Vanda Pharmaceuticals Inc.
Form 10-K
February 12, 2016
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UNITED STATES SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

Form 10-K

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

For the fiscal year ended December 31, 2015

¨ **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 D.C. 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	**Name of Each Exchange on Which Registered**
Common Stock, par value $0.001	The Nasdaq Stock Market LLC (NASDAQ Global Market)
Rights to Purchase Series A Junior Participating Preferred Stock	The Nasdaq Stock Market LLC (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 þ

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 þ

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 þ No ¨

Indicate by check mark whether the registrant has submitted electronically and posted on its corporate Web site, if any, every Interactive Data File required to be submitted and posted pursuant to Rule 405 of Regulation S-T (§ 232.405 of this chapter) during the preceding 12 months (or for such shorter period that the registrant was required to submit and post such files). Yes þ No ¨

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

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

Large accelerated filer ¨ Accelerated filer þ Non-accelerated filer ¨ Smaller reporting company ¨
(Do not check if a smaller reporting company)

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 þ

As of June 30, 2015, 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 $525.7 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 January 31, 2016 was 43,102,957.

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 2016 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, 2015, are incorporated by reference into Part III of this Form 10-K.

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PART I

CAUTIONARY NOTE REGARDING FORWARD-LOOKING STATEMENTS

Various statements throughout this report are forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995. Forward-looking statements may appear throughout this report. 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, forward-looking statements. Forward-looking statements are based upon current expectations that involve risks, changes in circumstances, assumptions and uncertainties. Important factors that could cause actual results to differ materially from those reflected in our forward-looking statements include, among others:

- the ability of Vanda Pharmaceuticals Inc. (we, our or Vanda) to successfully commercialize HETLIOZ® (tasimelteon) for the treatment of Non-24-Hour Sleep-Wake Disorder (Non-24) in the U.S. and Europe;
- uncertainty as to the market awareness of Non-24 and the market acceptance of HETLIOZ®;
- our ability to generate U.S. sales of Fanapt® (iloperidone) for the treatment of schizophrenia;
- the timing and costs of continuing to build a sales and marketing, supply chain, distribution, pharmacovigilance, compliance and safety infrastructure to promote Fanapt® in the U.S.;
- our dependence on third-party manufacturers to manufacture HETLIOZ® and Fanapt® in sufficient quantities and quality;
- our limited sales and marketing infrastructure;
- the regulatory status of Fanapt® in Europe;
- our ability to successfully commercialize HETLIOZ® and Fanapt® outside of the U.S.;
- our ability to prepare, file, prosecute, defend and enforce any patent claims and other intellectual property rights;
- a loss of rights to develop and commercialize our products under our license agreements;
- the ability to obtain and maintain regulatory approval of our products, and the labeling for any approved products;
- the timing and success of preclinical studies and clinical trials conducted by us and our development partners;
- a failure of our products to be demonstrably safe and effective;

the size and growth of the potential markets for our products and the ability to serve those markets;

our expectations regarding trends with respect to our revenues, costs, expenses and liabilities;

the scope, progress, expansion, and costs of developing and commercializing our products;

our failure to identify or obtain rights to new products;

a loss of any of our key scientists or management personnel;

limitations on our ability to utilize some of all of our prior net operating losses and orphan drug and research and development credits;

the cost and effects of litigation;

our ability to obtain the capital necessary to fund our research and development or commercial activities;

losses incurred from product liability claims made against us; and

use of our existing cash, cash equivalents and marketable securities.

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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 or referred to in this section. We caution investors not to rely too heavily on the forward-looking statements we make or that are made on our behalf. 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.

We encourage you to read *Management s Discussion and Analysis of our Financial Condition and Results of Operations* and our consolidated financial statements contained in this annual report on Form 10-K. We also encourage you to read Item 1A of Part I of this annual report on Form 10-K, entitled *Risk Factors*, which contains a more complete discussion of the risks and uncertainties associated with our business. In addition to the risks described above and in Item 1A of this 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.

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ITEM 1. BUSINESS

Overview

Vanda Pharmaceuticals Inc. (we, Vanda or the Company) is a biopharmaceutical company focused on the development and commercialization of products for the treatment of central nervous system disorders. Vanda commenced its operations in 2003 and our product portfolio includes:

HETLIOZ® (tasimelteon), a product for the treatment of Non-24-Hour Sleep-Wake Disorder (Non-24), was approved by the U.S. Food and Drug Administration (FDA) in January 2014 and launched commercially in the U.S. in April 2014. 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. This authorization is valid in the 28 countries that are members of the European Union, as well as European Economic Area members Iceland, Liechtenstein and Norway. HETLIOZ® has potential utility in a number of other circadian rhythm disorders and is presently in clinical development for the treatment of Jet Lag Disorder and Smith-Magenis Syndrome (SMS).

Fanapt® (iloperidone), a product for the treatment of schizophrenia, the oral formulation of which was being marketed and sold in the U.S. by Novartis Pharma AG (Novartis) until December 31, 2014. On December 31, 2014, Novartis transferred all the U.S. and Canadian commercial rights to the Fanapt® franchise to us. See Note 3, *Settlement Agreement with Novartis,* to the consolidated financial statements included in Part II of this annual report on Form 10-K for additional information. In September 2015, the FDA accepted for review a supplemental New Drug Application (sNDA) for Fanapt® for the maintenance treatment of schizophrenia in adults. In December 2015, we refiled with the European Medicines Agency (EMA) a Marketing Authorization Application (MAA) for Fanaptum® oral. Additionally, our distribution partners launched Fanapt® in Israel and Mexico in 2014.

Tradipitant (VLY-686), a small molecule neurokinin-1 receptor (NK-1R) antagonist, which is presently in clinical development for the treatment of chronic pruritus in atopic dermatitis.

Trichostatin A, a small molecule histone deacetylase (HDAC) inhibitor.

AQW051, a Phase II alpha-7 nicotinic acetylcholine receptor partial agonist.

Since we began operations in March 2003, we have devoted substantially all of our resources to the in-licensing, clinical development and commercialization of our products. Our products target prescription markets with significant unmet medical needs. Our ability to generate revenue and achieve profitability largely depends on our ability, alone or with others, to complete the development of our products, and to obtain the regulatory approvals for and manufacture, market and sell our products, and our ability to successfully commercialize HETLIOZ® for the treatment of Non-24 and Fanapt® for the treatment of schizophrenia. The results of our operations will vary significantly and depend on a number of factors, including risks related to our business, risks related to our industry, and other risks which are detailed in Item 1A of Part I entitled *Risk Factors* and Item 7 of Part II entitled *Management s Discussion and Analysis of Financial Condition and Results of Operations* of this annual report on Form 10-K.

