Vanda Pharmaceuticals Inc.
Form 10-K
February 26, 2013
Table of Contents

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, 2012

¨ **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 29, 2012, the aggregate market value of the Common Stock held by non-affiliates of the registrant was approximately $106.2 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, director and stockholders known by the registrant to own 10% or more of the outstanding stock based on public filings and other information known to the registrant have been excluded since such persons may be deemed affiliates. This determination of affiliate status is not necessarily a conclusive determination for other purposes.

The number of shares of the registrant s Common Stock, par value $0.001 per share, outstanding as of February 20, 2013 was 28,342,659.

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 2013 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, 2012, are incorporated by reference into Part III of this Form 10-K.

Table of Contents

Vanda Pharmaceuticals Inc.

Form 10-K

Table of Contents

Table of Contents

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 inability to reach agreement with the U.S. Food and Drug Administration regarding our regulatory approval strategy or proposed path to approval for tasimelteon for the treatment of Non-24-Hour Disorder (Non-24);
- the failure to obtain regulatory approval for our products or product candidates, particularly tasimelteon for the treatment of Non-24, or to comply with ongoing regulatory requirements;
- a loss of rights to develop and commercialize our products, product candidates or partnered products under our license and sublicense agreements.
- our failure to develop or obtain sales, marketing and distribution resources and expertise or to otherwise manage our growth;
- the extent and effectiveness of the development, sales and marketing and distribution support Fanapt® receives;
- our ability to successfully commercialize Fanapt® outside of the U.S. and Canada;
- delays in the completion of our or our partners clinical trials;
- a failure of our products, product candidates or partnered products to be demonstrably safe and effective;
- a lack of acceptance of our products, product candidates or partnered products in the marketplace, or a failure to become or remain profitable;
- our expectations regarding trends with respect to our revenues, costs, expenses and liabilities;
- our inability to obtain the capital necessary to fund our research and development or commercial activities;
- our failure to identify or obtain rights to new products or product candidates;

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

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

losses incurred from product liability claims made against us.

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 1 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

Table of Contents

we file with the Securities and Exchange Commission (SEC) from time to time, including on Form 10-Q and Form 8-K, which may supplement, modify, supersede or update those risk factors. There can be no assurance that the actual results or developments anticipated by us will be realized or, even if substantially realized, that they will have the expected consequences to, or effects on, us. Therefore no assurance can be given that the outcomes stated in such forward-looking statements and estimates will be achieved.

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. We believe that each of our products and partnered products will address markets with significant unmet medical needs. Our product portfolio includes tasimelteon, a compound for the treatment of circadian rhythm sleep disorders (CRSD), which is currently in clinical development for Non-24, Fanapt®, a compound for the treatment of schizophrenia, the oral formulation of which is currently being marketed and sold in the U.S. by Novartis Pharma AG (Novartis), and VLY-686, a small molecule neurokinin-1 receptor (NK-1R) antagonist.

Throughout this annual report on Form 10-K, we refer to Fanapt® within the U.S. and Canada as our partnered product and we refer to Fanapt® outside the U.S. and Canada, tasimelteon and VLY-686 as our products. All other compounds are referred to herein as our product candidates. In addition, we refer to our partnered products, products and product candidates collectively as our compounds. Moreover, we refer to drug products generally as drugs or products.

Since we began our operations in March 2003, we have devoted substantially all of our resources to the in-licensing and clinical development of our compounds. Our ability to generate revenue and achieve profitability largely depends on our ability, alone or with others, to complete the development of our products or product candidates, and to obtain the regulatory approvals for and manufacture, market and sell our products and product candidates, including tasimelteon for the treatment of Non-24-Hour Disorder (Non-24) and Novartis ability to successfully commercialize Fanapt® in the U.S. The results of our operations will vary significantly from year-to-year and quarter-to-quarter and depend on a number of factors, including risks related to our business, risks related to our industry, and other risks which are detailed in Item 1A of Part I of this annual report on Form 10-K, entitled Risk Factors.

Our activities will necessitate significant uses of working capital throughout 2013 and beyond. We are currently concentrating our efforts on the development of tasimelteon for the treatment of Non-24 and the preparation of a New Drug Application (NDA) for tasimelteon for the treatment of Non-24 that we plan to file with the U.S. Food and Drug Administration (FDA) in mid-2013. Additionally, we and our partners continue to pursue market approval of Fanapt® in a number of foreign jurisdictions, with Israel and Argentina having already approved Fanapt® for the treatment of schizophrenia.

Our founder and Chief Executive Officer, Mihael H. Polymeropoulos, M.D., started our operations early in 2003 after establishing and leading the Pharmacogenetics Department at Novartis. In acquiring and developing our compounds, 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.

Our products target prescription markets with significant unmet medical needs. We believe that tasimelteon may represent an important new treatment option for patients with CRSDs based on its potential to be the first compound approved as a circadian regulator with a demonstrated ability to reset the master body clock and align it to a constant 24-hour day. We believe that Fanapt® may address some of the shortcomings of other currently available drugs, based on its observed safety profile.

Table of Contents

Our strategy

Our goal is to create a leading biopharmaceutical company focused on developing and commercializing products that address critical unmet medical needs relating to central nervous system disorders 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:

Pursue the clinical development and regulatory approval of our products and product candidates. We believe that Vanda has built a team of capable drug developers that can take products through the development and regulatory processes towards our goal of regulatory approval in markets across the world. In markets where we do not have local expertise, we will leverage partners or consultants to assist towards us.

