			
Net product sales	$ 248,168	$ 227,188	$ 193,118
Total revenues	248,168	227,188	193,118
Operating expenses:			
Cost of goods sold excluding amortization	23,364	24,488	20,508
Research and development	55,577	48,649	43,594
Selling, general and administrative	140,510	129,736	105,751
Intangible asset amortization	1,478	1,505	1,527
Total operating expenses	220,929	204,378	171,380
Income from operations	27,239	22,810	21,738
Other income	4,416	6,218	3,608
Income before income taxes	31,655	29,028	25,346
Provision (benefit) for income taxes	8,318	(86,525)	138
Net income	$ 23,337	$ 115,553	$ 25,208
Net income per share:			
Basic	$ 0.43	$ 2.17	$ 0.50
Diluted	$ 0.42	$ 2.11	$ 0.48
Weighted average shares outstanding:			
Basic	54,427,683	53,137,562	50,859,947
Diluted	55,190,802	54,847,060	53,045,257

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

VANDA PHARMACEUTICALS INC.
CONSOLIDATED STATEMENTS OF COMPREHENSIVE INCOME

(in thousands)	Year Ended December 31, 2020	2019	2018
Net income	$ 23,337	$ 115,553	$ 25,208
Other comprehensive income (loss):			
Net foreign currency translation gain (loss)	68	6	(22)
Change in net unrealized gain (loss) on marketable securities	(102)	313	57
Tax benefit (provision) on other comprehensive income	24	(71)	—
Other comprehensive income (loss), net of tax	(10)	248	35
Comprehensive income	$ 23,327	$ 115,801	$ 25,243

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

VANDA PHARMACEUTICALS INC.
CONSOLIDATED STATEMENTS OF CHANGES IN STOCKHOLDERS' EQUITY

(in thousands, except for share amounts)	Common Stock		Additional Paid-in Capital	Accumulated Other Comprehensive Income (Loss)	Accumulated Deficit	Total
	Shares	Par Value				
Balances at December 31, 2017	44,938,133	$ 45	$ 492,802	$ (34)	$ (361,426)	$ 131,387
Net proceeds from public offering of common stock	6,325,000	6	100,864	—	—	100,870
Issuance of common stock from the exercise of stock options and settlement of restricted stock units	1,214,460	1	6,255	—	—	6,256
Stock-based compensation expense	—	—	11,666	—	—	11,666
Net income	—	—	—	—	25,208	25,208
Other comprehensive income, net of tax	—	—	—	35	—	35
Balances at December 31, 2018	52,477,593	52	611,587	1	(336,218)	275,422
Issuance of common stock from the exercise of stock options and settlement of restricted stock units	1,072,019	2	6,262	—	—	6,264
Stock-based compensation expense	—	—	13,458	—	—	13,458
Net income	—	—	—	—	115,553	115,553
Other comprehensive income, net of tax	—	—	—	248	—	248
Balances at December 31, 2019	53,549,612	54	631,307	249	(220,665)	410,945
Issuance of common stock from the exercise of stock options and settlement of restricted stock units	1,315,480	1	5,633	—	—	5,634
Stock-based compensation expense	—	—	13,360	—	—	13,360
Net income	—	—	—	—	23,337	23,337
Other comprehensive loss, net of tax	—	—	—	(10)	—	(10)
Balances at December 31, 2020	54,865,092	$ 55	$ 650,300	$ 239	$ (197,328)	$ 453,266

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

VANDA PHARMACEUTICALS INC.
CONSOLIDATED STATEMENTS OF CASH FLOWS

(in thousands)	Year Ended December 31, 2020	2019	2018
Cash flows from operating activities			
Net income	$ 23,337	$ 115,553	$ 25,208
Adjustments to reconcile net income to net cash provided by operating activities:			
Depreciation of property and equipment	1,386	1,387	1,429
Stock-based compensation	13,360	13,458	11,666
Amortization of premiums and accretion of discounts on marketable securities	179	(3,099)	(2,221)
Gain on sale of marketable securities	(229)	—	—
Intangible asset amortization	1,478	1,505	1,527
Deferred income taxes	6,189	(87,767)	—
Other non-cash adjustments, net	1,758	1,785	167
Changes in operating assets and liabilities:			
Accounts receivable	(3,767)	2,342	(11,207)
Prepaid expenses and other assets	4,068	(2,764)	(4,258)
Inventory	(2,876)	(722)	70
Accounts payable and other liabilities	3,759	3,508	(618)
Product revenue allowances	3,133	761	8,223
Net cash provided by operating activities	51,775	45,947	29,986
Cash flows from investing activities			
Acquisition of intangible asset	—	—	(25,000)
Purchases of property and equipment	(1,795)	(1,019)	(368)
Purchases of marketable securities	(346,622)	(394,517)	(282,395)
Sales and maturities of marketable securities	306,918	327,227	198,103
Net cash used in investing activities	(41,499)	(68,309)	(109,660)
Cash flows from financing activities			
Net proceeds from offering of common stock	—	—	100,870
Proceeds from exercise of stock options	5,634	6,264	6,256
Net cash provided by financing activities	5,634	6,264	107,126
Effect of exchange rate changes on cash, cash equivalents and restricted cash	53	(1)	(38)
Net change in cash, cash equivalents and restricted cash	15,963	(16,099)	27,414
Cash, cash equivalents and restricted cash			
Beginning of year	45,650	61,749	34,335
End of year	$ 61,613	$ 45,650	$ 61,749

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

VANDA PHARMACEUTICALS INC.

NOTES TO CONSOLIDATED FINANCIAL STATEMENTS

1. Business Organization and Presentation

Business Organization

Vanda Pharmaceuticals Inc. (the Company) is a global biopharmaceutical company focused on the development and commercialization of innovative therapies to address high unmet medical needs and improve the lives of patients. The Company commenced its operations in 2003 and operates in one reporting segment.

The Company's commercial portfolio is currently comprised of two products, HETLIOZ® for the treatment of Non-24-Hour Sleep-Wake Disorder (Non-24) and nighttime sleep disturbances in Smith-Magenis Syndrome (SMS) and Fanapt® for the treatment of schizophrenia. HETLIOZ® is the first treatment for patients with Non-24 and SMS approved by the United States Food and Drug Administration (FDA). In addition, the Company has a number of drugs in development, including:

- HETLIOZ® (tasimelteon) for the treatment of jet lag disorder, pediatric Non-24, delayed sleep phase disorder (DSPD) and autism spectrum disorder (ASD);
- Fanapt® (iloperidone) for the treatment of bipolar disorder and Parkinson's disease psychosis (PDP) and a long acting injectable (LAI) formulation for the treatment of schizophrenia;
- Tradipitant (VLY-686), a small molecule neurokinin-1 receptor (NK-1R) antagonist, for the treatment of gastroparesis, motion sickness, atopic dermatitis, and COVID-19 pneumonia;
- VTR-297, a small molecule histone deacetylase (HDAC) inhibitor for the treatment of hematologic malignancies and with potential use as a treatment for several oncology indications;
- Portfolio of Cystic Fibrosis Transmembrane Conductance Regulator (CFTR) activators and inhibitors, including VSJ-110 for the treatment of dry eye and ocular inflammation and BPO-27 for the treatment of secretory diarrhea disorders, including cholera; and
- VQW-765, a small molecule nicotinic acetylcholine receptor partial agonist, with potential use for the treatment of psychiatric disorders.

Basis of Presentation

The accompanying consolidated financial statements includes the accounts of Vanda Pharmaceuticals Inc. and its wholly-owned subsidiaries and have been prepared in accordance with accounting principles generally accepted in the United States of America (GAAP). All intercompany accounts and transactions have been eliminated in consolidation.

2. Summary of Significant Accounting Policies

Use of Estimates

The preparation of financial statements in conformity with GAAP requires management to make estimates that affect the reported amounts of assets and liabilities at the date of the financial statements, disclosure of contingent assets and liabilities, and the reported amounts of revenue and expenses during the reporting period. Management continually re-evaluates its estimates, judgments and assumptions, and management's evaluation could change. Actual results could differ from those estimates.

Cash, Cash Equivalents and Restricted Cash

For purposes of the Consolidated Balance Sheets and Consolidated Statements of Cash Flows, cash equivalents represent highly-liquid investments with a maturity date of three months or less at the date of purchase. Cash and cash equivalents include investments in money market funds with commercial banks and financial institutions, and commercial paper of high-quality corporate issuers. Restricted cash relates primarily to amounts held as collateral for letters of credit for leases for office space at the Company's Washington, D.C. headquarters.

The following table provides a reconciliation of cash, cash equivalents and restricted cash reported within the Consolidated Balance Sheets to the total end of period cash, cash equivalents and restricted cash reported within the Consolidated Statement of Cash Flows:

	December 31,	
(in thousands)	2020	2019
Cash and cash equivalents	$ 61,031	$ 45,072
Restricted cash included in:		
Prepaid expenses and other current assets	57	—
Non-current inventory and other	525	578
Total cash, cash equivalents and restricted cash	$ 61,613	$ 45,650

Marketable Securities

The Company classifies all of its marketable securities as available-for-sale securities. The Company's investment policy requires the selection of high-quality issuers. Available-for-sale securities are carried at fair market value, with unrealized gains and losses reported as a component of stockholders' equity in accumulated other comprehensive income. At each balance sheet date, the Company assesses available-for-sale securities in an unrealized loss position to determine whether it intends to sell or if it is more likely than not that the Company will be required to sell the security before recovery of its amortized cost basis. If either of the criteria regarding intent or requirement to sell is met, the security's amortized cost basis is written down to fair value. The Company also reviews its available-for-sale securities in an unrealized loss position to determine whether the unrealized loss is the result of a change in creditworthiness or other factors. If declines in the value of available for-sale securities are determined to be credit-related, a loss is recorded in earnings in the current period. Interest and dividend income is recorded when earned and included in other income. Premiums and discounts on marketable securities are amortized and accreted, respectively, to earliest call date and maturity, respectively, and included in other income. The Company uses the specific identification method in computing realized gains and losses on the sale of investments, which would be included in the Consolidated Statements of Operations when generated. All available-for-sale marketable securities are available for use in current operations and are classified as current.

Inventory

Inventory, which is recorded at the lower of cost or net realizable value, includes the cost of third-party manufacturing and other direct and indirect costs and is valued using the first-in, first-out method. The Company evaluates expiry risk by evaluating current and future product demand relative to product shelf life. The Company builds demand forecasts by considering factors such as, but not limited to, overall market potential, market share, market acceptance and patient usage. The Company capitalizes inventory costs associated with its products upon regulatory approval when, based on management's judgment, future commercialization is considered probable and the future economic benefit is expected to be realized; otherwise, such costs are expensed as research and development. Inventory levels are evaluated for the amount of inventory that would be sold within one year. At certain times, the level of inventory can exceed the forecasted level of cost of goods sold for the next 12 months. The Company classifies the estimate of such inventory as non-current.

Intangible Assets

Costs incurred for products not yet approved by the FDA and for which no alternative future use exists are recorded as research and development expense. Obligations for milestone payments to other pharmaceutical companies that may result in a capitalized intangible asset are recognized when it is deemed probable that the milestone event will occur. In the event a product has been approved by the FDA or an alternative future use exists for a product, patent and license costs are capitalized and amortized on a straight-line basis over the estimated useful economic life of the of the related product patents. For intangible assets related to HETLIOZ®, the estimated useful life is through July 2035, which is the estimated economic useful life of the related product patents. Intangible assets related Fanapt® have been fully amortized on a straight-line basis to November 2016. The useful life estimate for Fanapt® was based on the market participant methodology prescribed by ASC 805, and therefore does not reflect the impact of additional Fanapt® patents solely owned by the Company with varying expiration dates, the latest of which is December 2031.

Property and Equipment

Property and equipment are stated at cost less accumulated depreciation. Depreciation of most property and equipment is provided on a straight-line basis over the estimated useful lives of the assets. Leasehold improvements are amortized using a

straight-line basis over the lesser of the estimated useful lives of the assets or the terms of the related leases. The costs of additions and improvements are capitalized, and repairs and maintenance costs are charged to operations in the period incurred. Upon retirement or disposition of property and equipment, the cost and accumulated depreciation are removed from the accounts and any resulting gain or loss is reflected in the statement of operations for that period.

Leases

In accordance with Accounting Standards Codification (ASC) 842, *Leases*, effective January 1, 2019, the Company determines if an arrangement contains a lease at inception. Right-of-use (ROU) assets represent the Company's right to use an underlying asset for the lease term and lease liabilities represent the Company's obligation to make lease payments arising from that lease. For leases with a term greater than 12 months, ROU assets and liabilities are recognized at the lease commencement date based on the estimated present value of lease payments over the lease term. The lease term includes the option to extend the lease when it is reasonably certain the Company will exercise that option. When available, the Company uses the rate implicit in the lease to discount lease payments to present value. In the case the implicit rate is not available, the Company uses its incremental borrowing rate based on information available at the lease commencement date, including publicly available data for instruments with similar characteristics, to determine the present value of lease payments. The Company does not combine lease and non-lease elements for office leases. For existing office leases as of January 1, 2019, executory costs are excluded from lease expense, which is consistent with the Company's accounting under ASC 840, *Leases*. For all office leases entered into after January 1, 2019, executory costs are allocated between lease and non-lease elements based upon their relative stand-alone prices.