Our activities will necessitate significant uses of working capital throughout 2016 and beyond. We are currently concentrating our efforts on selling HETLIOZ® and Fanapt® commercially in the U.S. and our upcoming commercial launch of HETLIOZ® in Europe. Additionally, we continue to pursue market approval of HETLIOZ® in other regions and Fanapt® in Europe and other regions. We will continue to work with our distribution partners who launched Fanapt® in Mexico and Israel during 2014. We see opportunities to grow our commercial products through life cycle management strategies that include the addition of new indications and formulations. Our pipeline includes novel programs that could address largely unmet medical needs.

Our founder and Chief Executive Officer, Mihael H. Polymeropoulos, M.D., started Vanda s operations early in 2003 after establishing and leading the Pharmacogenetics Department at Novartis. In acquiring and developing our products, we have relied upon our deep expertise in the scientific disciplines of pharmacogenetics and pharmacogenomics. These scientific disciplines examine both genetic variations among people that influence response to a particular drug, and the multiple pathways through which drugs affect people.

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Our strategy

Our goal is to create a leading biopharmaceutical company focused on developing and commercializing novel 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;

Apply our pharmacogenetics and pharmacogenomics expertise to differentiate our products; and

Expand our product portfolio through the identification and acquisition of additional products.

Products

We have the following products on the market or under regulatory review:

Product	Indication	Country	Select Milestones
HETLIOZ®	Non-24	United States	FDA approval in January 2014;
(tasimelteon)			Commercial launch in April 2014
		Europe	EC approval in July 2015;
			Expected commercial launch in Germany in 2016
Fanapt® (Oral)	Schizophrenia	United States	FDA approval in May 2009;
(iloperidone)			Commercial launch in January 2010;
			U.S. and Canada rights sublicensed to Novartis in October 2009 and reacquired by Vanda in December 2014;
			Long term maintenance sNDA accepted for review by FDA in September 2015 with a PDUFA date in May 2016
Fanaptum® (Oral)		Europe	EMA accepted for evaluation our MAA in December 2015
(iloperidone)			
		Mexico	Market approval in October 2013;
			Commercial launch in the fourth quarter of 2014 by our local distribution partner, Probiomed S.A. de

	C.V.
Israel	Market approval August 2012; Commercial launch in the fourth quarter of 2014 by our local distribution partner, Megapharm Ltd.

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We have the following products in clinical development:

Product	Target Indication	Select Milestones
HETLIOZ®	Pediatric Non-24	Plan to initiate a pharmacokinetic study in the second quarter 2016;
(tasimelteon)		Plan to initiate a Phase III study in the second half of 2016
	SMS	Initiated open label interventional study in the fourth quarter 2015;
		Plan to initiate placebo controlled Phase III study in the second half of 2016
	Jet Lag Disorder	Completed observational study in the fourth quarter of 2015;
		Plan to initiate Phase III study in the second half of 2016
Fanapt® (Oral)	Schizophrenia	Positive results from a Phase III long-term maintenance study in patients with schizophrenia were announced in June 2015
(iloperidone)		
Tradipitant (VLY-686)	Pruritus in patients with Atopic Dermatitis	Plan to initiate a pruritus proof of concept study during 2016
Trichostatin A	Oncology	Plan to file an Investigational New Drug (IND) application in 2016
AQW051	CNS Disorders	Potential indications are under strategic evaluation including cognitive impairment

HETLIOZ®

Commercial opportunity: Non-24

In January 2014, HETLIOZ® was approved in the U.S. for the treatment of Non-24. Non-24 is a serious, rare and chronic circadian rhythm 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 (SCN), 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. HETLIOZ® was launched commercially in the U.S. in April 2014. In addition, in July 2015, the EC granted centralized marketing authorization with unified labeling for HETLIOZ® for the treatment of Non-24 in totally blind adults. This authorization is valid in the 28 countries that are members of the European Union, as well as European Economic Area members Iceland, Liechtenstein and Norway.

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 is a serious, rare and chronic circadian rhythm disorder characterized by the inability to synchronize the master body clock with the 24-hour day-night cycle. Non-24 affects a majority of totally blind individuals, or between 65,000 and 95,000 people in the U.S. Non-24 occurs almost entirely in individuals who lack the light sensitivity necessary to synchronize the master body clock in the brain with 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

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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.

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.

Therapeutic opportunity: Circadian Rhythm Sleep Disorders

Sleep disorders are segmented into three major categories: primary insomnia, secondary insomnia and circadian rhythm sleep disorders (CRSDs). Insomnia is a symptom complex that comprises difficulty falling asleep or staying asleep, or non-refreshing sleep, in combination with daytime dysfunction or distress. The symptom complex can be an independent disorder (primary insomnia) or be a result of another condition such as depression or anxiety (secondary insomnia). CRSDs result from a misalignment of the sleep/wake cycle and an individual s daily activities or lifestyle. The circadian rhythm is the rhythmic output of the human biological clock and is governed by the hormones melatonin and cortisol. Both the timing of behavioral events (activity, sleep, and social interactions) and the environmental light/dark cycle result in a sleep/wake cycle that follows the circadian rhythm. Examples of CRSDs include transient disorders such as jet lag and chronic disorders such as delayed sleep phase disorder, shift work sleep disorder and Non-24.

Therapeutic opportunity: Other

We are planning to develop HETLIOZ® for the treatment of pediatric Non-24. We expect to initiate a pediatric pharmacokinetic study in the second quarter of 2016 and a Phase III study in the second half of 2016.

We initiated an open label interventional study in patients with SMS in the fourth quarter of 2015. We expect to initiate a placebo controlled Phase III study in the second half of 2016. SMS is a rare genetic disorder caused by a deletion on chromosome 17. The U.S. National Institute of Health estimates that SMS affects approximately one in 20,000 births in the U.S.

We initiated an observational study in Jet Lag Disorder in the fourth quarter of 2015. We expect to initiate a Phase III study in the second half of 2016.

Fanapt®

Commercial Opportunity: Schizophrenia

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. In October 2009, we entered into an amended and restated sublicense agreement with Novartis. We had originally entered into a sublicense agreement with Novartis in June 2004 pursuant to which we obtained certain worldwide exclusive licenses from Novartis relating to Fanapt®. Pursuant to the amended and restated sublicense agreement, Novartis had 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 Vanda as part of the Settlement Agreement. See Note 3, *Settlement Agreement with Novartis*, to the consolidated financial statements included in Part II of this annual report on Form 10-K for additional information. In June 2015, we announced positive results from REPRIEVE, a Phase III long-term maintenance study that was conducted by Novartis. In September 2015, the FDA accepted for review a supplemental New Drug Application (sNDA) for Fanapt® for the maintenance treatment of schizophrenia in adults. The FDA has set a May 2016 PDUFA date for the Fanapt® sNDA.

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We continue to explore the regulatory path and commercial opportunity for Fanapt® oral formulation outside of the U.S. In December 2012, 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 European Union. The CHMP was of the opinion that the benefits of Fanaptum® did not outweigh its risks and recommended against marketing authorization. We initiated an appeal of this opinion and requested a re-examination of the decision by the CHMP, but withdrew our Marketing Authorization Application (MAA) in the first quarter of 2013 because the additional clinical data requested by the CHMP would not have been available in the timeframe allowed by the EMA s Centralized Procedure. In December 2015, we refiled a MAA with the EMA for Fanaptum® which included the results from the REPRIEVE study.