Establish our capability to commercialize products. We intend to establish a commercial capability to market our products in certain indications and geographies. Vanda has begun to hire experienced sales and marketing professionals to enable the commercialization of our products.

Enter into partnerships to supplement our capabilities and to extend our commercial reach. We intend to build commercial relationships to both supplement our capabilities in markets where we lead commercialization and to make our products available in markets where we do not intend to lead commercialization.

Apply our pharmacogenetics and pharmacogenomics expertise to differentiate our products and product candidates. We believe that our pharmacogenetics and pharmacogenomics expertise will yield new insights into our products and product candidates. These insights may enable us to target our products and product candidates to certain patient populations and to identify unexpected conditions for our products and product candidates to treat.

Expand our product portfolio through the identification and acquisition of additional compounds. We intend to continue to draw upon our clinical development expertise and pharmacogenetics and pharmacogenomics expertise to identify and pursue the acquisition of additional clinical-stage compounds.

Products and partnered products

We have the following products and partnered products on the market or in clinical development:

Product or Partnered Product	Target Indications	Select Milestones
Tasimelteon	Circadian Rhythm Sleep Disorders	Phase III trial (SET Study) for Non-24 completed in December 2012;
		Phase III trial (RESET Study) for Non-24 completed in January 2013;
		Two ongoing open label safety studies
	Major Depressive Disorder (MDD)	Phase IIb/III trial (MAGELLAN) completed in January 2013
	Insomnia	Phase III trial for transient insomnia completed in 2006;
		Phase III trial for chronic primary insomnia completed in 2008
Fanapt® (Oral)	Schizophrenia	FDA approval in May 2009;

		Commercial rights in the U.S. and Canada sublicensed to Novartis in October 2009;
Fanapt® (Injectable)	Schizophrenia	Launched in the U.S. by Novartis in January 2010 Phase II trial initiated by Novartis in 2011; Novartis has ceased the further clinical development of this formulation

Table of Contents

Tasimelteon

Tasimelteon is a circadian regulator in development for the treatment of Non-24. Tasimelteon is a melatonin agonist of the human MT1 and MT2 receptors, with greater specificity for MT2. Tasimelteon s ability to reset the master body clock in the suprachiasmatic nucleus (SCN), located in the hypothalamus, results in the entrainment of the body s melatonin and cortisol rhythms to align to the 24-hour day-night cycle. In December 2012 and January 2013, we announced positive results for two Phase III studies for tasimelteon in the treatment of Non-24. The SET Phase III study demonstrated that tasimelteon was able to entrain the master body clock as measured by melatonin and cortisol circadian rhythms. Tasimelteon was also shown to significantly improve clinical symptoms across a number of sleep and wake measures. These results provided robust evidence of direct and clinically meaningful benefits to patients with Non-24. The RESET Phase III study demonstrated the maintenance effect of 20 milligrams (mg) of tasimelteon to entrain melatonin and cortisol circadian rhythms in individuals with Non-24. Patients treated with tasimelteon maintained their clinical benefits while patients receiving placebo showed significant deterioration in measures of nighttime sleep, daytime naps and timing of sleep. The tasimelteon Non-24 program continues towards its goal of a projected mid-2013 NDA filing with the FDA. We will meet with the FDA in the first quarter of 2013 for a pre-NDA meeting on tasimelteon in the treatment of patients with Non-24.

In January 2010, the FDA granted orphan drug designation status for tasimelteon in Non-24 in blind individuals without light perception. 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 tasimelteon as an orphan medicinal product for the same indication.

Tasimelteon has also been studied in Major Depressive Disorder (MDD) and insomnia.

Therapeutic opportunity

Sleep disorders are segmented into three major categories: primary insomnia, secondary insomnia and 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 shift work sleep disorder and Non-24. Non-24 is a serious, rare circadian rhythm disorder that affects a majority of totally blind individuals who lack light perception and cannot entrain (reset) their master body clock to the 24-hour day. Based on market research we have conducted with LEK Consulting, we believe that CRSDs represent a significant portion of the market for sleep disorders.

While there are no FDA-approved treatments for CRSDs, there are a number of drugs approved and prescribed for patients with sleep disorders. The most commonly prescribed drugs are hypnotics, such as generic zolpidem, Ambien® (zolpidem) by sanofi-aventis (including Ambien CR®), Lunesta® (eszopiclone) by Dainippon Sumitomo Pharma, Sonata® (zaleplon) by Pfizer Inc. and Silenor® (doxepin) by Somaxon Pharmaceuticals, Inc. Hypnotics work by acting upon a set of brain receptors known as GABA receptors, which are separate and distinct from the melatonin receptors to which tasimelteon binds. Several drugs in development also utilize a mechanism of action involving binding to GABA receptors. Members of the benzodiazapine class of sedatives are also approved for insomnia, but their usage has declined due to an inferior safety profile compared to hypnotics. Anecdotal evidence also suggests that sedative antidepressants, such as trazodone and doxepin, are prescribed off-label for insomnia. FDA approved drugs for the treatment of insomnia also include Rozerem® (ramelteon) by Takeda Pharmaceuticals Company Limited, a compound with a mechanism of action

Table of Contents

similar to tasimelteon. 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.