Accounts Payable and Accrued Liabilities

The Company’s management is required to estimate accrued liabilities as part of the process of preparing financial statements. The estimation of accrued liabilities involves identifying services that have been performed on the Company’s behalf, and then estimating the level of service performed and the associated cost incurred for such services as of each balance sheet date in the financial statements. Accrued liabilities include research and development expenses, such as accrued costs under contracts with clinical monitors, data management organizations and investigators in conjunction with clinical trials, fees to contract manufacturers in conjunction with the production of clinical materials, consulting and professional fees, such as lawyers and fees for marketing and other commercialization activities, accrued compensation and employee benefits, such as accrued bonus, royalties payable under licensing agreements, and other accrued fees. Pursuant to management’s assessment of the services that have been performed on clinical trials and other contracts, the Company recognizes these expenses as the services are provided. Such management assessments include, but are not limited to: (i) an evaluation by the project manager of the work that has been completed during the period, (ii) measurement of progress prepared internally and/or provided by the third-party service provider, (iii) analyses of data that justify the progress, and (iv) management’s judgment. In the event that the Company does not identify certain costs that have begun to be incurred or the Company under- or over-estimates the level of services performed or the costs of such services, the Company’s reported expenses for such period would be too low or too high.

Revenue from Net Product Sales

In accordance with ASC 606, *Revenue from Contracts with Customers* (ASC 606), which the Company adopted January 1, 2018, the Company accounts for a contract when it has approval and commitment from both parties, the rights of the parties are identified, payment terms are identified, the contract has commercial substance and collectability of consideration is probable. The Company recognizes revenue when control of the product is transferred to the customer in an amount that reflects the consideration the Company expects to be entitled to in exchange for those product sales, which is typically once the product physically arrives at the customer. Sales taxes, value add taxes, and usage-based taxes are excluded from revenues.

The Company’s net product sales consist of sales of HETLIOZ® and Fanapt®. Net sales by product for the years ended December 31, 2020, 2019 and 2018 were as follows:

	Year Ended December 31,		
(*in thousands*)	2020	2019	2018
HETLIOZ® net product sales	$ 160,686	$ 142,980	$ 115,835
Fanapt® net product sales	87,482	84,208	77,283
Total net product sales	$ 248,168	$ 227,188	$ 193,118

HETLIOZ® is available in the United States (U.S.) for distribution through a limited number of specialty pharmacies, and is not available in retail pharmacies. Specialty pharmacy customers include Diplomat Pharmacy, Inc. (a subsidiary of

UnitedHealth Group) and Accredo (a subsidiary of Express Scripts). Fanapt® is available in the U.S. for distribution through a limited number of wholesalers and is available in retail pharmacies. Wholesaler customers include Cardinal Health, Inc., AmerisourceBergen Drug Corporation, and McKesson Corporation. The Company invoices and records revenue when its customers, specialty pharmacies and wholesalers, receive product from the third-party logistics warehouse, which is the point at which control is transferred to the customer. Revenues and accounts receivable are concentrated with these customers. Outside the U.S., the Company sells HETLIOZ® in Germany and has a distribution agreement for the commercialization of Fanapt® in Israel. Receivables are carried at transaction price net of allowance for credit losses. Allowance for credit losses is measured using historical loss rates based on the aging of receivables and incorporating current conditions and forward-looking estimates.

The following table presents each major customer that represented more than 10% of total revenues for the years ended December 31, 2020, 2019 and 2018:

	Year Ended December 31,		
Percent of Net Product Sales	**2020**	**2019**	**2018**
Distributor A	43 %	38 %	37 %
Distributor B	19 %	23 %	17 %
Distributor C	12 %	12 %	14 %
Distributor D	11 %	12 %	12 %
Distributor E	10 %	11 %	12 %

The following table presents each major customer that represented more than 10% of accounts receivable, net, as of December 31, 2020 and 2019:

	December 31,	
Percent of Accounts Receivable, Net	**2020**	**2019**
Distributor A	22 %	21 %
Distributor B	13 %	21 %
Distributor C	22 %	18 %
Distributor D	20 %	16 %
Distributor E	13 %	18 %

The transaction price is determined based upon the consideration to which the Company will be entitled in exchange for transferring product to the customer. The Company's product sales are recorded net of applicable product revenue allowances for which reserves are established and include discounts, rebates, chargebacks, service fees, co-pay assistance and product returns that are applicable for various government and commercial payors. The Company estimates the amount of variable consideration that should be included in the transaction price utilizing the most likely amount method and updates its estimate at each reporting date. Variable consideration is included in the transaction price if, in the Company's judgment, it is probable that a significant future reversal of cumulative revenue under the contract will not occur. Allowances for rebates, chargebacks and co-pay assistance are based upon the insurance benefits of the end customer, which are estimated using historical activity and, where available, actual and pending prescriptions for which the Company has validated the insurance benefits. Reserves for variable consideration are classified as product revenue allowances on the Consolidated Balance Sheets, with the exception of prompt-pay discounts that are classified as reductions of accounts receivable. The reserve for product returns for which the product may not be returned for a period of greater than one year from the balance sheet date is included as a component of other non-current liabilities in the Consolidated Balance Sheets. Uncertainties related to variable consideration are generally resolved in the quarter subsequent to period end, with the exception of Medicaid rebates, which are dependent upon the timing of when states submit reimbursement claims, and product returns that are resolved during the product expiry period specified in the customer contract. The Company currently records sales allowances for the following:

- *Prompt-pay:* Specialty pharmacies and wholesalers are offered discounts for prompt payment. The Company expects that the specialty pharmacies and wholesalers will earn prompt payment discounts and, therefore, deducts the full amount of these discounts from total product sales when revenues are recognized.
- *Rebates:* Allowances for rebates include mandated discounts under the Medicaid Drug Rebate Program as well as contracted rebate programs with other payors. Rebate amounts owed after the final dispensing of the product to a benefit plan participant are based upon contractual agreements or legal requirements with public sector benefit providers, such as Medicaid. The allowance for rebates is based on statutory or contracted discount rates and estimated patient utilization.

- *Chargebacks:* Chargebacks are discounts that occur when contracted indirect customers purchase directly from specialty pharmacies and wholesalers. Contracted indirect customers, which currently consist primarily of Public Health Service institutions and federal government entities purchasing via the Federal Supply Schedule, generally purchase the product at a discounted price. The specialty pharmacy or wholesaler, in turn, charges back the difference between the price initially paid by the specialty pharmacy or wholesaler and the discounted price paid to the specialty pharmacy or wholesaler by the contracted customer.
- *Medicare Part D Coverage Gap:* The Medicare Part D prescription drug benefit requires manufacturers to fund approximately 70% of the Medicare Part D insurance coverage gap for prescription drugs sold to eligible patients for applicable drugs. Vanda accounts for the Medicare Part D coverage gap using a point of sale model. Estimates for expected Medicare Part D coverage gap are based in part on historical activity and, where available, actual and pending prescriptions when the Company has validated the insurance benefits.
- *Service Fees:* The Company receives sales order management, data and distribution services from certain customers. These fees are based on contracted terms and are known amounts. The Company accrues service fees at the time of revenue recognition, resulting in a reduction of product sales and the recognition of an accrued liability, unless it is a payment for a distinct good or service from the customer in which case the fair value of those distinct goods or services are recorded as selling, general and administrative expense.
- *Co-payment Assistance:* Patients who have commercial insurance and meet certain eligibility requirements may receive co-payment assistance. Co-pay assistance utilization is based on information provided by the Company's third-party administrator.
- *Product Returns*: The Company generally offers direct customers a limited right to return as contractually defined with its customers. The Company considers several factors in the estimation process, including expiration dates of product shipped to customers, inventory levels within the distribution channel, product shelf life, historical return activity, including activity for product sold for which the return period has past, prescription trends and other relevant factors. The Company does not expect returned goods to be resalable. There was no right of return asset as of December 31, 2020 or 2019. The following table summarizes activity for product returns as of and for the years ended December 31, 2020, 2019 and 2018, all of which relates to sales of Fanapt®:

(in thousands)	Reserve for Product Returns
Balances at December 31, 2017	$ 4,119
Additions	2,684
Credits/payments	(1,616)
Balances at December 31, 2018	5,187
Additions	3,138
Credits/payments	(2,205)
Balances at December 31, 2019	6,120
Additions	3,844
Credits/payments	(5,266)
Balances at December 31, 2020	$ 4,698

Cost of Goods Sold

Cost of goods sold includes royalties payable, the cost of inventory sold, costs to write down inventory to net realizable value, manufacturing and supply chain costs and product shipping and handling costs related to sales of HETLIOZ® and Fanapt® to the Company's distribution partners.

Research and Development Expenses

Research and development expenses consist primarily of fees for services provided by third parties in connection with the clinical trials, costs of contract manufacturing services, milestone payments, costs of materials used in clinical trials and research and development, costs for regulatory consultants and filings, depreciation of capital resources used to develop products, related facilities costs, and salaries, other employee-related costs and stock-based compensation for research and development personnel. The Company expenses research and development costs as they are incurred for products in the development stage, including manufacturing costs and milestone payments made under license agreements prior to FDA approval. Upon and subsequent to FDA approval, manufacturing and milestone payments related to license agreements are

capitalized. Milestone payments are accrued when it is deemed probable that the milestone event will be achieved. Costs related to the acquisition of intellectual property are expensed as incurred if the underlying technology is developed in connection with the Company's research and development efforts and has no alternative future use.

Selling, General and Administrative Expenses

Selling, general and administrative expenses consist of salaries, stock-based compensation, facilities and third-party expenses. Selling, general and administrative expenses are associated with the activities of the corporate, finance, accounting, information technology, business development, commercial support, trade and distribution, sales, marketing, legal, medical affairs and human resource functions. Additionally, selling, general and administrative expenses included an estimate for the annual Affordable Care Act fee.

Stock-Based Compensation

Compensation costs for all stock-based awards to employees and directors are measured based on the grant date fair value of those awards and recognized over the period during which the employee or director is required to perform service in exchange for the award. The Company recognizes the expense over the award's vesting period. The fair value of stock options granted and restricted stock units (RSUs) awarded are amortized using the straight-line method. As stock-based compensation expense recognized in the Consolidated Statements of Operations is based on awards ultimately expected to vest, it has been reduced for estimated forfeitures. Forfeitures are estimated at the time of grant and revised, if necessary, in subsequent periods if actual forfeitures differ from those estimates.

Advertising Expense

The Company expenses the costs of advertising, including branded promotional expenses, as incurred. Branded advertising expenses, recorded in selling, general and administrative expenses, were $12.6 million, $3.2 million and $0.9 million for the years ended December 31, 2020, 2019 and 2018, respectively.

Foreign Currency

The reporting currency of the Company is the U.S. dollar. The functional currency of the Company's international subsidiaries is the local currency. Assets and liabilities denominated in foreign currencies, including intercompany balances for which settlement is anticipated in the foreseeable future, are translated at exchange rates in effect at the balance sheet date. Foreign currency equity balances are translated at historical rates. Revenues and expenses denominated in foreign currencies are translated at average exchange rates for the respective periods. Foreign currency translation adjustments are recorded in accumulated other comprehensive income.

Transactions denominated in currencies other than subsidiaries' functional currencies are recorded based on exchange rates at the time such transactions arise. Changes in exchange rates with respect to amounts recorded in the Consolidated Balance Sheets related to these items will result in unrealized foreign currency transaction gains and losses based upon period-end exchange rates. The Company also records realized foreign currency transaction gains and losses upon settlement of the transactions. Foreign currency transaction gains and losses are included in other income and were not material for the years ended December 31, 2020, 2019 and 2018, respectively.

Income Taxes

The Company accounts for income taxes using the asset and liability method. Under the asset and liability method, current income tax expense or benefit is the amount of income taxes expected to be payable or refundable for the current year. A deferred income tax asset or liability is recognized for future tax consequences attributable to differences between the financial statement carrying amounts of existing assets and liabilities and their respective tax bases and tax credits and loss carryforwards. Deferred tax assets are reduced by a valuation allowance when, in the opinion of management, it is more likely than not that some portion of the deferred tax assets will not be realized. Tax rate changes are reflected in income during the period such changes are enacted. Changes in ownership may limit the amount of net operating loss (NOL) carryforwards that can be utilized in the future to offset taxable income. Tax benefits are recognized from an uncertain tax position only if it is more likely than not that the position will be sustained on examination by the taxing authorities based on the technical merits of the position. The tax benefit recognized in the financial statements for a particular tax position is based on the largest benefit that is more likely than not to be realized upon settlement.