We have entered into agreements with the following partners for the commercialization of Fanapt® in the countries set forth below:

Country	Partner	Market Approval Date
Mexico	Probiomed S.A. de C.V.	October 2013
Israel	Megapharm Ltd.	August 2012

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 and currently comprise approximately 90% of schizophrenia prescriptions. See *Competition* below for a discussion of commonly prescribed atypical antipsychotics in addition to Fanapt®.

Pursuant to the Settlement Agreement with Novartis, we reacquired the U.S. and Canadian rights to the long-acting injectable (depot) formulation of Fanapt®. We are evaluating the commercial opportunity around the depot formulation.

Tradipitant (VLY-686)

Tradipitant is a small molecule NK-1R antagonist that we licensed from Eli Lilly and Company (Lilly) in April 2012. NK-1R antagonists have been evaluated in a number of indications including chemotherapy-induced nausea and vomiting (CINV), post-operative nausea and vomiting (PONV), alcohol dependence, anxiety, depression and pruritus. We commenced a Phase II clinical study of tradipitant in the treatment of chronic pruritus in patients with atopic dermatitis in 2014. Results from a Phase II study for the treatment of chronic pruritus in atopic dermatitis were announced in March 2015. This study showed no significant difference from placebo on the pre-specified primary endpoint. Vanda believes this proof of concept study was informative, in that through subsequent analyses, it revealed significant and clinically meaningful responses across multiple outcomes evaluated in individuals with higher blood plasma levels of tradipitant at the time of their pruritus assessments. We plan to initiate a pruritus proof of concept study in 2016.

Trichostatin A

Trichostatin A is a small molecule HDAC inhibitor with potential use as a treatment for several oncology indications. We plan to file an IND application in the first half of 2016.

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AQW051

AQW051 is a Phase II alpha-7 nicotinic acetylcholine receptor partial agonist that we licensed from Novartis on December 31, 2014 pursuant to the Settlement Agreement. We are currently in the process of transferring clinical data from Novartis and evaluating potential indications, including cognitive impairment.

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 Company (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®. In partial consideration for the license, we paid BMS an initial license fee of $0.5 million. We made developmental milestone payments to BMS totaling $12.0 million under the license agreement, including an $8.0 million milestone payment in the first quarter of 2014 as a result of the FDA s approval of our HETLIOZ NDA. The $8.0 million milestone payment was capitalized as an intangible asset and is being amortized over the expected HETLIOZ® patent life in the U.S. We are obligated to make a future milestone payment to BMS of $25.0 million in the event that cumulative worldwide sales of HETLIOZ® reach $250.0 million. 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 post the first commercial sale in the territory or the expiry of the new chemical entity patent in that territory. During the period prior to the expiry of the new chemical entity 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 new chemical entity patent existed or for the remainder of the 10 years after the expiry of the new chemical entity 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 our license agreement for HETLIOZ® to use our 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 the Settlement Agreement with Novartis, Novartis transferred all U.S. and Canadian rights in the Fanapt® franchise to Vanda on December 31, 2014.

A predecessor company of Sanofi, Hoechst Marion Roussel, Inc. (HMRI), discovered Fanapt® and completed early clinical work on the compound. In 1996, HMRI licensed its rights to the Fanapt® patents and patent applications to Titan Pharmaceuticals, Inc. (Titan) on an exclusive basis. In 1997, soon after it had acquired its rights, Titan sublicensed its rights to Fanapt® on an exclusive basis to Novartis. In June 2004, we acquired exclusive worldwide rights to these patents and patent applications as well as certain Novartis patents and patent applications to develop and commercialize Fanapt® through a sublicense agreement with Novartis. In partial consideration for this sublicense, we paid Novartis an initial license fee of $0.5 million and were obligated to make future milestone payments to Novartis of less than $100.0 million in the aggregate (the majority of which were tied to sales milestones), as well as royalty payments to Novartis at a rate which, as a percentage of net sales, was in the mid-twenties. As a result of the FDA s approval of the NDA for Fanapt® in May 2009, we met a milestone under the sublicense agreement, which required us to make a payment of $12.0 million to Novartis.

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In October 2009, we entered into an amended and restated sublicense agreement with Novartis, which amended and restated the June 2004 sublicense agreement. Pursuant to the amended and restated sublicense agreement, Novartis had exclusive commercialization rights to all formulations of Fanapt® in the U.S. and Canada. Novartis began selling Fanapt® in the U.S. during the first quarter of 2010. Novartis was responsible for the further clinical development activities in the U.S. and Canada. Pursuant to the amended and restated sublicense agreement, we received an upfront payment of $200.0 million and were eligible for additional payments totaling up to $265.0 million upon Novartis achievement of certain commercial and development milestones for Fanapt® in the U.S. and Canada. We also received royalties, which, as a percentage of net sales, were in the low double-digits, on net sales of Fanapt® in the U.S. and Canada. We retained exclusive rights to Fanapt® outside the U.S. and Canada and are obligated to make royalty payments to Sanofi S.A. on Fanapt® sales outside the U.S. and Canada.

Pursuant to the terms of the Settlement Agreement, Novartis transferred all U.S. and Canadian rights in the Fanapt® franchise to the Company on December 31, 2014. We are obligated to make royalty payments to Sanofi, S.A. (Sanofi) and Titan, at a percentage rate equal to 23% on annual U.S. net sales of Fanapt® up to $200.0 million, and at a percentage rate in the mid-twenties on sales over $200.0 million through November 2016. See Note 3, *Settlement Agreement with Novartis*, to the consolidated financial statements included in Part II of this annual report on Form 10-K for additional information. In February 2016, we amended the agreement with Sanofi and Titan to remove Titan as the entity through which royalty payments from us are directed to Sanofi following the expiration of the new chemical entity (NCE) patent for Fanapt® in the U.S. on November 15, 2016. Under the amended agreement, we will pay directly to Sanofi a fixed royalty of 3% of net sales from November 16, 2016 through December 31, 2019 related to manufacturing know-how. We will make a $2.0 million payment applied to this 3% manufacturing know-how royalty and will make additional royalty payments only to the extent that our cumulative royalty obligations during this period exceed the amount of the pre-payment. No further royalties on manufacturing know-how are payable by us after December 31, 2019. This amended agreement does not alter Titan s obligation under the License Agreement to make royalty payments to Sanofi prior to November 16, 2016 or our obligations under the Sublicense Agreement 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.

Tradipitant (VLY-686)

In April 2012, we entered into a license agreement with 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.

Pursuant to the agreement, we paid Lilly an initial license fee of $1.0 million and we will be responsible for all development costs for tradipitant. Lilly is also eligible to receive additional payments based upon achievement of specified development and commercialization milestones as well as tiered-royalties on net sales at percentage rates up to the low double digits. These milestones include $4.0 million for pre-NDA approval milestones and up to $95.0 million for future regulatory approval and sales milestones. We have agreed 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.