Limitations of current treatments

We believe that each of the drugs currently used to treat sleep disorders has inherent limitations that leave CRSD patients underserved. The key limitations include the potential for abuse, significant side effects, and a failure to address the underlying causes of CRSDs:

We believe that none of the drugs used and approved for sleep disorders, other than Rozerem®, work through the body s natural sleep/wake cycle, which is governed by melatonin. We believe that, for patients whose sleep disruption is due to a misalignment of this sleep/wake cycle (as is the case in CRSD), a drug that naturally modulates the sleep/wake cycle would be an attractive new alternative because it would address the underlying cause of the sleeplessness, rather than merely addressing its symptoms.

Many of the products prescribed commonly for sleep disorders, including Ambien®, Lunesta®, and Sonata®, are classified as Schedule IV controlled substances by the United States Drug Enforcement Administration (DEA) due to their potential for abuse, tolerance and withdrawal symptoms. Drugs that are classified as Schedule IV controlled substances are subject to restrictions on how such drugs are prescribed and dispensed.

Many drugs approved for and used in sleep disorders also induce a number of nuisance side effects beyond the more serious abuse and addiction effects associated with most approved products. These side effects include next-day grogginess, memory loss, unpleasant taste, dry mouth and hormonal changes.

Potential advantages of tasimelteon

We believe that tasimelteon may represent a breakthrough treatment option for patients with CRSDs based on the compound s demonstrated ability to reset the master body clock and align it with the 24-hour day. We believe that tasimelteon is unlikely to be scheduled as a controlled substance by the DEA because Rozerem®, which has a similar mechanism of action to tasimelteon, was shown not to have potential for abuse and was not classified as a Schedule IV controlled substance by the DEA. Tasimelteon also appears to be safe and well-tolerated, with no significant side effects or effects on next-day performance.

Overview of Phase III clinical trials for Non-24

In December 2012, we reported positive top-line results in a randomized, double-blind, multi-center, placebo-controlled Phase III trial (SET study) that enrolled 84 patients. Tasimelteon succeeded in the primary endpoint of entrainment of the melatonin (aMT6s) rhythm as compared to placebo. Additionally, tasimelteon demonstrated significant improvements across a number of sleep and wake parameters including measures of total sleep time, nap duration, and timing of sleep. Tasimelteon also showed significant improvements over placebo in the Non-24 Clinical Response Scale (N24CRS) as well as in the Clinical Global Impression of Change (CGI-C), an overall global functioning scale. These results provide robust evidence of a direct and clinically meaningful benefit to patients with Non-24. In the SET study, tasimelteon was demonstrated to be safe and well tolerated. The trial examined 20mg of tasimelteon dosed 30 minutes before bedtime versus placebo. The SET study was an 84 patient randomized, double-masked, placebo-controlled study in patients with Non-24. The primary endpoints for this study were entrainment of the melatonin (aMT6s) rhythm to the 24-hour clock and Clinical Response as measured by entrainment plus a score of greater than or equal to 3 on N24CRS.

In January 2013, we announced positive results for the second Phase III study of tasimelteon for the treatment of Non-24. The RESET study demonstrated the maintenance effect of 20mg of tasimelteon to entrain melatonin and cortisol circadian rhythms in individuals with Non-24. Patients treated with tasimelteon maintained their clinical benefits while patients receiving placebo showed significant deterioration in measures of nighttime sleep, daytime naps, and timing of sleep. The RESET study was a 20 patient randomized withdrawal

Table of Contents

study designed to demonstrate the maintenance effect of 20mg of tasimelteon in the treatment of blind individuals with Non-24. Patients were treated with tasimelteon for three months during an open-label run-in phase. Patients who responded to tasimelteon treatment during the run-in phase, as measured by entrainment of the melatonin rhythm (aMT6s) to the 24-hour day, were then randomized to receive either placebo or continue receiving tasimelteon 20mg for 2 months. The primary endpoint of the study was the maintenance of effect as measured by entrainment of the melatonin (aMT6s) rhythm.

Two open-label safety studies are ongoing for tasimelteon in Non-24. The 3202 and 3204 clinical trials are open-label, multicenter, studies in blind subjects with Non-24 to assess the safety of tasimelteon. The tasimelteon Non-24 program continues towards its goal of a projected mid-2013 NDA filing with the FDA. We will meet with the FDA in the first quarter of 2013 for a pre-NDA meeting on tasimelteon in the treatment of patients with Non-24.

Overview of Phase III clinical trials for insomnia

In November 2006, we reported positive top-line results in a randomized, double-blind, multi-center, placebo-controlled Phase III trial that enrolled 412 adults in a sleep laboratory setting using a phase-advance, first-night assessment model of induced transient insomnia. The trial examined tasimelteon dosed 30 minutes before bedtime at 20mg, 50mg and 100mg versus placebo.

Tasimelteon achieved significant results in multiple endpoints, demonstrating a benefit in both sleep onset, or time to fall asleep, and sleep maintenance, or ability to stay asleep. Based on these trial results, we believe that tasimelteon will compare favorably to efficacy achieved by currently approved insomnia drugs. The Phase III trial also demonstrated that tasimelteon was safe and well-tolerated, with no significant side effects versus placebo and no impairment of next-day performance or mood.

In June 2008, we reported positive top-line results in a randomized, double-blind, placebo-controlled Phase III trial in chronic primary insomnia that enrolled 324 patients. The trial examined tasimelteon at 20mg and 50mg versus placebo over a period of 35 days. The trial measured time to fall asleep and sleep maintenance, as well as next-day performance.