Certain Risks and Uncertainties

The outbreak of the novel coronavirus known as COVID-19 has resulted in government-imposed quarantines, travel restrictions and other public health safety measures. As this pandemic endures, the extent to which COVID-19 may impact the Company's business, financial condition and results of operations is uncertain and will depend on many factors outside of the Company's control.

The Company's products under development require approval from the FDA or other international regulatory agencies prior to commercial sales. There can be no assurance the products will receive the necessary clearance. If the Company is denied clearance or clearance is delayed, it may have a material adverse impact on the Company.

The Company's products are concentrated in rapidly changing, highly competitive markets, which are characterized by rapid technological advances, changes in customer requirements and evolving regulatory requirements and industry standards. Any failure by the Company to anticipate or to respond adequately to technological developments in its industry, changes in customer requirements or changes in regulatory requirements or industry standards or any significant delays in the development or introduction of products or services could have a material adverse effect on the Company's business, operating results and future cash flows.

The Company depends on single source suppliers for critical raw materials for manufacturing, as well as other components required for the administration of its products. The loss of these suppliers could delay the clinical trials or prevent or delay commercialization of the products.

Concentrations of Credit Risk

Financial instruments, which potentially subject the Company to significant concentrations of credit risk, consist primarily of cash, cash equivalents and marketable securities. The Company places its cash, cash equivalents and marketable securities with highly rated financial institutions. At December 31, 2020, the Company maintained all of its cash, cash equivalents and marketable securities in two financial institutions. Deposits held with these institutions may exceed the amount of insurance provided on such deposits. Generally, these deposits may be redeemed upon demand, and the Company believes there is minimal risk of losses on such balances.

Segment and Geographic Information

The Company operates in one reporting segment and, accordingly, no segment disclosures are presented herein. Foreign sales were not material for each of the years ended December 31, 2020, 2019 and 2018.

Recent Accounting Pronouncements

In December 2019, the Financial Accounting Standards Board (FASB) issued Accounting Standards Update (ASU) 2019-12, *Income Taxes (Topic 740), Simplifying the Accounting for Income Taxes,* which clarifies and simplifies certain aspects of the accounting for income taxes. The standard is effective for years beginning after December 15, 2020, and interim periods within annual periods beginning after December 15, 2020. The adoption of this standard on January 1, 2021 is not expected to have a material impact on the Company's consolidated financial statements.

In June 2016, the FASB issued ASU 2016-13, *Financial Instruments – Credit Losses,* which changed the impairment model for most financial assets and certain other financial instruments. The standard requires the use of a forward-looking "expected loss" model for instruments measured at amortized cost that generally will result in the earlier recognition of allowances for losses. The standard is effective for years beginning after December 15, 2019, and interim periods within annual periods beginning after December 15, 2019. The adoption of this standard on January 1, 2020 did not have a material impact on the Company's consolidated financial results.

3. Marketable Securities

The following is a summary of the Company's available-for-sale marketable securities as of December 31, 2020, which all have contractual maturities of less than two years:

(in thousands)	Amortized Cost	Gross Unrealized Gains	Gross Unrealized Losses	Fair Market Value
U.S. Treasury and government agencies	$ 165,966	$ 129	$ (3)	$ 166,092
Corporate debt	140,538	87	(8)	140,617
Total marketable securities	$ 306,504	$ 216	$ (11)	$ 306,709

The following is a summary of the Company's available-for-sale marketable securities as of December 31, 2019, which all have contractual maturities of less than two years:

(in thousands)	Amortized Cost	Gross Unrealized Gains	Gross Unrealized Losses	Fair Market Value
U.S. Treasury and government agencies	$ 88,535	$ 68	$ (2)	$ 88,601
Corporate debt	129,860	196	(1)	130,055
Asset-backed securities	48,355	49	(3)	48,401
Total marketable securities	$ 266,750	$ 313	$ (6)	$ 267,057

4. Fair Value Measurements

Authoritative guidance establishes a three-tier fair value hierarchy, which prioritizes the inputs used in measuring fair value. These tiers include:

- Level 1 — defined as observable inputs such as quoted prices in active markets
- Level 2 — defined as inputs other than quoted prices in active markets that are either directly or indirectly observable
- Level 3 — defined as unobservable inputs in which little or no market data exists, therefore requiring an entity to develop its own assumptions

The Company's assets classified in Level 1 and Level 2 as of December 31, 2020 and 2019 consist of cash equivalents and available-for-sale marketable securities. The valuation of Level 1 instruments is determined using a market approach and is based upon unadjusted quoted prices for identical assets in active markets. The valuation of Level 2 instruments is also determined using a market approach based upon quoted prices for similar assets in active markets, or other inputs that are observable for substantially the full term of the financial instrument. Level 2 securities include certificates of deposit, commercial paper, corporate notes and asset-backed securities that use as their basis readily observable market parameters.

The Company held certain assets that are required to be measured at fair value on a recurring basis as of December 31, 2020, as follows:

		Fair Value Measurement as of December 31, 2020 Using		
(in thousands)	Total Fair Value	Quoted Prices in Active Markets for Identical Assets (Level 1)	Significant Other Observable Inputs (Level 2)	Significant Unobservable Inputs (Level 3)
U.S. Treasury and government agencies	$ 166,092	$ 166,092	$ —	$ —
Corporate debt	140,617	—	140,617	—
Total assets measured at fair value	$ 306,709	$ 166,092	$ 140,617	$ —

The Company held certain assets that are required to be measured at fair value on a recurring basis as of December 31, 2019, as follows:

		Fair Value Measurement as of December 31, 2019 Using		
(in thousands)	Total Fair Value	Quoted Prices in Active Markets for Identical Assets (Level 1)	Significant Other Observable Inputs (Level 2)	Significant Unobservable Inputs (Level 3)
U.S. Treasury and government agencies	$ 88,601	$ 88,601	$ —	$ —
Corporate debt	137,025	—	137,025	—
Asset-backed securities	48,401	—	48,401	—
Total assets measured at fair value	$ 274,027	$ 88,601	$ 185,426	$ —

Total assets measured at fair value as of December 31, 2020 include no cash equivalents. Total assets measured at fair value as of December 31, 2019 include $7.0 million of cash equivalents.

The Company also has financial assets and liabilities, not required to be measured at fair value on a recurring basis, which primarily consist of cash, accounts receivable, restricted cash, accounts payable and accrued liabilities, product revenue allowances, and milestone obligations under license agreements, the carrying values of which materially approximate their fair values.

5. Inventory

Inventory consisted of the following as of December 31, 2020 and 2019:

(in thousands)	December 31, 2020	December 31, 2019
Current assets		
Work-in-process	$ 66	$ —
Finished goods	1,214	1,140
Total inventory, current	$ 1,280	$ 1,140
Non-Current assets		
Raw materials	$ 744	$ 659
Work-in-process	4,045	1,109
Finished goods	302	1,056
Total inventory, non-current	5,091	2,824
Total inventory	$ 6,371	$ 3,964

6. Property and Equipment

The following is a summary of the Company's property and equipment, at cost, as of December 31, 2020 and 2019:

(in thousands)	Estimated Useful Life (Years)	December 31, 2020	December 31, 2019
Computer and other equipment	3	$ 5,212	$ 4,398
Furniture and fixtures	5 - 7	1,495	1,491
Leasehold improvements	5 - 11	5,457	4,587
Total property and equipment, gross		12,164	10,476
Accumulated depreciation and amortization		(8,028)	(6,612)
Total property and equipment, net		$ 4,136	$ 3,864

Depreciation expense was $1.4 million for each of the years ended December 31, 2020, 2019 and 2018.

7. Leases

The Company's long-term leases primarily include operating leases and subleases for office space in Washington, D.C. and London, England. The Company recognized ROU assets and lease liabilities related to fixed payments for these long-term operating leases in its Consolidated Balance Sheet as of December 31, 2020 and 2019. The Company also has short-term leases, including office space in Berlin, Germany.

In June 2011, the Company entered into an operating lease agreement under which it leases 33,534 square feet of office space for its headquarters at 2200 Pennsylvania Avenue, N.W. in Washington, D.C. Subject to the prior rights of other tenants, the Company has the right to renew the lease for five years following its expiration in July 2028. As of December 31, 2020, the renewal period has not been included in the lease term. The Company has the right to sublease or assign all or a portion of the premises, subject to standard conditions. The lease may be terminated early by the Company or the landlord under certain circumstances.

In June 2016, the Company entered into a sublease agreement under which it subleases an additional 9,928 square feet of office space for its headquarters at 2200 Pennsylvania Avenue, N.W. in Washington, D.C. The sublease term began in

January 2017 and ends in July 2026 but may be terminated earlier by either party under certain circumstances. The Company has the right to sublease or assign all or a portion of the premises, subject to standard conditions.

In May 2016, the Company entered into an operating lease agreement under which it leases 2,880 square feet of office space in London, England. In November 2020, the Company extended the non-cancellable portion of the lease term from 2021 to 2023 and has the option to renew the lease for an additional three years following its expiration.

The following is a summary of the Company's ROU assets and operating lease liabilities as of December 31, 2020 and 2019:

(in thousands)	Classification on the Balance Sheet	December 31, 2020	December 31, 2019
Assets			
Operating lease assets	Operating lease right-of-use assets	$ 10,459	$ 11,180
Liabilities			
Operating lease current liabilities	Accounts payable and accrued liabilities	$ 2,117	$ 2,147
Operating lease non-current liabilities	Operating lease non-current liabilities	11,497	12,455
Total lease liabilities		$ 13,614	$ 14,602
Weighted average remaining lease term		7.1	8.1
Weighted average discount rate[1]		8.1 %	8.1 %

(1) Upon adoption of the new lease standard, discount rates used for existing leases were established at January 1, 2019.

For each of the years ended December 31, 2020 and 2019, the Company recognized operating lease cost of $2.3 million and short-term operating lease cost of $0.4 million. The Company also recognized $1.5 million and $1.4 million, respectively, of expense related to non-lease elements, such as building maintenance services and utilities, and executory costs associated with the operating leases. For existing leases as of January 1, 2019, executory costs are excluded from operating lease expense, which is consistent with the Company's accounting under ASC 840. For all leases entered into after January 1, 2019, executory costs are allocated between lease and non-lease elements based upon their relative stand-alone prices. For the year ended December 31, 2018, the Company recognized $3.6 million of rent expense, inclusive of lease expense, non-lease elements, and executory costs for short and long-term operating leases.

Cash paid for amounts included in the measurement of operating lease liabilities is included in operating cash flows and was $2.6 million and $2.5 million for the years ended December 31, 2020 and 2019, respectively.

The table below reconciles the Company's future cash obligations to operating lease liabilities recorded on the balance sheet as of December 31, 2020:

(in thousands)	Operating Leases
2021	$ 2,290
2022	2,611
2023	2,462
2024	2,488
2025	2,557
Thereafter	5,624
Total minimum lease payments	18,032
Less: amount of lease payments representing interest	(4,418)
Present value of future minimum lease payments	13,614
Less: current obligations under leases	(2,117)
Operating lease non-current liabilities	$ 11,497

8. Intangible Assets

HETLIOZ®. In January 2014, the Company announced that the FDA had approved the New Drug Application (NDA) for HETLIOZ®. As a result of this approval, the Company met a milestone under its license agreement with Bristol-Myers Squibb (BMS) that required the Company to make a license payment of $8.0 million to BMS. The $8.0 million is being amortized on a straight-line basis over the estimated economic useful life of the related product patents.

In April 2018, the Company met its final milestone under its license agreement with BMS when cumulative worldwide sales of HETLIOZ® reached $250.0 million. As a result of the achievement of this milestone, the Company made a payment to BMS of $25.0 million in 2018. The $25.0 million, which was capitalized as an intangible asset in the first quarter of 2015, was determined to be additional consideration for the acquisition of the HETLIOZ® intangible asset and is being amortized on a straight-line basis over the estimated economic useful life of the related product patents.

The estimated economic useful life of both the $8.0 million and the $25.0 million intangible assets were changed from February 2035 to July 2035 based on the July 2035 expiration date of U.S. patent number 10,376,487 (‘487 Patent) issued by the U.S. Patent and Trademark Office in August 2019.

The following is a summary of the Company’s intangible assets as of December 31, 2020:

		December 31, 2020		
(in thousands)	Estimated Useful Life	Gross Carrying Amount	Accumulated Amortization	Net Carrying Amount
HETLIOZ®	July 2035	$ 33,000	$ 11,441	$ 21,559

The following is a summary of the Company’s intangible assets as of December 31, 2019:

		December 31, 2019		
(in thousands)	Estimated Useful Life	Gross Carrying Amount	Accumulated Amortization	Net Carrying Amount
HETLIOZ®	July 2035	$ 33,000	$ 9,963	$ 23,037

As of December 31, 2020 and 2019, the Company also had $27.9 million of fully amortized intangible assets related to Fanapt®.