AQW051

In December 2014, we entered into a license agreement with Novartis 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 alpha-7 nicotinic acetylcholine receptor partial agonist, AQW051, for all human indications.

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Pursuant to the agreement, we will be responsible for all development costs for AQW051. Novartis is eligible to receive tiered royalties on net sales at percentage rates up to the low double digits. We have agreed to use commercially reasonable efforts to develop and commercialize AQW051.

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 AQW051.

Government regulation

Government authorities in the U.S., at the federal, state and local level, as well as foreign countries and local foreign governments, regulate the research, development, testing, manufacture, labeling, promotion, advertising, distribution, sampling, marketing, import and export of our products. Other than HETLIOZ® in the U.S. and the European Union and Fanapt® in the U.S., Israel and Mexico, all of our products will require regulatory approval by government agencies prior to commercialization. In particular, human pharmaceutical products are subject to rigorous pre-clinical and clinical trials and other approval procedures of the FDA and similar regulatory authorities in foreign countries. The process of obtaining these approvals and the subsequent compliance with appropriate domestic and foreign laws, rules and regulations require the expenditure of significant time and human and financial resources.

United States government regulation

FDA approval process

In the U.S., the FDA regulates drugs under the Federal Food, Drug and Cosmetic Act, as amended, and implements regulations. If we fail to comply with the applicable requirements at any time during the product development process, approval process, or after approval, we may become subject to administrative or judicial sanctions. These sanctions could include the FDA s refusal to approve pending applications, withdrawals of approvals, clinical holds, warning letters, product recalls, product seizures, total or partial suspension of our operations, injunctions, fines, civil penalties or criminal prosecution. Any such sanction could have a material adverse effect on our business.

The steps required before a drug may be marketed in the U.S. include:

- pre-clinical laboratory tests, animal studies and formulation studies under Current Good Laboratory Practices (cGLP);
- submission to the FDA of an investigational new drug application (IND), which must become effective before human clinical trials may begin;
- execution of adequate and well-controlled clinical trials to establish the safety and efficacy of the drug for each indication for which approval is sought;
- submission to the FDA of an NDA;
- satisfactory completion of an FDA inspection of the manufacturing facility or facilities at which the drug is produced to assess compliance with Current Good Manufacturing Practices (cGMP); and
- FDA review and approval of the NDA.

Pre-clinical studies generally are conducted in laboratory animals to evaluate the potential safety and activity of a drug. Violation of the FDA s cGLP regulations can, in some cases, lead to invalidation of the studies, requiring these studies to be replicated. In the U.S., drug developers

submit the results of pre-clinical trials, together with manufacturing information and analytical and stability data, to the FDA as part of the IND, which must become effective before clinical trials can begin in the U.S. An IND becomes effective 30 days after receipt by the FDA unless before that time the FDA raises concerns or questions about issues such as the

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proposed clinical trials outlined in the IND. In that case, the IND sponsor and the FDA must resolve any outstanding FDA concerns or questions before clinical trials can proceed. If these concerns or questions are unresolved, the FDA may not allow the clinical trials to commence.

Pilot studies generally are conducted in a limited patient population, approximately three to 25 subjects, to determine whether the drug warrants further clinical trials based on preliminary indications of efficacy. These pilot studies may be performed in the U.S. after an IND has become effective or outside of the U.S. prior to the filing of an IND in the U.S. in accordance with applicable government regulations and institutional procedures.

Clinical trials involve the administration of the investigational new drug to human subjects under the supervision of qualified investigators. Clinical trials are conducted under protocols detailing, among other things, the objectives of the study, the parameters to be used in assessing the safety and the effectiveness of the drug. Each protocol must be submitted to the FDA as part of the IND prior to beginning the trial.

Typically, clinical evaluation involves a time-consuming and costly three-Phase sequential process, but the phases may overlap. Each trial must be reviewed, approved and conducted under the auspices of an independent Institutional Review Board, and each trial must include the patient s informed consent.

Phase I: refers typically to closely-monitored clinical trials and includes the initial introduction of an investigational new drug into human patients or healthy volunteer subjects. Phase I trials are designed to determine the safety, metabolism and pharmacologic actions of a drug in humans, the potential side effects associated with increasing drug doses and, if possible, to gain early evidence of the drug s effectiveness. Phase I trials also include the study of structure-activity relationships and mechanism of action in humans, as well as studies in which investigational new drugs are used as research tools to explore biological phenomena or disease processes. During Phase I trials, sufficient information about a drug s pharmacokinetics and pharmacological effects should be obtained to permit the design of well-controlled, scientifically valid Phase II studies. The total number of subjects and patients included in Phase I trials varies, but is generally in the range of 20 to 80 people.

Phase II: refers to controlled clinical trials conducted to evaluate appropriate dosage and the effectiveness of a drug for a particular indication or indications in patients with a disease or condition under study and to determine the common short-term side effects and risks associated with the drug. These trials are typically well-controlled, closely monitored and conducted in a relatively small number of patients, usually involving no more than several hundred subjects.

Phase III: refers to expanded controlled and uncontrolled clinical trials. These trials are performed after preliminary evidence suggesting effectiveness of a drug has been obtained. Phase III trials are intended to gather additional information about the effectiveness and safety that is needed to evaluate the overall benefit-risk relationship of the drug and to provide an adequate basis for physician labeling. Phase III trials usually include several hundred to several thousand subjects.

Phase I, II and III testing may not be completed successfully within any specified time period, if at all. The FDA closely monitors the progress of each of the three phases of clinical trials that are conducted in the U.S. and may, at its discretion, reevaluate, alter, suspend or terminate the testing based upon the data accumulated to that point and the FDA s assessment of the risk/benefit ratio to the patient. A clinical program is designed after assessing the causes of the disease, the mechanism of action of the active pharmaceutical ingredient of the drug and all clinical and pre-clinical data of previous trials performed. Typically, the trial design protocols and efficacy endpoints are established in consultation with the FDA. Upon request through a special protocol assessment, the FDA can also provide specific guidance on the acceptability of protocol design for clinical trials. The FDA, we or our partners may suspend or terminate clinical trials at any time for various reasons, including a finding that the subjects or patients are being exposed to an unacceptable health risk. The FDA can also request additional clinical trials be conducted as a condition to drug approval. During all clinical trials, physicians monitor the patients to determine effectiveness and to observe and report any reactions or other safety risks that may result from use of the drug.

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Assuming successful completion of the required clinical trials, drug developers submit the results of pre-clinical studies and clinical trials, together with other detailed information including information on the manufacture and composition of the drug, to the FDA, in the form of an NDA, requesting approval to market the drug for one or more indications. In most cases, the NDA must be accompanied by a substantial user fee. The FDA reviews an NDA to determine, among other things, whether a drug is safe and effective for its intended use.