Overview of Phase IIb/ III clinical trials for major depressive disorder

In January 2013, Vanda reported top-line results of the Phase IIb/III clinical study (MAGELLAN) in MDD, investigating the efficacy and safety of tasimelteon as a monotherapy in the treatment of patients with MDD. The clinical study did not meet the primary endpoint of change from baseline in the Hamilton Depression Scale (HAMD-17) after 8 weeks of treatment as compared to placebo. Tasimelteon was shown to be safe and well-tolerated, consistent with observations in prior studies. Based on these proof of concept clinical study results, Vanda decided to discontinue all activities in this indication. MAGELLAN was a proof of concept, two arm (tasimelteon 20mg and placebo), 8-week, double-masked, randomized, phase IIb/III clinical study in patients with MDD. The study enrolled 507 patients in 43 sites in the U.S.

Intellectual property

Tasimelteon and its formulations, genetic markers and uses are covered by a total of 11 patent and patent application families worldwide. The primary new chemical entity patent covering tasimelteon expires normally in 2017 in the U.S. and in most European markets. We believe that, like Fanapt®, tasimelteon 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. In Europe, data exclusivity will protect tasimelteon for at least ten years from approval. Outside the U.S. and Europe, data exclusivity will protect tasimelteon from generic competition for varying number of years depending on the country. Additional patent applications directed to specific sleep disorders and to methods of administration, if issued, would provide exclusivity for such indications and methods of administration. Patent applications directed to the treatment of Non-24, if granted, would provide exclusivity for this indication until at least 2033.

Our rights to the new chemical entity patent covering tasimelteon and related intellectual property have been acquired through a license with Bristol-Myers Squibb Company (BMS). Please see License agreements below for a discussion of this license.

Table of Contents

Fanapt®

Fanapt® is a compound 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. On 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 has exclusive commercialization rights to all formulations of Fanapt® in the U.S. and Canada. In January 2010, Novartis launched Fanapt® in the U.S. Novartis is responsible for the further clinical development activities in the U.S. and Canada, including the development of a long-acting injectable (or depot) formulation of Fanapt®. In October 2012, Novartis informed us that it had determined to cease the development of the long-acting injectable (or depot) formulation of Fanapt®.

We continue to explore the regulatory path and commercial opportunity for Fanapt® oral formulation outside of the U.S. and Canada. In December 2012, the European Medicines Agency s (EMA) Committee for Medicinal Product 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 at this point in time. In January 2013, we formally appealed the EMA s negative opinion and requested a re-examination of the decision by the CHMP. We have entered into agreements with the following partners for the commercialization of Fanapt® in the countries set forth below:

Country	Partner
Mexico	Probiomed S.A. de C.V.
Israel	Megapharm Ltd.

In August 2012, the Israeli Ministry of Health granted market approval for Fanapt® for the treatment of schizophrenia. In November 2012, we were notified, that Fanapt® had been granted market approval in Argentina for the treatment of schizophrenia.

Our rights to the new chemical entity patent covering Fanapt® and related intellectual property have been acquired through a license with Novartis. Please see License agreements below for a discussion of this license.

Therapeutic opportunity

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 additionally 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. Currently approved atypical antipsychotics include, in addition to Fanapt®, 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 , by Eli Lilly and Company, Seroquel® (quetiapine) by AstraZeneca PLC, Abilify® (aripiprazole) by BMS/Otsuka Pharmaceutical Co., Ltd., Geodon® (ziprasidone) by Pfizer Inc., Saphris® (asenapine) by Schering-Plough, Latuda® (lurasidone) by Dainippon Sumitomo Pharma, and generic clozapine.

The long-acting injectable (or depot) formulation of Fanapt® is administered once every four weeks and we believe will be a compelling complement to the oral formulation for both physicians and patients. Novartis conducted a two-month Phase I/IIa safety trial of this formulation in schizophrenia patients, in which it

Table of Contents

demonstrated the benefit of consistent release over a four-week time period with no greater side effects relative to oral dosing. In October 2012, Novartis informed us that it had determined to cease the development of the depot formulation.

Intellectual property

Fanapt® and its metabolites, formulations, genetic markers and uses are covered by a total of 18 patent and patent application families worldwide. 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. In the U.S., the United States Drug Price Competition and Patent Term Restoration Act of 1984, more commonly known as the Hatch-Waxman Act provides for an extension of new chemical entity patents for a period of up to five years following the expiration of the patent covering that compound to compensate for time spent in development. Fanapt® has qualified for the full five-year patent term extension and so the term of the new chemical entity patent in the U.S. has been extended until November 2016. In addition, we expect that Fanapt® will be eligible for six months of pediatric exclusivity potentially extending the term of the new chemical entity patent in the U.S. until May 2017. In Europe, statutes provide 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, assuming that pediatric exclusivity is granted by the FDA and that we receive regulatory approval in Europe, we expect that Novartis rights to commercialize Fanapt® will be exclusive until May 2017 in the U.S. and 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. The patent for the microsphere long-acting injectable (or depot) formulation of Fanapt® expires in 2024 in the U.S. and 2022 in most of the major markets in Europe. The pending patent application for the aqueous microcrystals long acting injectable (or depot) formulation of Fanapt® will expire in 2023 in the U.S. The patent for the aqueous microcrystals long acting injectable (or depot) formulation of Fanapt® will expire in 2023 in most of the major markets in Europe. Several other patent applications covering metabolites, uses, formulations and genetic markers relating to Fanapt® extend beyond 2020.

We acquired worldwide, exclusive rights to the new chemical entity patent covering Fanapt® and certain related intellectual property from Novartis under a sublicense agreement we entered into in 2004, which was amended and restated in 2009. Please see License agreements below for a more complete description of the rights we acquired from and relinquished to Novartis with respect to Fanapt®.