Intangible assets are amortized over their estimated useful economic life using the straight-line method. Amortization expense for the years ended December 31, 2020, 2019 and 2018 was as follows:

	Year Ended December 31,		
(in thousands)	2020	2019	2018
HETLIOZ®	$ 1,478	$ 1,505	$ 1,527

The following is a summary of the future intangible asset amortization schedule as of December 31, 2020:

(in thousands)	Total	2021	2022	2023	2024	2025	Thereafter
HETLIOZ®	$ 21,559	$ 1,478	$ 1,478	$ 1,478	$ 1,478	$ 1,478	$ 14,169

9. Accounts Payable and Accrued Liabilities

The following is a summary of the Company’s accounts payable and accrued liabilities as of December 31, 2020 and 2019:

(in thousands)	December 31, 2020	December 31, 2019
Compensation and employee benefits	$ 10,951	$ 6,597
Research and development expenses	6,173	5,893
Royalties payable	5,817	5,904
Consulting and other professional fees	5,052	5,376
Operating lease liabilities	2,117	2,147
Milestone obligations under license agreements	350	—
Other	1,049	1,673
Total accounts payable and accrued liabilities	$ 31,509	$ 27,590

10. Commitments and Contingencies

Guarantees and Indemnifications

The Company has entered into a number of standard intellectual property indemnification agreements in the ordinary course of its business. Pursuant to these agreements, the Company indemnifies, holds harmless, and agrees to reimburse the indemnified party for losses suffered or incurred by the indemnified party, generally the Company's business partners or customers, in connection with any U.S. patent or any copyright or other intellectual property infringement claim by any third party with respect to the Company's products. The term of these indemnification agreements is generally perpetual from the date of execution of the agreement. The maximum potential amount of future payments the Company could be required to make under these indemnification agreements is unlimited. Since inception, the Company has not incurred costs to defend lawsuits or settle claims related to these indemnification agreements. The Company also indemnifies its officers and directors for certain events or occurrences, subject to certain conditions.

License Agreements

The Company's rights to develop and commercialize its products are subject to the terms and conditions of licenses granted to the Company by other pharmaceutical companies.

HETLIOZ®. In February 2004, the Company entered into a license agreement with BMS under which it received an exclusive worldwide license under certain patents and patent applications, and other licenses to intellectual property, to develop and commercialize HETLIOZ®. As of December 31, 2020, the Company has paid BMS $37.5 million in upfront fees and milestone obligations, including $33.0 million of regulatory approval and commercial milestones capitalized as intangible assets (see Note 8). The Company has no remaining milestone obligations to BMS. Additionally, the Company is obligated to make royalty payments on HETLIOZ® net sales to BMS in any territory where the Company commercializes HETLIOZ® for a period equal to the greater of 10 years following the first commercial sale in the territory or the expiry of the new chemical entity (NCE) patent in that territory. During the period prior to the expiry of the NCE patent in a territory, the Company is obligated to pay a 10% royalty on net sales in that territory. The royalty rate is decreased by half for countries in which no NCE patent existed or for the remainder of the 10 years after the expiry of the NCE patent. The Company is also obligated under the license agreement to pay BMS a percentage of any sublicense fees, upfront payments and milestone and other payments (excluding royalties) that it receives from a third party in connection with any sublicensing arrangement, at a rate which is in the mid-twenties. The Company is obligated to use its commercially reasonable efforts to develop and commercialize HETLIOZ®.

Fanapt®. Pursuant to the terms of a settlement agreement with Novartis Pharma AG (Novartis), Novartis transferred all U.S. and Canadian rights in the *Fanapt®* franchise to the Company on December 31, 2014. The Company paid directly to Sanofi S.A. (Sanofi) a fixed royalty of 3% of net sales through December 2019 related to manufacturing know-how. The Company is also obligated to pay Sanofi a fixed royalty on Fanapt® net sales equal to 6% on Sanofi know-how not related to manufacturing under certain conditions for a period of up to 10 years in markets where the NCE patent has expired or was not issued. The Company is obligated to pay this 6% royalty on net sales in the U.S. through November 2026.

Tradipitant. In April 2012, the Company entered into a license agreement with Eli Lilly and Company (Lilly) pursuant to which the Company acquired an exclusive worldwide license under certain patents and patent applications, and other licenses to intellectual property, to develop and commercialize an NK-1R antagonist, tradipitant, for all human indications. Lilly is eligible to receive future payments based upon achievement of specified development, regulatory approval and commercialization milestones as well as tiered-royalties on net sales at percentage rates up to the low double digits. As of December 31, 2020, the Company has paid Lilly $3.0 million in upfront fees and development milestones. As of December 31, 2020, remaining milestone obligations include a $2.0 million development milestone due upon the filing of the first marketing authorization for tradipitant in either the U.S. or European Union (E.U.), $10.0 million and $5.0 million for the first approval of a marketing authorization for tradipitant in the U.S. and E.U., respectively, and up to $80.0 million for sales milestones. The Company is obligated to use its commercially reasonable efforts to develop and commercialize tradipitant.

Portfolio of CFTR activators and inhibitors. In March 2017, the Company entered into a license agreement with the University of California San Francisco (UCSF), under which the Company acquired an exclusive worldwide license to develop and commercialize a portfolio of CFTR activators and inhibitors. Pursuant to the license agreement, the Company will develop and commercialize the CFTR activators and inhibitors and is responsible for all development costs under the license agreement, including current pre-investigational new drug development work. UCSF is eligible to receive future payments based upon achievement of specified development and commercialization milestones as well as single-digit royalties on net sales. As of December 31, 2020, the Company has paid UCSF $1.2 million in upfront fees and development milestones, including a $0.2 million development milestone payment in March 2019. As of December 31, 2020, remaining milestone obligations include

$12.2 million for development milestones and $33.0 million for future regulatory approval and sales milestones. Included in the $12.2 million of development milestones is a $350,000 milestone due upon the conclusion of a Phase I study for each licensed product but not to exceed $1.1 million in total for the CFTR portfolio. In the fourth quarter of 2020, the Company determined the $350,000 milestone to be probable and accrued it as a current liability as of December 31, 2020.

VQW-765. In connection with a settlement agreement with Novartis relating to Fanapt®, the Company received an exclusive worldwide license under certain patents and patent applications, and other licenses to intellectual property, to develop and commercialize VQW-765, a Phase II alpha-7 nicotinic acetylcholine receptor partial agonist. Pursuant to the license agreement, the Company is obligated to use its commercially reasonable efforts to develop and commercialize VQW-765 and is responsible for all development costs. The Company has no milestone obligations; however, Novartis is eligible to receive tiered-royalties on net sales at percentage rates up to the mid-teens.

Purchase Commitments

In the course of its business, the Company regularly enters into agreements with clinical organizations to provide services relating to clinical development and clinical manufacturing activities under fee service arrangements. The Company's current agreements for clinical, marketing and other services may be terminated on generally 90 days' notice without incurring additional charges, other than charges for work completed but not paid for through the effective date of termination and other costs incurred by the Company's contractors in closing out work in progress as of the effective date of termination.

11. Public Offering of Common Stock

In March 2018, the Company completed a public offering of 6,325,000 shares of its common stock, including the exercise of the underwriters' option to purchase an additional 825,000 shares of common stock, at a price to the public of $17.00 per share. Net cash proceeds from the public offering were $100.9 million, after deducting the underwriting discounts and commissions and offering expenses.

12. Accumulated Other Comprehensive Income

The accumulated balances related to each component of other comprehensive income (loss), net of taxes, were as follows for the years ended December 31, 2020 and 2019:

(in thousands)	December 31, 2020	December 31, 2019
Foreign currency translation	$ 81	$ 13
Unrealized gain on marketable securities	158	236
Accumulated other comprehensive income	$ 239	$ 249

13. Stock-Based Compensation

As of December 31, 2020, there were 5,246,381 shares subject to outstanding options and RSUs under the 2006 Equity Incentive Plan (2006 Plan) and the Amended and Restated 2016 Equity Incentive Plan (2016 Plan, and together with the 2006 Plan, Plans). The 2006 Plan expired by its terms in April 2016, and the Company adopted the 2016 Plan. Outstanding options under the 2006 Plan remain in effect and the terms of the 2006 Plan continue to apply, but no additional awards can be granted under the 2006 Plan. In June 2016, the Company's stockholders approved the 2016 Plan. The 2016 Plan has been amended and restated three times to increase the number of shares reserved for issuance, among other administrative changes. Each of the amendments and restatements of the 2016 Plan was approved by the Company's stockholders. There is a total of 8,790,000 shares of common stock authorized for issuance under the 2016 Plan, 3,991,612 shares of which remained available for future grant as of December 31, 2020.

Stock Options

The Company has granted option awards under the Plans with service conditions (service option awards) that are subject to terms and conditions established by the compensation committee of the board of directors. Service option awards have 10-year contractual terms. Service option awards granted to employees and new directors upon their election vest and become exercisable over four years, with the first 25% of the shares subject to service option awards vesting on the first anniversary of the grant date and the remaining 75% of the shares subject to the service option awards in 36 equal monthly installments thereafter. Subsequent annual service option awards granted to directors vest and become exercisable in full on the first anniversary of the grant date. Certain service option awards granted to employees and executive officers provide for partial

acceleration of vesting if the employee or executive officer is subject to an involuntary termination, and full acceleration of vesting if the employee or executive officer is subject to an involuntary termination within 24 months after a change in control of the Company. Service option awards granted to directors provide for accelerated vesting if there is a change in control of the Company or if the director's service terminates as a result of the director's death or total and permanent disability.

As of December 31, 2020, $6.9 million of unrecognized compensation costs related to unvested service option awards are expected to be recognized over a weighted average period of 1.2 years. No option awards are classified as a liability as of December 31, 2020.

A summary of option activity under the Plans for the years ended December 31, 2020, 2019, and 2018 is as follows:

(in thousands, except for share and per share amounts)	Number of Shares	Weighted Average Exercise Price at Grant Date	Weighted Average Remaining Term (Years)	Aggregate Intrinsic Value
Outstanding at December 31, 2017	4,719,784	$ 10.03	5.63	$ 24,421
Granted	567,500	19.22		
Forfeited	(232,527)	13.99		
Exercised	(685,715)	9.12		5,945
Outstanding at December 31, 2018	4,369,042	11.15	5.28	65,438
Granted	687,500	18.38		
Forfeited	(53)	7.94		
Expired	(15,000)	14.78		
Exercised	(546,344)	11.47		2,482
Outstanding at December 31, 2019	4,495,145	12.21	5.58	22,148
Granted	627,500	11.27		
Forfeited	(225,000)	18.83		
Expired	(557,604)	14.21		
Exercised	(733,223)	7.68		2,868
Outstanding at December 31, 2020	3,606,818	12.24	5.76	8,511
Exercisable at December 31, 2020	2,556,394	11.52	4.53	7,302
Vested and expected to vest at December 31, 2020	3,482,804	12.22	5.64	8,337

The weighted average grant-date fair value of options granted was $5.53, $10.19 and $10.66 per share for the years ended December 31, 2020, 2019 and 2018, respectively. Proceeds from the exercise of stock options amounted to $5.6 million, $6.3 million and $6.3 million for the years ended December 31, 2020, 2019 and 2018, respectively.

Restricted Stock Units

An RSU is a stock award that entitles the holder to receive shares of the Company's common stock as the award vests. The fair value of each RSU is based on the closing price of the Company's stock on the date of grant. The Company has granted RSUs under the Plans with service conditions (service RSUs) that are subject to terms and conditions established by the compensation committee of the board of directors. Service RSUs granted to employees vest in four equal annual installments provided that the employee remains employed with the Company. Certain service RSUs granted to employees and executive officers provide for accelerated vesting if the employee or executive officer is subject to an involuntary termination within 24 months after a change in control. Annual service RSUs granted to directors vest on the first anniversary of the grant date and provide for accelerated vesting if there is a change in control of the Company.

As of December 31, 2020, $18.3 million of unrecognized compensation costs related to unvested service RSUs are expected to be recognized over a weighted average period of 1.6 years. No RSUs are classified as a liability as of December 31, 2020.

A summary of RSU activity for the Plans for the years ended December 31, 2020, 2019, and 2018 is as follows:

	Number of Shares	Weighted Average Grant Date Fair Value
Unvested at December 31, 2017	1,357,838	$ 12.72
Granted	714,086	18.93
Forfeited	(229,603)	15.19
Vested	(528,745)	12.69
Unvested at December 31, 2018	1,313,576	15.68
Granted	937,328	19.46
Forfeited	(75,444)	18.93
Vested	(526,175)	14.54
Unvested at December 31, 2019	1,649,285	18.04
Granted	832,162	11.28
Forfeited	(260,127)	17.35
Vested	(581,757)	16.54
Unvested at December 31, 2020	1,639,563	15.26

The grant date fair value for the 581,757 shares underlying RSUs that vested during the year ended December 31, 2020 was $9.6 million.