Before approving an NDA, the FDA will inspect the facility or facilities where the drug is manufactured. The FDA will not approve the application unless cGMP compliance is satisfactory. The FDA will issue an approval letter if it determines that the application, manufacturing process and manufacturing facilities are acceptable. If the FDA determines that the NDA, manufacturing process or manufacturing facilities are not acceptable, it will issue a complete response letter (CRL), in which it will outline the deficiencies in the submission and will often request additional testing or information. Notwithstanding the submission of any requested additional information, the FDA may ultimately decide that the NDA does not satisfy the regulatory criteria for approval and refuse to approve the NDA.

The testing and approval process requires substantial time, effort and financial resources, and each may take several years to complete. The FDA may not grant approval on a timely basis, or at all. We or our partners may encounter difficulties or unanticipated costs in our efforts to secure necessary governmental approvals, which could delay or preclude us or our partners from marketing our products. Furthermore, the FDA may prevent a drug developer from marketing a drug under a label for its desired indications or place other conditions on distribution as a condition of any approvals, which may impair commercialization of the drug. After approval, some types of changes to the approved drug, such as adding new indications, manufacturing changes and additional labeling claims, are subject to further FDA review and approval. Similar regulatory procedures must also be complied within countries outside the U.S.

If the FDA approves the NDA, the drug becomes available for physicians to prescribe in the U.S. After approval of our products, we have to comply with a number of post-approval requirements, including delivering periodic reports to the FDA, submitting descriptions of any adverse reactions reported, and complying with drug sampling and distribution requirements. We and our partners also are required to provide updated safety and efficacy information and to comply with requirements concerning advertising and promotional labeling. Also, our quality control and manufacturing procedures must continue to conform to cGMP after approval. Drug manufacturers and their subcontractors are required to register their facilities and are subject to periodic unannounced inspections by the FDA to assess compliance with cGMP which imposes certain procedural and documentation requirements relating to quality assurance and quality control. Accordingly, manufacturers must continue to expend time, money and effort in the area of production and quality control to maintain compliance with cGMP and other aspects of regulatory compliance. The FDA may require post market testing and surveillance to monitor the drug s safety or efficacy, including additional studies, known as Phase IV trials, to evaluate long-term effects.

In addition to studies requested by the FDA after approval, we or our partners may have to conduct other trials and studies to explore use of the approved product for treatment of new indications, which require FDA approval. The purpose of these trials and studies is to broaden the application and use of the product and its acceptance in the medical community.

We use, and will continue to use, third-party manufacturers to produce our products in clinical and commercial quantities. Future FDA inspections may identify compliance issues at our facilities or at the facilities of our contract manufacturers that may disrupt production or distribution, or require substantial resources to correct. In addition, discovery of problems with a product or the failure to comply with requirements may result in restrictions on a product, manufacturer or holder of an approved NDA, including withdrawal or recall of the product from the market or other voluntary or FDA-initiated action that could delay further marketing. Newly discovered or developed safety or effectiveness data may require changes to a product s approved labeling, including the addition of new warnings and contraindications.

In September 2007, the Food and Drug Administration Amendments Act (FDAAA), was enacted into law, amending the U.S. Federal Food, Drug, and Cosmetic Act and the Public Health Service Act. The FDAAA made a number of substantive and incremental changes to the review and approval processes in ways that could make it

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more difficult or costly to obtain approval for new pharmaceutical products, or to produce, market and distribute existing pharmaceutical products. Most significantly, the law changed the FDA s handling of postmarked drug product safety issues by giving the FDA authority to require post approval studies or clinical trials, to request that safety information be provided in labeling, or to require an NDA applicant to submit and execute a Risk Evaluation and Mitigation Strategy (REMS).

The FDAAA made certain changes to the user fee provisions to permit the use of user fee revenue to fund the FDA s drug product safety activities and the review of Direct-to-Consumer advertisements. The Food and Drug Administration Safety and Innovation Act of 2012, which became effective in October 2012, reauthorized the authority of the FDA to collect user fees to fund the FDA s review activities.

In addition, new government requirements may be established that could delay or prevent regulatory approval of our products under development.

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 Approved Drug Products with Therapeutic Equivalence Evaluations, commonly known as the Orange Book. Drugs listed in the Orange Book can, in turn be cited by potential competitors in support of approval of an abbreviated new drug application (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 pre-clinical 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 FDA s 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 new chemical entity, 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.

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Foreign regulation

Whether or not we or our partners 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 United States government regulation. However, the foreign equivalent of an IND is not a prerequisite to performing pilot studies or Phase I clinical trials.

Under European Union regulatory systems, we may submit 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 European Union 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 or our partners.

Patents and proprietary rights; Hatch-Waxman protection

We and our partners will be able to protect our products from unauthorized use by third parties only to the extent that our products are covered by valid and enforceable patents, either licensed in from third parties or generated internally, that give us or our partners sufficient proprietary rights. Accordingly, patents and other proprietary rights are essential elements of our business.

HETLIOZ®, Fanapt®, tradipitant and AQW051 are covered by new chemical entity and other patents and patent applications. The patents cover the active pharmaceutical ingredient and provide patent protection for all formulations containing these active pharmaceutical ingredients. For more on these license and sublicense arrangements, see *License agreements* above. In addition, we have generated our own intellectual property, and filed patent applications covering this intellectual property, for HETLIOZ® and Fanapt.

The table below is a summary of select patents for our commercial products.

	Number	Type	Country
HETLIOZ®	US 5,856,529	NCE	Issued in 39 countries including US, EU and Japan
	US 8,785,492	Method of treatment	US issued, pending in 15 countries and EU
	US 9,060,995	Method of treatment	US issued, pending in 15 countries and EU
	US 7,754,902	Synthesis	US
	US 8,097,738	Synthesis	US
	US 8,558,017	Synthesis	US
Fanapt®	RE 39198	NCE	US
	US 8,586,610	Method of treatment	US & Japan, pending in Canada, EU, Australia
	US 9,138,432	Method of treatment	US, pending in Japan, Canada, EU, Australia
	PCT/EP2002/012073	Iloperidone microparticle depot formulation	US, EU & Japan, issued in 29 countries

PCT/EP2003/007619	Iloperidone aq. crystal depot formulation	US, EU & Japan, issued in 34 countries
PCT/EP2002/013937	Method of treatment	US, EU & Japan, issued in 30 countries

HETLIOZ®

Our rights to the new chemical entity patent covering HETLIOZ® and related intellectual property have been acquired through a license with BMS. HETLIOZ® and its formulations, genetic markers and uses are covered by a total of 14 patent and patent application families worldwide. The primary new chemical entity patent covering HETLIOZ® expires normally in 2017 in the U.S. and in most European markets. The Hatch-Waxman Act provides for an extension of new chemical entity patents for a period of up to five years following

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the expiration of the patent covering that compound to compensate for time spent in development. We believe that HETLIOZ® will meet the various criteria of the Hatch-Waxman Act and will receive five additional years of patent protection in the U.S., which would extend its new chemical entity patent protection in the U.S. until 2022. An application for the five year patent term extension has been filed and is being processed by the U.S. Patent and Trademark Office. In July 2014, a new method of use patent was issued to us by the U.S. Patent and Trademark Office for HETLIOZ® in the treatment of Non-24. This method of use patent is expected to expire in 2033, potentially further extending the exclusivity protection of HETLIOZ®. In June 2015, an additional method of use patent was issued to us by the U.S. Patent and Trademark Office for HETLIOZ®. This method of use patent is also expected to expire in 2033. Both the new chemical entity patent and the method of use patents are listed in the FDA s Orange Book.