VLY-686

VLY-686 is an 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 are currently examining the clinical and commercial profile of VLY-686. This strategic evaluation will further inform potential indications for an early development clinical program.

Intellectual property

VLY-686 is covered by a total of three patent and patent application families worldwide. The new chemical patent covering VLY-686 expires in April 2023, except in the U.S., where it expires in June 2024 absent any applicable patent term adjustments.

License agreements

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

Tasimelteon

In February 2004, we entered into a license agreement with 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 tasimelteon. In partial consideration for the license, we paid BMS an initial license

Table of Contents

fee of $0.5 million. We made a milestone payment to BMS of $1.0 million under this license agreement in 2006 relating to the initiation of our first Phase III clinical trial for tasimelteon. We would be obligated to make future milestone payments to BMS and Massachusetts General Hospital (MGH) of less than $40.0 million in the aggregate (the majority of which are tied to sales milestones). In the event that a tasimelteon NDA is accepted for filing by the FDA, we will incur milestone obligations of $3.8 million. Additionally, we would be obligated to make royalty payments based on the net sales of tasimelteon at a rate which, as a percentage of net sales, is in the low teens. We would also be obligated under this 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 tasimelteon to use our commercially reasonable efforts to develop and commercialize tasimelteon and to meet certain milestones in initiating and completing certain clinical work.

The license agreement with BMS was amended in May 2012 to, among other things, extend the deadline by which we must enter into a development and commercialization agreement with a third party for tasimelteon until the earliest of: (i) the date mutually agreed upon by BMS and us following the provision by us to BMS of a full written report of the Phase III clinical studies on which we intend to rely for filing for marketing authorization for tasimelteon in its first major market country (Phase III report); (ii) the date of the acceptance by a regulatory authority of the filing by us for marketing authorization for tasimelteon in a major market country following the provision by us to BMS of the Phase III report; or (iii) December 31, 2013.

If we have not entered into a development and commercialization agreement with respect to certain major market countries by the foregoing deadline, then BMS will have the option to exclusively develop and commercialize tasimelteon on its own in those countries not covered by such an agreement on pre-determined financial terms, including milestone and royalty payments. In addition to the foregoing, pursuant to the May 2012 amendment, our deadline for filing an NDA with the FDA for tasimelteon was extended until January 1, 2014.

Either party may terminate the tasimelteon license agreement under certain circumstances, including a material breach of the agreement by the other. In the event that BMS has not exercised its option to reacquire the rights to tasimelteon and 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®

We acquired exclusive worldwide rights to patents and patent applications for Fanapt® through a sublicense agreement with Novartis. A predecessor company of sanofi-aventis, Hoechst Marion Roussel, Inc. (HMRI), discovered Fanapt® and completed early clinical work on the compound. In 1996, following a review of its product portfolio, 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 October 2009, we entered into an amended and restated sublicense agreement with Novartis which amended and restated our June 2004 sublicense agreement with Novartis relating to Fanapt®. Pursuant to the amended and restated sublicense agreement, 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. Novartis is responsible for the further clinical development activities in the U.S. and Canada, including the development of a long-acting injectable (or depot) formulation of Fanapt®. In October 2012, Novartis informed us that it had determined to cease the development of the long-acting injectable (or depot) formulation of Fanapt®. Pursuant to the amended and restated sublicense agreement, we received an upfront payment of $200.0 million and are eligible for additional payments totaling up to $265.0 million upon the achievement of certain commercial and development milestones for Fanapt® in the U.S. and Canada. Based on the current sales performance of Fanapt® in the U.S. and the decision by Novartis to cease development of the long-acting injectable (or depot) formulation of Fanapt®, we expect that some or all of these commercial and development

Table of Contents

milestones will not be achieved by Novartis. We also receive royalties, which, as a percentage of net sales, are in the low double-digits, on net sales of Fanapt® in the U.S. and Canada. We retain exclusive rights to Fanapt® outside the U.S. and Canada and we have exclusive rights to use any of Novartis data for Fanapt® for developing and commercializing Fanapt® outside the U.S. and Canada. At Novartis option, we will enter into good faith discussions with Novartis relating to the co-commercialization of Fanapt® outside of the U.S. and Canada or, alternatively, Novartis will receive a royalty on net sales of Fanapt® outside of the U.S. and Canada.

We may lose our rights to develop and commercialize Fanapt® outside the U.S. and Canada if we fail to comply with certain requirements in the amended and restated sublicense agreement regarding our financial condition, or if we fail to comply with certain diligence obligations regarding our development or commercialization activities or if we otherwise breach the amended and restated sublicense agreement and fail to cure such breach. Our rights to develop and commercialize Fanapt® outside the U.S. and Canada may be impaired if we do not cure breaches by Novartis of similar obligations contained in its sublicense agreement with Titan for Fanapt®. In addition, if Novartis breaches the amended and restated sublicense agreement with respect to its commercialization activities in the U.S. or Canada, we may terminate Novartis commercialization rights in the applicable country and we would no longer receive royalty payments from Novartis in connection with such country in the event of such termination.

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, VLY-686, 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. 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 VLY-686.

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 VLY-686.

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 Fanapt® in the U.S., Israel and Argentina, all of our compounds 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.

Table of Contents

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, or 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 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.

Table of Contents

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.