Stock-Based Compensation Expense

Stock-based compensation expense recognized for the years ended December 31, 2020, 2019 and 2018 comprised of the following:

	Year Ended December 31,		
(in thousands)	2020	2019	2018
Research and development	$ 3,804	$ 3,207	$ 1,290
Selling, general and administrative	9,556	10,251	10,376
Total stock-based compensation expense	$ 13,360	$ 13,458	$ 11,666

The fair value of each option award is estimated on the date of grant using the Black-Scholes-Merton option pricing model that uses the assumptions noted in the following table. Expected volatility rates are based on the historical volatility of the Company's publicly traded common stock and other factors. The risk-free interest rates are based on the U.S. Treasury yield for a period consistent with the expected term of the option in effect at the time of the grant. The Company has never paid cash dividends to its stockholders and does not plan to pay dividends in the foreseeable future. Assumptions used in the Black-Scholes-Merton option pricing model for employee and director stock options granted during the years ended December 31, 2020, 2019 and 2018 were as follows:

	Year Ended December 31,		
	2020	2019	2018
Expected dividend yield	— %	— %	— %
Weighted average expected volatility	51 %	58 %	58 %
Weighted average expected term (years)	6.07	5.95	5.90
Weighted average risk-free rate	1.14 %	2.26 %	2.68 %

14. Employee Benefit Plan

The Company has a defined contribution plan under IRC Section 401(k). This plan covers substantially all employees who meet minimum age and service requirements and allows participants to defer a portion of their annual compensation on a pre-tax basis. Currently, the Company matches fifty percent up to the first six percent of employee contributions. All matching contributions have been paid by the Company. The Company match vests over a 4-year period and amounted to $0.9 million, $0.8 million and $0.9 million for the years ended December 31, 2020, 2019 and 2018, respectively.

15. Income Taxes

The following is a summary of the domestic and foreign components of income before income taxes for the years ended December 31, 2020, 2019 and 2018:

	Year Ended December 31,		
(in thousands)	2020	2019	2018
Domestic	$ 31,667	$ 28,794	$ 25,123
Foreign	(12)	234	223
Total income before income taxes	$ 31,655	$ 29,028	$ 25,346

The following is a summary of the provision (benefit) for income taxes for the years ended December 31, 2020, 2019 and 2018:

	Year Ended December 31,		
(in thousands)	2020	2019	2018
Current:			
Federal	$ —	$ —	$ —
State	2,061	1,161	53
Foreign	68	81	99
Deferred:			
Federal	6,076	(85,624)	—
State	155	(2,127)	—
Foreign	(42)	(16)	(14)
Provision (benefit) for income taxes	$ 8,318	$ (86,525)	$ 138

The Company assesses the need for a valuation allowance against its deferred tax asset each quarter through the review of all available positive and negative evidence. Deferred tax assets are reduced by a tax valuation allowance when, in the opinion of management, it is more likely than not that some portion of the deferred tax assets will not be realized. The analysis depends on historical and projected taxable income. Projected taxable income includes significant assumptions related to revenue, commercial expenses and research and development activities. During 2019, after considering all available positive and negative evidence, including but not limited to cumulative income in recent periods, historical, current and future projected results and significant risks and uncertainties related to forecasts, the Company concluded that it was more likely than not that substantially all of its deferred tax assets in the U.S. are realizable in future periods. A valuation allowance was retained against certain District of Columbia state deferred tax assets as of December 31, 2020, and 2019.

The following is reconciliation between the federal statutory tax rate and the Company's effective tax rate for the years ended December 31, 2020, 2019 and 2018:

	Year Ended December 31,		
	2020	2019	2018
Federal tax at statutory rate	21.0 %	21.0 %	21.0 %
State taxes	2.6 %	1.8 %	1.7 %
Change in valuation allowance (1)	(3.5)%	(357.6)%	(16.4)%
Research and development credit (2)	(5.4)%	(10.9)%	(9.1)%
Orphan drug credit (2)	(1.3)%	17.1 %	(2.7)%
Section 162(m) limitation	1.7 %	2.7 %	3.1 %
Other tax rate changes	0.2 %	(0.5)%	(0.7)%
Other changes in state deferred taxes (3)	— %	— %	5.9 %
Uncertain tax positions (2)	4.7 %	26.3 %	— %
Stock-based compensation	5.1 %	(1.0)%	(3.9)%
Other items	1.2 %	3.0 %	1.6 %
Effective tax rate	26.3 %	(298.1)%	0.5 %

(1) Reductions in 2020 valuation allowances are attributable to 2020 income before income taxes. Reductions in 2019 valuation allowances include $7.5 million related to 2019 U.S. income before income taxes, $10.7 related to adjustments for prior period credit carryforwards and uncertain tax positions and $85.6 million related to a change in

beginning-of-the-year balances that resulted from a change in circumstances that caused a change in judgment about the realizability of U.S. deferred tax assets in future years. Reductions in 2018 valuation allowances are attributable to 2018 income before income taxes.

(2) 2019 activity includes adjustments to prior year credit carryforwards and prior year tax positions. As a result of the tax valuation allowance previously recorded against deferred tax assets in the U.S., these adjustments resulted in no change in tax expense.

(3) Includes adjustments to state deferred taxes based on changes to filing jurisdictions.

The following is a summary of the components of the Company's net deferred tax assets and the related tax valuation allowance as of December 31, 2020 and 2019. Certain prior period amounts in the table have been reclassified to conform to the current period presentation.

(in thousands)	December 31, 2020	December 31, 2019
Deferred tax assets:		
Net operating loss carryforwards	$ 43,623	$ 52,034
Stock-based compensation	4,653	5,298
Accrued expenses	2,429	1,266
Allowance for returns and credit losses	1,169	1,468
Research and development and orphan drug credit carryforwards	37,737	36,041
Other	3,279	4,572
Total deferred tax assets	92,890	100,679
Deferred tax liabilities:		
Intangible assets	(1,911)	(1,994)
Other	(2,412)	(2,850)
Total deferred tax liabilities	(4,323)	(4,844)
Deferred tax assets, net	88,567	95,835
Less: Valuation allowance	7,051	8,155
Net deferred tax assets	$ 81,516	$ 87,680

The following is a summary of changes in the Company's tax valuation allowance for the years ended December 31, 2020, 2019 and 2018:

(in thousands)	Balance at Beginning of Year	Additions	Reductions	Balance at End of Year
Year Ended:				
December 31, 2020	$ 8,155	$ —	$ (1,104)	$ 7,051
December 31, 2019	111,950	—	(103,795)	8,155
December 31, 2018	116,110	4,036	(8,196)	111,950

The Company has NOL and other tax credit carryforwards in several jurisdictions. As of December 31, 2020, the Company has $35.2 million of deferred tax assets relating to U.S. federal NOL carryforwards, along with deferred tax assets of $13.4 million and $24.4 million related to U.S. federal research and development credits and orphan drug credits, respectively. These tax attributes will begin to expire in 2031, 2024 and 2030, respectively. In addition, the Company has $8.4 million of deferred tax assets relating to U.S. state NOL carryforwards, which primarily relate to the District of Columbia. State NOLs for the District of Columbia will begin to expire in 2032 and other state NOLs will begin to expire in 2029.

Tax benefits are recognized from an uncertain tax position only if it is more likely than not that the position will be sustained on examination by the taxing authorities based on the technical merits of the position. The tax benefit recognized in the financial statements for a particular tax position is based on the largest benefit that is more likely than not to be realized upon settlement.

A reconciliation of the beginning and ending amount of gross unrecognized tax benefits is as follows:

	Year Ended December 31,		
(in thousands)	2020	2019	2018
Unrecognized tax benefits at the beginning of the year	$ 9,741	$ —	$ —
Increases (decreases) related to prior year tax positions	(121)	8,223	—
Increases related to current year tax positions	1,613	1,518	—
Unrecognized tax benefits at the end of the year	$ 11,233	$ 9,741	$ —

The amount of uncertain tax benefits that, if recognized, would impact the effective tax rate is $11.2 million. No material income tax interest or penalties have been recorded, and unrecognized tax benefits are not expected to change materially over the next 12 months. Income tax returns filed by the Company for all periods are open to examination by tax jurisdictions. As of December 31, 2020, the Company is not under examination by any federal or state tax jurisdiction.

Certain tax attributes of the Company, including NOLs and credits, would be subject to a limitation should an ownership change as defined under the Internal Revenue Code of 1986, as amended (IRC), Section 382, occur. The limitations resulting from a change in ownership could affect the Company's ability to utilize its NOLs and credit carryforward (tax attributes). Ownership changes occurred in the years ending December 31, 2014 and December 31, 2008. The Company believes that the ownership changes in 2014 and 2008 will not impact its ability to utilize NOL and credit carryforwards; however, future ownership changes may cause the Company's existing tax attributes to have additional limitations.

16. Earnings per Share

Basic earnings per share (EPS) is calculated by dividing the net income by the weighted average number of shares of common stock outstanding. Diluted EPS is computed by dividing the net income by the weighted average number of shares of common stock outstanding, plus potential outstanding common stock for the period. Potential outstanding common stock includes stock options and shares underlying RSUs, but only to the extent that their inclusion is dilutive.

The following table presents the calculation of basic and diluted net income per share of common stock for the years ended December 31, 2020, 2019 and 2018:

	Year Ended December 31,		
(in thousands, except for share and per share amounts)	2020	2019	2018
Numerator:			
Net income	$ 23,337	$ 115,553	$ 25,208
Denominator:			
Weighted average shares outstanding, basic	54,427,683	53,137,562	50,859,947
Effect of dilutive securities	763,119	1,709,498	2,185,310
Weighted average shares outstanding, diluted	55,190,802	54,847,060	53,045,257
Net income per share, basic and diluted:			
Basic	$ 0.43	$ 2.17	$ 0.50
Diluted	$ 0.42	$ 2.11	$ 0.48
Antidilutive securities excluded from calculations of diluted net income per share	3,407,409	1,932,024	903,265

17. Legal Matters

Fanapt®. In 2014 and 2015, Roxane Laboratories, Inc. (Roxane) and its affiliates, West-Ward Pharmaceuticals International Limited and West-Ward Pharmaceuticals Corp (West-Ward), Inventia Healthcare Pvt. Ltd. (Inventia), Lupin Ltd. and Lupin Pharmaceuticals, Inc. (Lupin), Taro Pharmaceuticals USA, Inc. and Taro Pharmaceutical Industries, Ltd. (Taro), and Apotex Inc. and Apotex Corp. (Apotex) (collectively, the Fanapt® Defendants) each submitted an Abbreviated New Drug Applications (ANDA) to the FDA seeking approval to market generic versions of Fanapt® prior to the expiration of certain of the Company's patents covering Fanapt®, including U.S. Patent No. 8,586,610 ('610 Patent) and U.S. Patent No. 9,138,432 ('432 Patent). In response, the Company filed separate lawsuits in 2014 and 2015 against each of the Fanapt® Defendants in the U.S. District Court for the District of Delaware (Delaware District Court) for patent infringement.

In August 2016, the Delaware District Court ruled in the Company's favor, permanently enjoining Roxane from manufacturing, using, selling, offering to sell, distributing or importing any generic iloperidone product described in Roxane's

ANDA until the expiration of the ‘610 Patent in November 2027, or May 2028 if the Company obtains pediatric exclusivity. This ruling was affirmed on appeal by the Federal Circuit Court of Appeals in April 2018. West-Ward, having replaced Roxane as defendant following the acquisition of Roxane by West-Ward’s parent company, Hikma Pharmaceuticals PLC (Hikma), petitioned the U.S. Supreme Court for a writ of certiorari, which was denied in January 2020. The Company’s lawsuit against Hikma regarding the ‘432 Patent remains pending.

The Company entered into separate license agreements with each of Taro, Apotex and Lupin resolving these lawsuits in October 2016, December 2016 and July 2020, respectively. The license agreements grant Taro, Apotex and Lupin non-exclusive licenses to manufacture and commercialize a version of Fanapt® in the U.S. effective as of the expiration of the ‘610 Patent or earlier under certain limited circumstances. The Company entered into a confidential stipulation with Inventia regarding any potential launch of its generic versions of Fanapt®, but the Company’s lawsuit against Inventia regarding the ‘610 and ‘432 Patents remains pending.