In Europe, the law provides for ten years of data exclusivity (with the potential for an additional year if the drug is developed for a significant new indication). As such, in Europe, data exclusivity will protect HETLIOZ® for at least ten years from approval. A completed Pediatric Investigation Plan could further extend this exclusivity for two years in an orphan indication, for a total of 12 years of exclusivity. It is also possible that the term of the new chemical entity patent in Europe could be extended by issuance of a supplementary protection certificate (SPC). The European Patent Office has granted the Company s patent application directed to the 20 mg/day dose. This patent will expire normally in 2027. Patent applications directed to the treatment of Non-24, if granted, would provide exclusivity in Europe for this indication until at least 2033.

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 major markets.

Fanapt®

The new chemical entity patent for Fanapt® is owned by Sanofi, and other patents and patent applications relating to Fanapt® previously owned by Novartis are now owned by Vanda. We originally obtained exclusive worldwide rights to develop and commercialize the products covered by these patents through license and sublicense arrangements. Then, pursuant to an amended sublicense agreement with Novartis, Novartis retained exclusive commercialization rights to all formulations of Fanapt® in the U.S. and Canada. However, as of December 2014, pursuant to an asset transfer agreement, we acquired all rights in Fanapt®, including in the U.S. and Canada.

Fanapt® and its metabolites, formulations, genetic markers and uses are covered by a total of 17 patent and patent application families in the U.S., Europe, and other markets. The primary new chemical entity patent covering Fanapt® was set to expire normally in 2011 in the U.S. and expired in 2010 in major markets outside the U.S. Fanapt® has qualified for the full five-year patent term extension under the Hatch-Waxman Act and so the term of the new chemical entity patent in the U.S. has been extended until November 2016. In November 2013, a patent directed to a method of treating patients with Fanapt® based on genotype was issued to the Company by the U.S. Patent and Trademark Office. This patent, which was listed in the FDA s Orange Book in January 2015, is set to expire in 2027, potentially further extending the exclusivity protection of Fanapt®. Additional method of treatment patents were issued and listed in the Orange Book with the latest expected expiry in December 2031. We have asserted our patents against Roxane Laboratories and several other paragraph IV filers. See Note 18, *Legal Matters*, to the consolidated financial statements included in Part II of this annual report on Form 10-K for additional information.

In Europe, the law provides for ten years of data 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 this 10-year (or 11-year) period in most European countries. Consequently, we expect our rights to commercialize Fanapt® will be exclusive for at least 10 years from approval in Europe. Outside the U.S. and Europe, data exclusivity will protect Fanapt® from generic competition for varying numbers of years depending upon the country. Several other patent applications covering metabolites, uses, formulations and

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genetic markers relating to Fanapt® extend beyond 2020. The patent family for the microsphere depot formulation of Fanapt® expires in 2024 in the U.S. and 2022 in most of the major markets in Europe. The patent family for the aqueous microcrystals depot formulation of Fanapt® expires in 2023 in the U.S. and in most of the major markets in Europe.

Tradipitant

Lilly owns a new chemical entity patent as well as patent applications directed to polymorphic forms of, and methods of making tradipitant. Thus, tradipitant is covered by a total of three patent and patent application families worldwide, which have been licensed to the Company. The new chemical entity patent covering tradipitant expires in 2023, except in the U.S., where it expires normally in 2024 subject to any extension that may be received under Hatch-Waxman. We have filed additional patent applications based on discoveries made during recent studies with tradipitant.

AQW051

Novartis owns a new chemical entity patent as well as patent applications directed to methods of using AQW051, AQW051 formulations, and combinations of AQW051 with other active pharmaceutical ingredients. The new chemical entity patent expires normally in 2023 in the U.S., Europe, and other markets.

Trichostatin A

Trichostatin A 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 Trichostatin A and plan on filing additional applications based on discoveries made throughout the development plan of this molecule.

Other Patents

Aside from the new chemical entity patents and other in-licensed patents relating to Fanapt®, HETLIOZ®, tradipitant, and AQW051, we have numerous patent and patent application families, most of which have been filed in key markets including the U.S., relating to our products and development compounds. In addition, we have several other patent application families 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, 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.

Third-party reimbursement and pricing controls

The Patient Protection and Affordable Care Act, as amended by the Health Care and Education Affordability Reconciliation Act of 2010, collectively referred to as the ACA, has changed and is expected to further significantly change the way healthcare is financed by both governmental and private insurers. The provisions of the ACA became effective over various periods from 2010 through 2014. We cannot predict the complete impact of the ACA on pharmaceutical companies because many of the ACA s reforms require the promulgation of detailed regulations to implement the statutory provisions, which has not yet occurred. While we cannot predict the complete impact on federal reimbursement policies this law will have in general or specifically on any product we commercialize, the ACA may result in downward pressure on pharmaceutical reimbursement, which could negatively affect market acceptance of new products. The rebates, discounts, taxes and other costs

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resulting from the ACA may have a significant effect on our profitability in the future. In addition, potential reductions of the per capita rate of growth in Medicare spending under the ACA, could potentially limit access to certain treatments or mandate price controls for our products. Moreover, although the United States Supreme Court has upheld the constitutionality of most of the ACA, some states have indicated that they intend not to implement certain sections of the ACA, and some members of the U.S. Congress are still working to repeal the ACA. We cannot predict whether these challenges will continue or other proposals will be made or adopted, or what impact these efforts may have on us or our partners.

In the U.S. and elsewhere, sales of pharmaceutical products depend in significant part on the availability of reimbursement to the consumer from third-party payors, such as government and private insurance plans. Third-party payors are increasingly challenging the prices charged for medical products and services. It will be time consuming and expensive for us or our partners to go through the process of seeking reimbursement from Medicare and private payors. Our products may not be considered cost-effective, and coverage and reimbursement may not be available or sufficient to allow us or our partners to sell our compounds on a competitive and profitable basis. The passage of the Medicare Prescription Drug and Modernization Act of 2003 imposes additional requirements for the distribution and pricing of prescription drugs which may affect the marketing of our products.

In many foreign markets, including the countries in the European Union and Japan, pricing of pharmaceutical products is subject to governmental control. In the U.S., there have been, and we expect that there will continue to be, a number of federal and state proposals to implement similar governmental pricing control. While we cannot predict whether such legislative or regulatory proposals will be adopted, the adoption of such proposals could have a material adverse effect on our business, financial condition and profitability.