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 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 or partnered products or product candidates. 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 or partnered products or product candidates, 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

Table of Contents

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 or partnered product and its acceptance in the medical community.

We use, and will continue to use, third-party manufacturers to produce our products and product candidates 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, or the FDAAA, was enacted into law, amending both the FDC 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 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, or 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 and product candidates 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, or 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.

Table of Contents

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. Federal law 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.

Foreign regulation

Whether or not we or our partners obtain FDA approval for a product or product candidate, we must obtain approval by the comparable regulatory authorities of foreign countries before we can commence clinical trials or marketing of the product or product candidate 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.

Third-party reimbursement and pricing controls

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 compounds 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 compounds.

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

Table of Contents

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

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

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.

We continue to explore the regulatory path and commercial opportunity for Fanapt® oral formulation outside of the U.S. and Canada. In December 2012, the 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 at this point in time. In January 2013, we formally appealed the EMA s negative opinion and requested a re-examination of the decision by the CHMP. We have entered into agreements with the following partners for the commercialization of Fanapt® in the countries set forth below:

Country	Partner
Mexico	Probiomed S.A. de C.V.
Israel	Megapharm Ltd.

In August 2012, the Israeli Ministry of Health granted market approval for Fanapt® for the treatment of schizophrenia. In November 2012, we were notified that Fanapt® had been granted market approval in Argentina for the treatment of schizophrenia.

Patents and proprietary rights; Hatch-Waxman protection

We and our partners will be able to protect our compounds from unauthorized use by third parties only to the extent that our compounds 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.

Fanapt®, tasimelteon and VLY-686 are covered by new chemical entity and other patents. These patents cover the active pharmaceutical ingredient and provide patent protection for all formulations containing these active pharmaceutical ingredients. The new chemical entity patent for Fanapt® is owned by sanofi-aventis, and other patents and patent applications relating to Fanapt® are owned by Novartis. BMS owns the new chemical entity patent for tasimelteon and Lilly owns the new chemical entity patent for VLY-686. We originally obtained exclusive worldwide rights to develop and commercialize the compounds covered by these patents through license and sublicense arrangements. However, pursuant to the amended and restated sublicense agreement with Novartis, Novartis obtained exclusive commercialization rights to all formulations of Fanapt® in the U.S. and Canada. For more on these license and sublicense arrangements, please see License agreements above. In addition, we have generated intellectual property, and filed patent applications covering this intellectual property, for Fanapt® and tasimelteon.

The 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 of the U.S. The new chemical entity patent covering tasimelteon expires in 2017 in the U.S. and most European markets. The new chemical entity patent covering VLY-686 expires in April 2023, except in the U.S., where it expires in June 2024 absent any applicable patent term adjustments. Additionally, Fanapt® has qualified for the full five-year patent term extension and so the term of the new chemical entity patent in the U.S. has been extended until November 2016. A similar extension is expected to be available for tasimelteon and may also be available for VLY-686. Fanapt® will also be eligible for 6 months of additional protection for completing studies in the pediatric population potentially extending the term of the new

Table of Contents

chemical entity parent in the U.S. until May 2017. These studies, for which Novartis is responsible, are required by the FDA approval letter. In Europe, statutes provide for ten years of data exclusivity, with the potential for an additional year if the company develops the drug 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, assuming that pediatric exclusivity is granted by the FDA and that we receive regulatory approval in Europe, we expect that Novartis rights to commercialize Fanapt® will be exclusive until May 2017 in the U.S. and our rights in Europe would be exclusive for at least 10 years from approval in Europe. Data exclusivity periods in other countries vary from country to country. The patent for the microsphere long-acting injectable (or depot) formulation of Fanapt® expires in 2024 in the U.S. and 2022 in most of the major markets in Europe. The pending patent application for the aqueous microcrystals long acting injectable (or depot) formulation of Fanapt® will expire in 2023 in the U.S. The patent for the aqueous microcrystals long acting injectable (or depot) formulation of Fanapt® will expire in 2023 in most of the major markets in Europe. Several other patent applications covering metabolites, uses, formulations and genetic markers relating to Fanapt® extend beyond 2020.

Aside from the new chemical entity patents and other in-licensed patents relating to Fanapt®, tasimelteon and VLY-686, as of December 31, 2012 we had 29 patent and patent application families, most of which have been filed in key markets including the U.S., relating to Fanapt® and tasimelteon. In addition, we had five other patent applications relating to compounds not presently in clinical studies. The claims in these various patents and patent applications are directed to compositions of matter, including claims covering other product candidates, pharmaceutical compositions and methods of use.

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 is 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.

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 $45.4 million, $29.0 million and $12.3 million in research and development expenses in the years ended December 31, 2012, 2011 and 2010, respectively.

Manufacturing

We currently depend on, and expect to continue to depend on, a small number of third-party manufacturers to produce sufficient quantities of our products and product candidates for use in our clinical studies. We are not obligated to obtain our products and product candidates from any particular third-party manufacturer and we believe that we would be able to obtain our products and product candidates from a number of third-party manufacturers at comparable cost.

We intend to rely on third-party contract manufacturers to produce sufficient quantities for large-scale commercialization of our products and product candidates once approved for commercial use. If we do enter into commercial manufacturing arrangements with third parties, these third-party manufacturers will be subject to

Table of Contents

extensive governmental regulation. Specifically, regulatory authorities in the markets which we intend to serve will require that drugs be manufactured, packaged and labeled in conformity with cGMP or equivalent foreign standards. We intend to engage only those contract manufacturers who have the capability to manufacture drugs in compliance with cGMP and other applicable standards in bulk quantities for commercial use.