HETLIOZ®. Between April and February 2021, the Company filed numerous patent infringement lawsuits in the Delaware District Court against Teva Pharmaceuticals USA, Inc. (Teva), MSN Pharmaceuticals Inc. and MSN Laboratories Private Limited (MSN) and Apotex (collectively with Teva and MSN, the HETLIOZ® Defendants) after having received multiple Paragraph IV certification notice letters (Paragraph IV Letters) from each of the HETLIOZ® Defendants alleging that the Company’s patents covering HETLIOZ®, U.S. Patent Nos. RE46,604, 9,060,995, 9,539,234, 9,549,913, 9,730,910, 9,844,241, 10,071,977, 10,149,829, 10,376,487, 10,449,176, 10,610,510, 10,610,511, and 10,829,465, were invalid, unenforceable and/or would not be infringed by the manufacture, use or sale of their generic versions of HETLIOZ®, as described in the ANDAs submitted to the FDA by each of the HETLIOZ® Defendants. These lawsuits have been consolidated and are schedule for trial in March 2022.

Other Matters. In February 2019, a qui tam action filed against the Company was unsealed by order of the U.S. District Court for the District of Columbia (DC District Court). The qui tam action, which was filed under seal in March 2017, was brought by a former Company employee on behalf of the U.S., 28 states and the District of Columbia (collectively, the Plaintiff States) and the policyholders of certain insurance companies under the Federal False Claims Act and state law equivalents to the Federal False Claims Act and related state laws. The complaint alleged that the Company violated these laws through the promotion and marketing of its products Fanapt® and HETLIOZ® and sought, among other things, treble damages, civil penalties for each alleged false claim, and attorneys’ fees and costs. By virtue of the DC District Court having unsealed the original complaint, the Company learned that in January 2019, the U.S. Department of Justice (the DOJ), as well as the Plaintiff States, elected not to intervene in the qui tam action at that time. In May 2019, the plaintiff filed an amended complaint under seal repeating the same allegations and seeking the same relief. According to a filing unsealed in June 2019, the DOJ reaffirmed its decision not to intervene and incorporated its prior filing, indicating that neither the DOJ nor the Plaintiff States were intervening regarding the original complaint. Although the DOJ and the Plaintiff States have elected not to intervene, the plaintiff may litigate this action and the DOJ and the Plaintiff States may later seek to intervene in the action. In August 2019, the Company filed a motion to dismiss, and in October 2019 the plaintiff filed a reply. In May 2020, the DC District Court dismissed the plaintiff’s complaint in its entirety, without prejudice. In June 2020, the plaintiff filed a second amended complaint with similar allegations and seeking the same relief. In July 2020, the Company filed another motion to dismiss and in October 2020 the plaintiff filed a reply. The DC District Court will hear the Company's motion to dismiss on February 24, 2021. The Company intends to continue to vigorously defend itself in the case.

In February 2019, a securities class action, *Gordon v. Vanda Pharmaceuticals Inc.*, was filed in the U.S. District Court for the Eastern District of New York naming the Company and certain of its officers as defendants. An amended complaint was filed in July 2019. The amended complaint, filed on behalf of a purported stockholder, asserts claims on behalf of a putative class of all persons who purchased the Company’s publicly traded securities between November 4, 2015 and February 11, 2019, for alleged violations of Sections 10(b) and 20(a) of the Securities Exchange Act of 1934, as amended, and Rule 10b-5 promulgated thereunder. The amended complaint alleges that the defendants made false and misleading statements and/or omissions regarding Fanapt®, HETLIOZ® and the Company’s interactions with the FDA regarding tradipitant between November 3, 2015 and February 11, 2019. In March 2020, the Company filed a motion to dismiss the complaint. The Company believes that it has meritorious defenses and intends to vigorously defend this lawsuit. The Company does not anticipate that this litigation will have a material adverse effect on its business, results of operations or financial condition. However, this lawsuit is subject to inherent uncertainties, the actual cost may be significant, and the Company may not prevail. The Company believes it is entitled to coverage under its relevant insurance policies, subject to a retention, but coverage could be denied or prove to be insufficient.

In July 2019, a shareholder derivative complaint, *Samuel Williams v. Mihael Polymeropoulos, et al.*, was filed in the U.S. District Court for the Eastern District of New York naming certain current and former Company directors and officers as defendants. In September 2019, a shareholder derivative complaint, *Michael Bavaro v. Mihael Polymeropoulos, et al.*, was filed

in the Delaware District Court naming certain current and former Company directors and officers as defendants. In October 2019, the Company filed a motion to transfer the *Bavaro* case to the Eastern District of New York, where the *Gordon* and *Williams* cases are pending. In March 2020, the Delaware District Court transferred the *Bavaro* case to the Eastern District of New York, consolidating the *Williams* and *Bavaro* cases, and the plaintiffs filed a consolidated complaint in April 2020. These complaints, filed on behalf of purported stockholders, derivatively on behalf of the Company, assert claims for alleged breach of fiduciary duties by certain of the Company's current and former directors and officers. The Company believes that it has meritorious defenses and intends to vigorously defend this lawsuit. The Company does not anticipate that this litigation will have a material adverse effect on its business, results of operations or financial condition. However, this lawsuit is subject to inherent uncertainties, the actual cost may be significant, and the Company may not prevail. The Company believes it is entitled to coverage under its relevant insurance policies, subject to a retention, but coverage could be denied or prove to be insufficient.

In July 2017, the Committee for Medicinal Products for Human Use (CHMP) issued a negative opinion recommending against approval of Fanaptum® (oral iloperidone tablets) for the treatment of schizophrenia in adult patients in the E.U. The CHMP was of the opinion that the benefits of Fanaptum® did not outweigh its risks and recommended against marketing authorization. In March 2018, the Company filed an application seeking annulment of the EMA's negative opinion and the subsequent European Commission decision refusing marketing authorization of Fanaptum in the E.U. General Court. In December 2019, the General Court issued its judgment dismissing the action, leaving the EMA opinion and Commission decision intact. In February 2020, the Company filed an appeal of this judgment with the Court of Justice of the E.U.

18. Quarterly Financial Data (Unaudited)

The following is a summary of quarterly financial data for the years ended December 31, 2020 and 2019:

(in thousands, except for per share amounts)	First Quarter	Second Quarter	Third Quarter	Fourth Quarter
Year Ended December 31, 2020				
Revenues	$ 58,000	$ 62,207	$ 60,308	$ 67,653
Gross profit (1)	52,423	55,991	54,041	60,871
Income (loss) from operations	(125)	9,171	7,742	10,451
Net income	486	8,714	5,947	8,190
Net income per share, basic	$ 0.01	$ 0.16	$ 0.11	$ 0.15
Net income per share, diluted	$ 0.01	$ 0.16	$ 0.11	$ 0.15
Year Ended December 31, 2019				
Revenues	$ 47,713	$ 59,060	$ 59,485	$ 60,930
Gross profit (1)	42,220	52,313	52,327	54,335
Income (loss) from operations	(2,087)	9,895	10,759	4,243
Net income (loss)	(612)	11,526	100,423	4,216
Net income (loss) per share, basic	$ (0.01)	$ 0.22	$ 1.88	$ 0.08
Net income (loss) per share, diluted	$ (0.01)	$ 0.21	$ 1.84	$ 0.08

(1) Gross profit includes revenues less cost of goods sold excluding amortization, and less intangible asset amortization.

VANDA PHARMACEUTICALS INC.

EXHIBIT INDEX

Exhibit Number	Description
3.1	Form of Amended and Restated Certificate of Incorporation of the registrant (filed as Exhibit 3.8 to Amendment No. 2 to the registrant's registration statement on Form S-1 (File No. 333-130759) on March 17, 2006 and incorporated herein by reference).
3.2	Fourth Amended and Restated Bylaws of the registrant, as amended and restated on December 17, 2015 (filed as Exhibit 3.1 to the registrant's current report on Form 8-K (File No. 001-34186) on December 21, 2015 and incorporated herein by reference).
4.1	Specimen certificate representing the common stock of the registrant (filed as Exhibit 4.4 to Amendment No. 2 to the registrant's registration statement on Form S-1 (File No. 333-130759) on March 17, 2006, and incorporated herein by reference).
10.1#	Amended and Restated License, Development and Commercialization Agreement, dated July 24, 2005, by and between Bristol-Myers Squibb Company and the registrant (relating to HETLIOZ®) (filed as Exhibit 10.3 to Amendment No. 1 to the registrant's registration Statement on Form S-1 (File No. 333-130759) on February 16, 2006 and incorporated herein by reference).
10.2	Form of Indemnification Agreement entered into by directors and executive officers (filed as Exhibit 10.11 to the registrant's registration statement on Form S-1 (File No. 333-130759) on December 29, 2005 and incorporated herein by reference).
10.3†	2006 Equity Incentive Plan, as amended (filed as Exhibit 10.17 to Amendment No. 2 to the registrant's Registration Statement on Form S-1 (File No. 333-130759), as filed on March 17, 2006, and incorporated herein by reference).
10.4†	Amendment to Amended and Restated Employment Agreement, dated December 16, 2010, by and between Mihael H. Polymeropoulos and the registrant (filed as Exhibit 10.39 to the registrant's annual report on Form 10-K (File No. 001-34186) on March 10, 2011 and incorporated herein by reference).
10.5	Amended and Restated Tax Indemnity Agreement, dated December 16, 2010, by and between Mihael H. Polymeropoulos and the registrant (filed as Exhibit 10.41 to the registrant's annual report on Form 10-K (File No. 001-34186) on March 10, 2011 and incorporated herein by reference).
10.6	Lease, effective as of July 25, 2011, by and between Square 54 Office Owner LLC and the registrant (filed as Exhibit 10.42 to the registrant's quarterly report on Form 10-Q (File No. 001-34186) on November 7, 2011 and incorporated herein by reference).
10.7	Amendment to Amended and Restated License, Development and Commercialization Agreement, dated as of April 15, 2010, by and between Bristol-Myers Squibb Company and the registrant (filed as Exhibit 10.38 to the registrant's current report on Form 8-K (File No. 001-34186) on April 19, 2010 and incorporated herein by reference).
10.8	Amendment to Amended and Restated License, Development and Commercialization Agreement, dated as of May 24, 2012, by and between Bristol-Myers Squibb Company and the registrant (filed as Exhibit 10.46 to the registrant's current report on Form 8-K (File No. 001-34186) on May 30, 2012 and incorporated herein by reference).
10.9#	License, Development and Commercialization Agreement, dated as of April 12, 2012, by and between Eli Lilly and Company and the registrant (filed as Exhibit 10.48 to the registrant's quarterly report on Form 10-Q (File No. 001-34186) on August 3, 2012 and incorporated herein by reference).
10.10	Amendment to Amended and Restated License, Development and Commercialization Agreement, dated as of April 25, 2013, by and between Bristol-Myers Squibb Company and the registrant (filed as Exhibit 10.50 to the registrant's current report on Form 8-K (File No. 001-34186) on April 29, 2013 and incorporated herein by reference).
10.11#	Manufacturing Agreement, dated January 24, 2014, by and between Patheon Pharmaceuticals Inc. and the registrant (relating to HETLIOZ®) (filed as Exhibit 10.53 to the registrant's quarterly report on Form 10-Q (File No. 001-34186) on May 8, 2014 and incorporated herein by reference).
10.12	Amendment to Lease Agreement, dated March 18, 2014, by and between Square 54 Office Owner LLC and the registrant (filed as Exhibit 10.54 to the registrant's quarterly report on Form 10-Q (File No. 001-34186) on May 8, 2014 and incorporated herein by reference).