Marketing and sales

HETLIOZ® was approved in the U.S. for the treatment of Non-24 in January 2014 and commercially launched in the U.S. in April 2014. Additionally, HETLIOZ® was approved in the Europe Union for the treatment of Non-24 in July 2015 and we expect to commercially launch the product in Germany in 2016.

Given the range of potential indications for HETLIOZ®, we may pursue one or more partnerships for the development and commercialization of HETLIOZ® worldwide.

Fanapt® was approved in the U.S. for the treatment of schizophrenia in May 2009 and commercially launched in the U.S. in January 2010. In October 2009, we entered into an amended and restated sublicense agreement with Novartis pursuant to which Novartis has exclusive commercialization rights to all formulations of Fanapt® in the U.S. and Canada. Novartis began selling Fanapt® in the U.S. during the first quarter of 2010. Pursuant to the terms of the Settlement Agreement with Novartis, Novartis transferred all U.S. and Canadian rights in the Fanapt® franchise to Vanda on December 31, 2014.

Fanapt® was launched in Israel and Mexico by our distribution partners in 2014. We continue to explore the regulatory path and commercial opportunity for Fanapt® oral formulation outside of the U.S. and Canada.

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.

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In January 2014, we entered into a manufacturing agreement with Patheon Pharmaceuticals Inc. (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 for HETLIOZ® to Patheon and have agreed to certain minimum yearly order requirements. 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 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 twelve 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 the Settlement Agreement, we assumed Novartis manufacturing agreement with Patheon for the manufacture of commercial supplies of Fanapt®. Under the Fanapt® manufacturing agreement, we may procure bulk, partially packaged and finished supplies of various dosages of Fanapt® for sale worldwide. We are responsible for sourcing the supply of the active pharmaceutical ingredient (iloperidone), and Patheon will manufacture 1, 2, 4, 6, 8, 10 and 12 mg tablets pursuant to orders placed by us. The Fanapt® manufacturing agreement contains specific forecasting, order lead time, minimum order quantities, yield requirements, delivery terms and alternative manufacturing provisions. Generally, all product shipped to us must have a remaining shelf life of more than four-fifths of its total shelf life, but no less than one year of shelf life remaining for certain products. The Fanapt® manufacturing agreement continues on a year-to-year basis, and can be terminated by either party on at least 12 months prior notice, or prior to the end of the then current term for uncured breach, insolvency/bankruptcy, or by us if a regulatory action prevents the supply of iloperidone to Patheon or otherwise the purchase or sale of 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.

We incurred $29.1 million, $19.2 million and $28.5 million in research and development expenses in the years ended December 31, 2015, 2014 and 2013, respectively.

Customers

Our revenue for the years ended December 31, 2015, 2014 and 2013 consisted of revenue from product sales, license revenue, and royalty revenue. Six customers, each based in the U.S., accounted for 94% of our total revenue for the year ended December 31, 2015. No other customer accounted for more than 10% of revenue in 2015. One company, headquartered in Switzerland with our revenue generated from sales in the U.S., accounted for 74% of our total revenue for the year ended December 31, 2014. No other customer accounted for more than 10% of revenue in 2014. One company, headquartered in Switzerland with our revenue generated from sales in the U.S., accounted for 100% of our total revenue for the year ended December 31, 2013. No other customer accounted for more than 10% of revenue in 2013. Future revenue is uncertain and may fluctuate significantly from period to period. We have not experienced any losses relating to receivables from customers.

Competition

The pharmaceutical industry and the central nervous system segment of that 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

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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, there are no FDA approved direct competitors. Sedative-Hypnotic treatments 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® (agemelatine) by Servier, Circadin® (long-acting melatonin) by Neurim Pharmaceuticals 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 depot formulation Risperdal® Consta® and Invega® (paliperidone), including the depot formulation Invega® Sustenna®, each by Ortho-McNeil-Janssen Pharmaceuticals, Inc., Zyprexa® (olanzapine), including the depot formulation Zyprexa® Relprevv , each by Eli Lilly and Company, Seroquel® (quetiapine) by AstraZeneca PLC, Abilify® (aripiprazole) by BMS/Otsuka America Pharmaceutical Inc., Abilify® Maintena® (the depot formulation of Abilify®) by Lundbeck/Otsuka America Pharmaceutical Inc., Geodon® (ziprasidone) by Pfizer Inc., Saphris® (asenapine) by Actavis plc, Latuda® (lurasidone) by Sunovion Pharmaceuticals Inc., Rexulti® (brexpiprazole) by Otsuka Pharmaceutical, Inc., Aristada (aripiprazole lauroxil) extended-release injectible suspension by Alkermes, Inc. 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.

Employees

We had 118 full-time employees as of December 31, 2015, compared with 64 as of December 31, 2014. 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.

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 (the Exchange Act). The public

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may read and copy any materials that we file with the SEC at the SEC s Public Reference Room at 100 F Street, NE, Washington, D.C. 20549. The public may obtain information on the operation of the Public Reference Room by calling the SEC at 1-800-SEC-0330. Also, the SEC maintains an internet 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 current 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 on Form 10-K or elsewhere. The following information should be read in conjunction with the consolidated financial statements and related notes in Part I, Item 1, Financial Statements and Part I, Item 2, 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 heavily dependent on the commercial success of HETLIOZ®.

Our future success is currently substantially dependent upon the commercial success of HETLIOZ® for the treatment of Non-24-Hour Sleep-Wake Disorder (Non-24). In January 2014, the 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 blind adults. This authorization is valid in the 28 countries that are members of the European Union, as well as European Economic Area members Iceland, Liechtenstein and Norway.

Because we have limited information with regard to the market acceptance of HETLIOZ® in the U.S. or elsewhere abroad, we may have to revise our commercial strategy for, or estimates regarding the market acceptance of, HETLIOZ® or our strategy to commercialize the product.

Market acceptance of and demand for HETLIOZ® depends on many factors, including, but not limited to:

- cost of treatment;
- pricing and availability of alternative products;
- the cost and success of our Non-24 awareness campaign;

our ability to obtain third-party coverage or reimbursement for HETLIOZ®;

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perceived efficacy relative to other available therapies;

shifts in the medical community to new treatment paradigms or standards of care;

relative convenience and ease of administration; and

prevalence and severity of adverse side effects associated with treatment.

In addition, 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 our Non-24 awareness campaign in the U.S., evaluate foreign market opportunities for HETLIOZ® and continue to grow our operational capabilities, both domestically and abroad. This represents a significant investment in the commercial success of HETLIOZ ®, which is uncertain.

If we do not successfully commercialize HETLIOZ® in the U.S., Europe or other jurisdictions in which HETLIOZ® may be approved for sale, our ability to generate increased product sales revenue may be jeopardized and, consequently, our business may be seriously harmed.