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 market segment also includes several smaller emerging companies whose activities are directly focused on our target markets and areas of expertise. Our compounds, once approved for commercial use, will compete with numerous therapeutic treatments offered by these competitors. While we believe that our compounds 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 compounds or technologies obsolete or noncompetitive.

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

For tasimelteon in the treatment of CRSDs, there are no approved direct competitors. Insomnia treatments include, Rozerem® (ramelteon) by Takeda Pharmaceuticals Company Limited, hypnotics such as Ambien® (zolpidem) by sanofi-aventis (including Ambien CR®), Lunesta® (eszopiclone) by Dainippon Sumitomo Pharma, Sonata® (zaleplon) by Pfizer Inc., Silenor® (doxepin) by Somaxon Pharmaceuticals, Inc., generic compounds 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.

For Fanapt® in the treatment of schizophrenia, the atypical antipsychotics 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 , by Eli Lilly and Company, Seroquel® (quetiapine) by AstraZeneca PLC, Abilify® (aripiprazole) by BMS/Otsuka Pharmaceutical Co., Ltd., Geodon® (ziprasidone) by Pfizer Inc., Saphris® (asenapine) by Schering-Plough, Latuda® (lurasidone) by Dainippon Sumitomo Pharma, 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 compounds 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 compounds less attractive.

Employees

As of December 31, 2012, we had 40 full-time employees. Of these employees, 24 were primarily engaged in research and development activities. 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.

Table of Contents

Available Information

Vanda Pharmaceuticals Inc. files 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 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

Investing in our common stock involves a high degree of risk. You should consider carefully the risks and uncertainties described below, together with all of the other information in this report, including the consolidated financial statements and the related notes appearing at the end of this annual report on Form 10-K, with respect to any investment in shares of our common stock. If any of the following risks actually occurs, our business, financial condition, results of operations and future prospects would likely be materially and adversely affected. In that event, the market price of our common stock could decline and you could lose all or part of your investment.

Risks related to our business and industry

If the FDA does not accept for filing the NDA that we intend to submit for tasimelteon for the treatment of Non-24, regulatory authorities determine that our clinical trial results for tasimelteon for the treatment of Non-24 do not demonstrate adequate safety and efficacy, or the FDA does not approve an applicable PDUFA date, continued development of tasimelteon will be significantly delayed or terminated, our business will be significantly harmed, and the market price of our stock could decline.

We commenced our Phase III program for tasimelteon for the treatment of Non-24-Hour Disorder (Non-24) in the third quarter of 2010. In December 2012, we reported positive top-line results in a randomized, double-blind, multi-center, placebo-controlled Phase III trial (SET study) that enrolled 84 patients. In January 2013, we announced positive results for the second Phase III study of tasimelteon for the treatment of Non-24. In addition, we have two ongoing open-label safety studies for tasimelteon in treatment of Non-24. Based on the results of our completed trials, we intend to submit a New Drug Application (NDA) with the U.S. Food and Drug Administration (FDA) in mid-2013. We will meet with the FDA in the first quarter of 2013 for a pre-NDA meeting on tasimelteon in the treatment of patients with Non-24. Any adverse developments or results or perceived adverse developments or results with respect to our pre-NDA meeting with the FDA, our regulatory submission or the tasimelteon Phase III program will significantly harm our business and could cause the market price of our stock to decline. Examples of such adverse developments include, but are not limited to:

- the FDA determining that additional clinical studies are required with respect to the Phase III program in Non-24;
- safety, efficacy or other concerns arising from clinical or non-clinical studies in this program; or
- the FDA determining that the Phase III program in Non-24 raises safety concerns or does not demonstrate adequate efficacy.

Table of Contents

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

The research, testing, manufacturing and marketing of compounds such as those that we have developed or we or in regard to partnered products, our partners, are developing are subject to extensive regulation by federal, state and local government authorities, including the FDA. To obtain regulatory approval of such compounds, we or our partners must demonstrate to the satisfaction of the applicable regulatory agency that, among other things, the compound is safe and effective for its intended use. In addition, we or our partners must show that the manufacturing facilities used to produce such compounds are in compliance with current Good Manufacturing Practices regulations or cGMP.

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

- a compound may not be shown to be safe or effective;
- the FDA may interpret data from pre-clinical and clinical trials in different ways than we or our partners do;
- the FDA may not approve our or our partners manufacturing processes or facilities;
- a compound may not be approved for all the indications we or our partners request;
- the FDA may change its approval policies or adopt new regulations;
- the FDA may not meet, or may extend, the Prescription Drug User Fee Act (PDUFA) date with respect to a particular NDA; and
- the FDA may not agree with our or our partners regulatory approval strategies or components of the regulatory filings, such as clinical trial designs.

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

Moreover, 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;

total or partial suspension of production;

refusal of the government to grant future approvals;

withdrawal of approvals; and

criminal prosecution.

Any delay or failure to obtain regulatory approvals for our compounds will result in increased costs, could diminish competitive advantages that we may attain and would adversely affect the marketing and sale of our compounds. Other than Fanapt® in the U.S., Israel and Argentina, we have not received regulatory approval to market any of our compounds in any jurisdiction.

Table of Contents

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

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

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

Pursuant to our amended and restated sublicense agreement with Novartis, we retained the right to develop and commercialize Fanapt® outside the U.S. and Canada. We intend to market our compounds outside the U.S. and Canada with one or more commercial partners. In order to market our compounds 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 compounds in any market. The failure to obtain these approvals could harm our business materially.