Exhibit Number	Description
10.13	Settlement Agreement and Mutual General Release, dated December 22, 2014, by and among Novartis Pharma AG and the registrant (filed as Exhibit 10.55 to the registrant's annual report on Form 10-K (File No. 001-34186) on March 13, 2015 and incorporated herein by reference).
10.14#	Asset Transfer Agreement, dated December 22, 2014, by and among Novartis Pharma AG, Novartis AG and the registrant (relating to Fanapt®) (filed as Exhibit 10.56 to the registrant's annual report on Form 10-K/A (File No. 001-34186) on June 10, 2015 and incorporated herein by reference).
10.15#	Sublicense Agreement, dated November 20, 1997, by and between Titan Pharmaceuticals, Inc. and Novartis Pharma AG (filed as Exhibit 10.30 to Titan Pharmaceutical Inc.'s registration statement on Form S-3 (File No. 333-42367) on December 16, 1997 and incorporated herein by reference).
10.16#	Amendment No. 1 to Sublicense Agreement by and between Titan Pharmaceuticals, Inc. and Novartis Pharma AG, dated November 30, 1998 (filed as Exhibit 10.58 to the registrant's annual report on Form 10-K (File No. 001-34186) on March 13, 2015 and incorporated herein by reference).
10.17#	Amendment No. 2 to Sublicense Agreement, dated April 10, 2001, by and between Titan Pharmaceuticals, Inc. and Novartis Pharma AG (filed as Exhibit 10.59 to the registrant's annual report on Form 10-K/A (File No. 001-34186) on June 10, 2015 and incorporated herein by reference).
10.18#	Amendment No. 3 to Sublicense Agreement, dated June 4, 2004, by and between Titan Pharmaceuticals, Inc. and Novartis Pharma AG (filed as Exhibit 10.60 to the registrant's annual report on Form 10-K (File No. 001-34186) on March 13, 2015 and incorporated herein by reference).
10.19	Stock Purchase Agreement, dated December 22, 2014, by and between Novartis AG and the registrant (filed as Exhibit 10.61 to the registrant's annual report on Form 10-K (File No. 001-34186) on March 13, 2015 and incorporated herein by reference).
10.20#	License Agreement, dated December 22, 2014, by and between Novartis Pharma AG and the registrant (relating to AQW051) (filed as Exhibit 10.62 to the registrant's annual report on Form 10-K (File No. 001-34186) on March 13, 2015 and incorporated herein by reference).
10.21	Agreement, dated February 2, 2016, by and among Titan Pharmaceuticals, Inc., Aventisub LLC, the successor-in-interest to Aventisub II Inc. Sanofi-Aventis and the registrant (filed as Exhibit 10.1 to the registrant's current report on Form 8-K (File No. 001-34186) on February 4, 2016 and incorporated herein by reference).
10.22†	Vanda Pharmaceuticals Inc. Amended and Restated 2016 Equity Incentive Plan, effective as of June 11, 2020 (filed as Exhibit 10.1 to the registrant's registration statement on Form S-8 (File No. 333-239103) on June 11, 2020 and incorporated herein by reference).
10.23†	Form of Notice of Stock Option Grant and Stock Option Agreement under Amended and Restated 2016 Equity Incentive Plan (filed as Exhibit 10.2 to the registrant's registration statement on Form S-8 (File No. 333-218774) on June 15, 2017 and incorporated herein by reference).
10.24†	Form of Restricted Stock Unit Award Agreement under Amended and Restated 2016 Equity Incentive Plan (filed as Exhibit 10.3 to the registrant's registration statement on Form S-8 (File No. 333-218774) on June 15, 2017 and incorporated herein by reference).
10.25†	UK Sub Plan under the Amended and Restated 2016 Equity Incentive Plan (filed as Exhibit 10.4 to the registrant's registration statement on Form S-8 (File No. 333-218774) on June 15, 2017 and incorporated herein by reference).
10.26†	Form of Stock Option Grant and Stock Option Agreement under the UK Sub Plan under the Amended and Restated 2016 Equity Incentive Plan (filed as Exhibit 10.5 to the registrant's registration statement on Form S-8 (File No. 333-218774) on June 15, 2017 and incorporated herein by reference).
10.27†	Form of Restricted Stock Unit Award Agreement under the UK Sub Plan under the Amended and Restated 2016 Equity Incentive Plan (filed as Exhibit 10.6 to the registrant's registration statement on Form S-8 (File No. 333-218774) on June 15, 2017 and incorporated herein by reference).
10.28#	Manufacturing Agreement, dated May 6, 2016, by and between Patheon Pharmaceuticals Inc. and the registrant (relating to Fanapt®) (filed as Exhibit 10.42 to the registrant's quarterly report on Form 10-Q (File No. 001-34186) on July 28, 2016 and incorporated herein by reference).
10.29	Second Amendment to Lease Agreement, dated June 20, 2016, by and between Square 54 Office Owner LLC and the registrant (filed as Exhibit 10.43 to the registrant's quarterly report on Form 10-Q (File No. 001-34186) on July 28, 2016 and incorporated herein by reference).

Exhibit Number	Description
10.30	Sublease Agreement, dated June 22, 2016, by and between Hunton & Williams LLP and the registrant (filed as Exhibit 10.44 to the registrant's quarterly report on Form 10-Q (File No. 001-34186) on July 28, 2016 and incorporated herein by reference).
10.31#	License Agreement, dated October 24, 2016, by and among Taro Pharmaceuticals USA, Inc., Taro Pharmaceuticals Industries Ltd. and the registrant (filed as Exhibit 10.45 to the registrant's annual report on Form 10-K (File No. 001-34186) on February 17, 2017 and incorporated herein by reference).
10.32#	License Agreement, dated December 7, 2016, by and between Apotex, Inc. and the registrant (filed as Exhibit 10.46 to the registrant's annual report on Form 10-K (File No. 001-34186) on February 17, 2017 and incorporated herein by reference).
10.33	Third Amendment to Lease Agreement, dated March 28, 2018, by and between Square 54 Office Owner LLC and the registrant (filed as Exhibit 10.38 to the registrant's quarterly report on Form 10-Q (File No. 001-34186) on May 2, 2018 and incorporated herein by reference).
10.34	Fourth Amendment to Lease Agreement, dated March 29, 2018, by and between Square 54 Office Owner LLC and the registrant (filed as Exhibit 10.39 to the registrant's quarterly report on Form 10-Q (File No. 001-34186) on May 2, 2018 and incorporated herein by reference).
10.35†	Amended and Restated Employment Agreement, dated April 30, 2018, by and between Gunther Birznieks and the registrant (filed as Exhibit 10.40 to the registrant's quarterly report on Form 10-Q (File No. 001-34186) on May 2, 2018 and incorporated herein by reference).
10.36†	Employment Agreement, dated August 13, 2018, by and between Timothy Williams and the registrant (filed as Exhibit 10.41 to the registrant's quarterly report on Form 10-Q (File No. 001-34186) on November 7, 2018 and incorporated herein by reference).
10.37†	Employment Agreement, dated July 3, 2019, by and between Aranthan "AJ" Jones II and the registrant (filed as Exhibit 10.40 to the registrant's quarterly report on Form 10-Q (File No. 001-34186) on November 7, 2019 and incorporated herein by reference).
10.38†	Employment Agreement, dated August 5, 2019, by and between Joakim Wijkstrom and the registrant (filed as Exhibit 10.41 to the registrant's quarterly report on Form 10-Q (File No. 001-34186) on November 7, 2019 and incorporated herein by reference).
10.39†	Amended and Restated Employment Agreement, dated May 5, 2020, by and between Kevin Moran and the registrant (filed as Exhibit 10.42 to the registrant's quarterly report on Form 10-Q (File No. 001-34186) on May 7, 2020 and incorporated herein by reference).
10.40*	Fifth Amendment to Lease Agreement, dated April 11, 2019, by and between Square 54 Office Owner LLC and the registrant.
10.41*	Sixth Amendment to Lease Agreement, dated May 7, 2020, by and between Square 54 Office Owner LLC and the registrant.
21.1*	List of Subsidiaries.
23.1*	Consent of PricewaterhouseCoopers LLP, Independent Registered Public Accounting Firm.
31.1*	Certification of the Chief Executive Officer, as required by Section 302 of the Sarbanes-Oxley Act of 2002.
31.2*	Certification of the Chief Financial Officer as required by Section 302 of the Sarbanes-Oxley Act of 2002.
32.1*	Certification of the Chief Executive Officer and Chief Financial Officer as required by Section 906 of the Sarbanes-Oxley Act of 2002.
101*	The following financial information from this annual report on Form 10-K for the fiscal year ended December 31, 2020, formatted in Inline Extensible Business Reporting Language (iXBRL) and furnished electronically herewith: (i) Consolidated Balance Sheets as of December 31, 2020 and 2019; (ii) Consolidated Statements of Operations for the years ended December 31, 2020, 2019 and 2018; (iii) Consolidated Statements of Comprehensive Income (Loss) for the years ended December 31, 2020, 2019 and 2018; (iv) Consolidated Statements of Changes in Stockholders' Equity for the years ended December 31, 2020, 2019 and 2018; (v) Consolidated Statements of Cash Flows for the years ended December 31, 2020, 2019 and 2018; and (vi) Notes to the Consolidated Financial Statements.
104	Cover Page Interactive Data File (embedded within the Inline XBRL document).

† Indicates management contract or compensatory plan.

Exhibit Number	Description
#	Confidential treatment has been granted with respect to certain provisions of this exhibit.
*	Filed herewith.

EXECUTION COPY

AMENDMENT NO. 5 TO LEASE

THIS AMENDMENT NO. 5 TO LEASE ("**Amendment No. 5**") is made as of the 11th day of April, 2019 ("**Effective Date**"), by and between SQUARE 54 OFFICE OWNER LLC, a Delaware limited liability company ("**Landlord**"), and VANDA PHARMACEUTICALS INC., a Delaware corporation ("**Tenant**").

WITNESSETH:

WHEREAS, by Lease dated as of July 25, 2011 (the "**Initial Lease**"), as amended by that Amendment No. 1 to Lease dated as of March 18, 2014 ("**Amendment No. 1**"), and that Amendment No. 2 to Lease dated as of June 20, 2016 ("**Amendment No. 2**"), and that Amendment No. 3 to Lease dated as of March 28, 2018 ("**Amendment No. 3**"), and that Amendment No. 4 to Lease dated as of March 29, 2018 ("**Amendment No. 4**") (the Initial Lease, Amendment No. 1, Amendment No. 2, Amendment No. 3 and Amendment No. 4, collectively, the "**Lease**"), Landlord is leasing to Tenant thirty-three thousand five hundred thirty-four (33,534) square feet of rentable area (the "**Premises**") located in the East Tower of the building located at 2200 Pennsylvania Avenue, N.W., Washington, D.C. (the "**Building**"), which includes, without limitation, three thousand two hundred seventy-four (3,274) square feet of rentable area located on the second (2nd) floor more particularly defined as the "**Amendment No. 3 Expansion Space**";

WHEREAS, Landlord granted Tenant the Amendment No. 3 Allowance to be applied to Tenant alterations costs in the Amendment No. 3 Expansion Space; and

WHEREAS, Landlord and Tenant desire to amend the Lease to extend the period during which Tenant may requisition the Amendment No. 3 Allowance and to modify certain other terms of the Lease in accordance with and subject to the terms and conditions set forth below.

NOW, THEREFORE, in consideration of the mutual covenants and premises contained herein and other good and valuable consideration, the receipt and sufficiency of which are hereby acknowledged, Landlord and Tenant hereby agree to amend the Lease as follows:

1. Defined Terms. All capitalized terms used herein and not otherwise defined herein shall have the same meanings as provided for such terms in the Lease.

2. Extension of Time for Amendment No. 3 Allowance. Amendment No. 3 is hereby amended by deleting the phrase "within twelve (12) months after the Expansion Commencement Date" in the second-to-last line of Section 6(d)(iii) and inserting the phrase "on or before June 30, 2020" in its stead.

3. Ratification. Except as otherwise expressly modified by the terms of this Amendment No. 5, the Lease shall remain unchanged and continue in full force and effect. All

terms, covenants and conditions of the Lease not expressly modified herein are hereby confirmed and ratified and remain in full force and effect, and, as further amended hereby, constitute valid and binding obligations of Landlord and Tenant enforceable according to the terms thereof.

4. Broker. Landlord and Tenant each represent and warrant to the other that neither of them has employed or dealt with any broker, agent or finder in carrying on the negotiations relating to this Amendment No. 5. Landlord and Tenant shall indemnify and hold the other harmless from and against any claim or claims for brokerage or other commissions asserted by any broker, agent or finder engaged by Landlord or Tenant or with whom Landlord or Tenant has dealt in connection with this Amendment No. 5.

5. Authority.

(a) Tenant hereby represents and warrants to Landlord that Tenant is a duly organized and existing corporation and is in good standing under the laws of the State of Delaware and the District of Columbia, that all necessary corporate action has been taken to enter into this Amendment No. 5 and that the person signing this Amendment No. 5 on behalf of Tenant has been duly authorized to do so.

(b) Landlord hereby represents and warrants to Tenant that Landlord is a duly organized and existing limited liability company and is in good standing under the laws of the State of Delaware and the District of Columbia, that all necessary company action has been taken to enter into this Amendment No. 5 and that the person signing this Amendment No. 5 on behalf of Landlord has been duly authorized to do so.

6. Landlord and Tenant Representations and Acknowledgements.

(a) To the best of Tenant's knowledge, Landlord has performed all of its obligations under the Lease. To the best of Tenant's knowledge, Landlord is not in default under the Lease as of the date hereof, and Tenant is unaware of any condition or circumstance which, but for the passage of time or delivery of notice, or both, would constitute an event of default by Landlord under the Lease. Tenant has no current claims, defenses or set-offs of any kind to the payment or performance of Tenant's obligations under the Lease. Nothing contained herein shall be deemed to waive any sums due from Tenant to Landlord, or any default or event which, with the passage of time or delivery of notice, or both, would constitute a default by Tenant under the Lease as of the date hereof.

(b) To the best of Landlord's knowledge, Tenant has performed all of its obligations under the Lease. To the best of Landlord's knowledge, Tenant is not in default under the Lease as of the date hereof, and Landlord is unaware of any condition or circumstance which, but for the passage of time or delivery of notice, or both, would constitute an event of default by Tenant under the Lease. Landlord has no current claims, defenses or set-offs of any kind to the payment or performance of Landlord's obligations under the Lease. Nothing contained herein shall be deemed to waive any sums due from Landlord to Tenant, or any default or event which,

with the passage of time or delivery of notice, or both, would constitute a default by Landlord under the Lease as of the date hereof.