We recently acquired further rights to Fanapt® in the United States, and began selling, marketing and distributing Fanapt® in the United States in the first quarter of 2015, and our ability to generate meaningful product sales from Fanapt® will depend on the success of this product in the marketplace.

Our ability to generate meaningful product sales from Fanapt® will depend on many factors, including the following:

the unfavorable outcome or other negative effects of any pending litigation relating to Fanapt®;

the effectiveness of our sales and marketing efforts in support of Fanapt®;

the ability of patients to be able to afford Fanapt® or obtain health care coverage that covers Fanapt®;

acceptance of, and ongoing satisfaction, with Fanapt® by the medical community, patients receiving therapy and third party payors;

a satisfactory efficacy and safety profile as demonstrated in a broad patient population;

the size of the market for Fanapt®;

the ability of our manufacturing partners to successfully expand and sustain capacity to meet demand;

cost and availability of raw materials;

safety concerns in the marketplace for schizophrenia therapies;

regulatory developments relating to the manufacture or continued use of Fanapt®;

decisions as to the timing of product launches, pricing and discounts;

the competitive landscape for approved and developing therapies that will compete with Fanapt®; and

our or our partners ability to obtain regulatory approval for Fanapt® in additional countries.

For reasons outside of our control, including those mentioned above, sales of Fanapt® may not meet our or financial or industry analysts expectations. Any significant negative developments relating to Fanapt®, such as the loss of patent protection, safety or efficacy issues, the introduction or greater acceptance of competing products or adverse regulatory or legislative developments, will have an adverse effect on our financial condition and results of operations.

As a company, we have minimal experience selling, marketing or distributing products, which may make commercializing our products difficult.

At present, we as a company have minimal marketing experience. Therefore, in order for us to successfully commercialize HETLIOZ®, Fanapt® or our other products, we must either acquire or continue to internally develop sales, marketing and distribution capabilities, or enter into collaborations with partners to perform these services for us. We may, in some instances, rely significantly on sales, marketing and distribution arrangements with our collaborative partners and other third parties.

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For the commercialization of HETLIOZ®, Fanapt® or our other products, we may not be able to establish additional sales, marketing and distribution capabilities or partnerships on acceptable terms or at all. In regard to our current foreign partners and any additional distribution arrangements or other agreements we may enter into, our success will be materially dependent upon the performance of our partners. Factors that may inhibit our efforts to commercialize our products without partners or licensees include:

- our inability to recruit and retain adequate numbers of effective sales and marketing personnel;
- the inability of sales personnel to obtain access to or persuade adequate numbers of physicians to prescribe our products;
- the lack of complementary products to be offered by our sales personnel, which may put us at a competitive disadvantage with respect to companies with broader product lines; and
- unforeseen costs associated with growing our own sales and marketing team or with entering into a partnering agreement with an independent sales and marketing organization.

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.

We may enter into third party collaborations from time to time in order to 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. Areas in which we may potentially enter into third-party collaboration arrangements include joint sales and marketing arrangements for sales and marketing in certain European Union 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 which 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 which 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.

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Even after we or our partners 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 or our partners are developing and the effectiveness of our and our partners 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 clinical development and supply of HETLIOZ®, Fanapt® and our other products.

As of December 31, 2015, we had 118 full-time employees and, as a result, we rely, and expect to continue to rely, on outsourcing arrangements for a significant portion of our activities, including distribution, clinical research and development, data collection and analysis and manufacturing, as well as for certain functions as a public company. We may 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® or Fanapt® supply chains could materially affect our ability to successfully commercialize 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® 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 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® 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.

We and our partners face heavy government regulation. We and our partners are also continually at risk of the FDA or applicable foreign agency requiring us or them to discontinue marketing any products that have obtained, or in the future may obtain, regulatory approval.

Following marketing approval of a product, we and our partners will continue to face heavy governmental regulation. The marketing, distribution and manufacture of approved products remain subject to extensive ongoing regulatory requirements. Failure to comply with applicable regulatory requirements could result in, among other things:

warning letters;

fines;

civil penalties;

injunctions;

recall or seizure of products;

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total or partial suspension of production;

refusal of the government to grant future approvals;

withdrawal of approvals; and

criminal prosecution.

If we or our partners become subject to any of these foregoing items, our business, results of operations and financial condition could be materially adversely affected.

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

Our and our partners activities, including the sale and marketing of our products, are subject to extensive government regulation and oversight, including regulation under the federal Food, Drug and Cosmetic Act and other federal and state statutes. We are also subject to the provisions of the Federal Anti-Kickback Statute and several similar state laws, which prohibit payments intended to induce physicians or others either to purchase or arrange for or recommend the purchase of healthcare products or services. While the federal law applies only to products or services for which payment may be made by a federal healthcare program, state laws may apply regardless of whether federal funds may be involved. These laws constrain the sales, marketing and other promotional activities of manufacturers, suppliers or sponsors, including third-parties performing similar functions, of drugs and biologicals, by limiting the kinds of financial arrangements, including sales programs, with hospitals, physicians, and other potential purchasers of drugs and biologicals. Other federal and state laws generally prohibit individuals or entities from knowingly presenting, or causing to be presented, claims for payment from Medicare, Medicaid, or other third party payors that are false or fraudulent, or are for items or services that were not provided as claimed. Anti-kickback and false claims laws prescribe civil and criminal penalties for noncompliance that can be substantial, including the possibility of exclusion from federal healthcare programs (including Medicare and Medicaid).

Pharmaceutical and biotechnology companies have been the target of lawsuits and investigations alleging violations of government regulation, including claims asserting antitrust violations, violations of the Federal False Claim Act, the Anti-Kickback Statute, the Prescription Drug Marketing Act and other violations in connection with off-label promotion of products and Medicare and/or Medicaid reimbursement or related to environmental matters and claims under state laws, including state anti-kickback and fraud laws.

While we continually strive to comply with these complex requirements, interpretations of the applicability of these laws to marketing practices are ever evolving. If any such actions are instituted against us or our partners and we or they are not successful in defending such actions or asserting our rights, those actions could have a significant and material adverse impact on our business, including the imposition of significant fines or other sanctions. Even an unsuccessful challenge could cause adverse publicity and be costly to respond to, and thus could have a material adverse effect on our business, results of operations and financial condition.

We intend to seek regulatory approvals for our products in additional foreign jurisdictions, but we may not obtain any such approvals.

We intend to market our products, alone or with others, in foreign jurisdictions. In order to market our products in foreign jurisdictions, we or our partners may be required to obtain separate regulatory approvals and to comply with numerous and varying regulatory requirements. 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. Additionally, the foreign regulatory approval process may include all of the risks associated with obtaining FDA approval. For all of these reasons, we or our partners may not obtain foreign regulatory approvals on a timely basis, if at all. 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. We or our partners may not be able to file for regulatory approvals and may not receive necessary approvals to commercialize our products in any market. The failure to obtain these approvals could harm our business materially.

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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 only 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