7. Mutual Negotiation. Landlord and Tenant each hereby covenants and agrees that each and every provision of this Amendment No. 5 has been jointly and mutually negotiated and authorized by both Landlord and Tenant, and in the event of any dispute arising out of any provision of this Amendment No. 5, Landlord and Tenant each does hereby waive any claim of authorship against the other party.

8. General Provisions. Landlord and Tenant agree that the terms and conditions of this Amendment No. 5 shall also be subject to the same provisions regarding confidentiality as are contained within Section 25.20 of the Initial Lease.

9. Binding Effect. This Amendment No. 5 shall not be effective and binding unless and until fully executed and delivered by each of the parties hereto. All of the covenants contained in this Amendment No. 5, including, but not limited to, all covenants of the Lease as modified hereby, shall be binding upon and inure to the benefit of the parties hereto, their respective heirs, legal representatives, and permitted successors and assigns.

[Remainder of page intentionally blank.
Signature page follows.]

IN WITNESS WHEREOF, Landlord and Tenant have executed this Amendment No. 5 to Lease as of the date and year first above written.

LANDLORD:

SQUARE 54 OFFICE OWNER LLC,
a Delaware limited liability company

By: BP/DC PROPERTIES, INC.,
a Maryland corporation, its sole member and manager

By: /s/ John J. Stroman
Name: John J. Stroman
Title: Vice President, Leasing

TENANT:

VANDA PHARMACEUTICALS INC.,
a Delaware corporation

By: /s/ Mihael H. Polymeropoulos
Name: Mihael H. Polymeropoulos
Title: President and CEO

EXECUTION COPY

AMENDMENT NO. 6 TO LEASE

THIS AMENDMENT NO. 6 TO LEASE ("**Amendment No. 6**") is made as of the 7th day of May, 2020 ("**Effective Date**"), by and between SQUARE 54 OFFICE OWNER LLC, a Delaware limited liability company ("**Landlord**"), and VANDA PHARMACEUTICALS INC., a Delaware corporation ("**Tenant**").

WITNESSETH:

WHEREAS, by Lease dated as of July 25, 2011 (the "**Initial Lease**"), as amended by that Amendment No. 1 to Lease dated as of March 18, 2014 ("**Amendment No. 1**"), and that Amendment No. 2 to Lease dated as of June 20, 2016 ("**Amendment No. 2**"), and that Amendment No. 3 to Lease dated as of March 28, 2018 ("**Amendment No. 3**"), and that Amendment No. 4 to Lease dated as of March 29, 2018 ("**Amendment No. 4**"), and that Amendment No. 5 to Lease dated as of April 11, 2019 ("**Amendment No. 5**") (the Initial Lease, Amendment No. 1, Amendment No. 2, Amendment No. 3, Amendment No. 4 and Amendment No. 5, collectively, the "**Lease**"), Landlord is leasing to Tenant thirty-three thousand five hundred thirty-four (33,534) square feet of rentable area (the "**Premises**") located in the East Tower of the building located at 2200 Pennsylvania Avenue, N.W., Washington, D.C. (the "**Building**"), which includes, without limitation, three thousand two hundred seventy-four (3,274) square feet of rentable area located on the second (2nd) floor more particularly defined as the "**Amendment No. 3 Expansion Space**";

WHEREAS, Landlord granted Tenant the Amendment No. 3 Allowance to be applied to Tenant alterations costs in the Amendment No. 3 Expansion Space;

WHEREAS, pursuant to section 6(d)(iii) of Amendment No. 3, as amended by Amendment No. 5, the period during which Tenant may requisition the Amendment No. 3 Allowance was extended to June 30, 2020; and

WHEREAS, Landlord and Tenant desire to amend the Lease to further extend the period during which Tenant may requisition the Amendment No. 3 Allowance to June 30, 2021, and to modify certain other terms of the Lease in accordance with and subject to the terms and conditions set forth below.

NOW, THEREFORE, in consideration of the mutual covenants and premises contained herein and other good and valuable consideration, the receipt and sufficiency of which are hereby acknowledged, Landlord and Tenant hereby agree to amend the Lease as follows:

1. Defined Terms. All capitalized terms used herein and not otherwise defined herein shall have the same meanings as provided for such terms in the Lease.

2. Extension of Time for Amendment No. 3 Allowance. The last sentence of Section 6(d)(iii) of Amendment No. 3, as amended, is hereby deleted in its entirety and replaced with the following: "Any portion of the Amendment No. 3 Allowance that has not been requisitioned in accordance with the foregoing on or before June 30, 2021 shall be deemed waived and forfeited."

3. Ratification. Except as otherwise expressly modified by the terms of this Amendment No. 6, the Lease shall remain unchanged and continue in full force and effect. All terms, covenants and conditions of the Lease not expressly modified herein are hereby confirmed and ratified and remain in full force and effect, and, as further amended hereby, constitute valid and binding obligations of Landlord and Tenant enforceable according to the terms thereof.

4. Broker. Landlord and Tenant each represent and warrant to the other that neither of them has employed or dealt with any broker, agent or finder in carrying on the negotiations relating to this Amendment No. 6. Landlord and Tenant shall indemnify and hold the other harmless from and against any claim or claims for brokerage or other commissions asserted by any broker, agent or finder engaged by Landlord or Tenant or with whom Landlord or Tenant has dealt in connection with this Amendment No. 6.

5. Authority.

(a) Tenant hereby represents and warrants to Landlord that Tenant is a duly organized and existing corporation and is in good standing under the laws of the State of Delaware and the District of Columbia, that all necessary corporate action has been taken to enter into this Amendment No. 6 and that the person signing this Amendment No. 6 on behalf of Tenant has been duly authorized to do so.

(b) Landlord hereby represents and warrants to Tenant that Landlord is a duly organized and existing limited liability company and is in good standing under the laws of the State of Delaware and the District of Columbia, that all necessary company action has been taken to enter into this Amendment No. 6 and that the person signing this Amendment No. 6 on behalf of Landlord has been duly authorized to do so.

6. Landlord and Tenant Representations and Acknowledgements.

(a) To the best of Tenant's knowledge, Landlord has performed all of its obligations under the Lease. To the best of Tenant's knowledge, Landlord is not in default under the Lease as of the date hereof, and Tenant is unaware of any condition or circumstance which, but for the passage of time or delivery of notice, or both, would constitute an event of default by Landlord under the Lease. Tenant has no current claims, defenses or set-offs of any kind to the payment or performance of Tenant's obligations under the Lease. Nothing contained herein shall be deemed to waive any sums due from Tenant to Landlord, or any default or event which, with the passage of time or delivery of notice, or both, would constitute a default by Tenant under the Lease as of the date hereof.

(b) To the best of Landlord's knowledge, Tenant has performed all of its obligations under the Lease. To the best of Landlord's knowledge, Tenant is not in default under the Lease as of the date hereof, and Landlord is unaware of any condition or circumstance which, but for the passage of time or delivery of notice, or both, would constitute an event of default by Tenant under the Lease. Landlord has no current claims, defenses or set-offs of any kind to the payment or performance of Landlord's obligations under the Lease. Nothing contained herein shall be deemed to waive any sums due from Landlord to Tenant, or any default or event which, with the passage of time or delivery of notice, or both, would constitute a default by Landlord under the Lease as of the date hereof.

7. Mutual Negotiation. Landlord and Tenant each hereby covenants and agrees that each and every provision of this Amendment No. 6 has been jointly and mutually negotiated and authorized by both Landlord and Tenant, and in the event of any dispute arising out of any provision of this Amendment No. 6, Landlord and Tenant each does hereby waive any claim of authorship against the other party.

8. General Provisions. Landlord and Tenant agree that the terms and conditions of this Amendment No. 6 shall also be subject to the same provisions regarding confidentiality as are contained within Section 25.20 of the Initial Lease.

9. Binding Effect. This Amendment No. 6 shall not be effective and binding unless and until fully executed and delivered by each of the parties hereto. All of the covenants contained in this Amendment No. 6, including, but not limited to, all covenants of the Lease as modified hereby, shall be binding upon and inure to the benefit of the parties hereto, their respective heirs, legal representatives, and permitted successors and assigns.

[Remainder of page intentionally blank.
Signature page follows.]

IN WITNESS WHEREOF, Landlord and Tenant have executed this Amendment No. 6 to Lease as of the date and year first above written.

LANDLORD:

SQUARE 54 OFFICE OWNER LLC,
a Delaware limited liability company

By: BP/DC PROPERTIES, INC.,
a Maryland corporation, its sole member and manager

By: /s/ John J. Stroman
Name: John J. Stroman
Title: SVP, Leasing

TENANT:

VANDA PHARMACEUTICALS INC.,
a Delaware corporation

By: /s/ Mihael H. Polymeropoulos
Name: Mihael H. Polymeropoulos
Title: CEO

Exhibit 21.1

Vanda Pharmaceuticals Inc.
List of Subsidiaries

Name of Wholly-Owned Subsidiary	Jurisdiction of Organization	Name under which the subsidiary conducts business
Vanda Pharmaceuticals Limited	United Kingdom	Vanda Pharmaceuticals Limited
Vanda Pharmaceuticals GmbH	Switzerland	Vanda Pharmaceuticals GmbH
Vanda Pharmaceuticals Germany GmbH	Germany	Vanda Pharmaceuticals Germany GmbH
Vanda Pharmaceuticals Netherlands B.V.	Netherlands	Vanda Pharmaceuticals Netherlands B.V.

Exhibit 23.1

CONSENT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

We hereby consent to the incorporation by reference in the Registration Statements on Form S-8 (No. 333-133368, No. 333-138070, No. 333-141571, No. 333-148924, No. 333-156995, No. 333-164567, No. 333-171962, No. 333-179265, No. 333-186509, No. 333-193614, No. 333-201754, No. 333-209144, No. 333-212255, No. 333-218774, No. 333-225599 and No. 333-239103) of Vanda Pharmaceuticals Inc. of our report dated February 11, 2021 relating to the financial statements and the effectiveness of internal control over financial reporting, which appears in this Form 10-K.

/s/ PricewaterhouseCoopers LLP

Baltimore, Maryland
February 11, 2021

EXHIBIT 31.1

CERTIFICATION OF CHIEF EXECUTIVE OFFICER
PURSUANT TO SECTION 302 OF THE SARBANES-OXLEY ACT OF 2002

I, Mihael H. Polymeropoulos, certify that:

1. I have reviewed this annual report on Form 10-K of Vanda Pharmaceuticals Inc.;

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 our 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 our 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; and

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.

February 11, 2021

/s/ Mihael H. Polymeropoulos, M.D.

Mihael H. Polymeropoulos, M.D.
President and Chief Executive Officer
(Principal Executive Officer)

EXHIBIT 31.2

CERTIFICATION OF CHIEF FINANCIAL OFFICER
PURSUANT TO SECTION 302 OF THE SARBANES-OXLEY ACT OF 2002

I, Kevin Moran, certify that:

1. I have reviewed this annual report on Form 10-K of Vanda Pharmaceuticals Inc.;

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 our 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 our 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; and

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.

February 11, 2021

/s/ Kevin Moran

Kevin Moran
Senior Vice President, Chief Financial Officer and Treasurer
(Principal Financial Officer and Principal Accounting Officer)

EXHIBIT 32.1

CERTIFICATION OF CHIEF EXECUTIVE OFFICER AND CHIEF FINANCIAL OFFICER

Pursuant to Section 906 of the Sarbanes-Oxley Act of 2002
(Subsections (a) and (b) of Section 1350, Chapter 63 of Title 18, United States Code)

Pursuant to Section 906 of the Sarbanes-Oxley Act of 2002 (subsections (a) and (b) of section 1350, chapter 63 of title 18, United States Code), each of the undersigned officers of Vanda Pharmaceuticals Inc., (the "Company"), does hereby certify, to the best of such officer's knowledge, that:

The Annual Report on Form 10-K for the year ended December 31, 2020 (the Form 10-K) of the Company fully complies with the requirements of Section 13(a) or 15(d) of the Securities Exchange Act of 1934, and the information contained in the Form 10-K fairly presents, in all material respects, the consolidated financial condition and results of operations of the Company.

February 11, 2021 /s/ Mihael H. Polymeropoulos, M.D.

Mihael H. Polymeropoulos, M.D.
President and Chief Executive Officer
(Principal Executive Officer)

February 11, 2021 /s/ Kevin Moran

Kevin Moran
Senior Vice President, Chief Financial Officer and Treasurer
(Principal Financial Officer and Principal Accounting Officer)

A signed original of this written statement required by Section 906 has been provided to the Company and will be retained by the Company and furnished to the Securities and Exchange Commission (SEC) or its staff upon request. This certification "accompanies" the Form 10-K to which it relates, is not deemed filed with the SEC 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.