We continue to explore the regulatory path and commercial opportunity for Fanapt® oral formulation outside of the U.S. and Canada. In December 2012, the European Medicines Agency s (EMA) Committee for Medicinal Product 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 at this point in time. In January 2013, we formally appealed the EMA s negative opinion and requested a re-examination of the decision by the CHMP. We may not be successful in obtaining a positive decision from CHMP of our appeal.

Even after we or our partners obtain regulatory approvals of a product, acceptance of such compound in the marketplace is uncertain and failure to achieve market acceptance will prevent or delay our ability to generate revenues.

Even after obtaining regulatory approvals for the sale of our compounds, the commercial success of these compounds will depend, among other things, on their acceptance by physicians, patients, third-party payors and other members of the medical community as a therapeutic and cost-effective alternative to competing products

Table of Contents

and treatments. The degree of market acceptance of any compound 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 compound, our ability to attract and maintain corporate partners, including pharmaceutical companies, to assist in commercializing our compounds, 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 compounds fail to gain market acceptance, we may be unable to earn sufficient revenue to continue our business. If our approved compounds 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.

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

Our activities will necessitate significant uses of working capital throughout 2013 and beyond. As of December 31, 2012, our total cash and cash equivalents and marketable securities were $120.4 million. Our long term capital requirements are expected to depend on many factors, including, among others:

- our ability to commercialize tasimelteon globally;
- the amount of royalty and milestone payments received from our commercial partners;
- our ability to commercialize Fanapt® outside the U.S. and Canada;
- costs of developing and maintaining sales, marketing and distribution channels and our ability to sell our products;
- costs involved in establishing manufacturing capabilities for commercial quantities of our products;
- the number of potential formulations, products and product candidates in development;
- progress with pre-clinical studies and clinical trials;
- time and costs involved in obtaining regulatory (including FDA) approval;
- costs involved in preparing, filing, prosecuting, maintaining and enforcing patent, trademark and other intellectual property claims;
- competing technological and market developments;
- market acceptance of our products;

costs for recruiting and retaining employees and consultants;

costs for training physicians; and

legal, accounting, insurance and other professional and business related costs.

We expect to continue to receive royalty payments and hope to receive commercial and development milestone payments relating to Fanapt® in connection with our amended and restated sublicense agreement with Novartis. Based on the current sales performance of Fanapt® in the U.S. and the decision by Novartis to cease development of the long-acting injectable (or depot) formulation of Fanapt®, we expect that some or all of these commercial and development milestones will not be achieved by Novartis. As a result, we may need to raise additional capital to fund our anticipated operating expenses and execute on our business plans. In our capital-raising efforts, we may seek to sell debt securities or additional equity securities or obtain a bank credit facility, or enter into partnerships or other collaboration agreements. The sale of additional equity or debt securities, if convertible, could result in dilution to our stockholders and may also result in a lower price for our common stock. The incurrence of indebtedness would result in increased fixed obligations and could also result in covenants that could restrict our operations. However, we may not be able to raise additional funds on acceptable

Table of Contents

terms, or at all. If we are unable to secure sufficient capital to fund our planned activities, we may not be able to continue operations, or we may have to enter into partnerships or other collaboration agreements that could require us to share commercial rights to our products to a greater extent or at earlier stages in the drug development process than is currently intended. These partnerships or collaborations, if consummated prior to proof-of-efficacy or safety of a given product, could impair our ability to realize value from that product. If additional financing is not available when required or is not available on acceptable terms, we may be unable to fund our operations and planned growth, develop or enhance our technologies or products, take advantage of business opportunities or respond to competitive market pressures, any of which would materially harm our business, financial condition and results of operations.

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

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

- developing products and product candidates;
- undertaking pre-clinical testing and clinical trials;
- obtaining FDA and other regulatory approvals of products and product candidates; and
- manufacturing, marketing and selling products.

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

Fanapt® (and our other compounds, if successfully developed and approved for commercial sale) will compete with a number of drugs and therapies currently manufactured and marketed by major pharmaceutical and other biotechnology companies. Our compounds may also compete with new products currently under development by others or with products which may cost less than our compounds. Physicians, patients, third party payors and the medical community may not accept or utilize any of our compounds that may be approved. If Fanapt® and our other compounds (if and when approved) do not achieve significant market acceptance, our business, results of operations and financial condition would be materially adversely affected. We believe the primary competitors for Fanapt® and tasimelteon are as follows:

- For tasimelteon in the treatment of CRSDs, there are no approved direct competitors. Insomnia treatments include, Rozerem® (ramelteon) by Takeda Pharmaceuticals Company Limited, hypnotics such as Ambien® (zolpidem) by sanofi-aventis (including Ambien CR®), Lunesta® (eszopiclone) by Dainippon Sumitomo Pharma, Sonata® (zaleplon) by Pfizer Inc., Silenor® (doxepin) by Somaxon Pharmaceuticals, Inc., generic compounds 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.

- For Fanapt® in the treatment of schizophrenia, the atypical antipsychotics 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 , by Eli Lilly and Company, Seroquel® (quetiapine) by AstraZeneca PLC, Abilify® (aripiprazole) by BMS/Otsuka Pharmaceutical Co.,

23

Table of Contents

Ltd., Geodon® (ziprasidone) by Pfizer Inc., Saphris® (asenapine) by Schering-Plough, Latuda® (lurasidone) by Dainippon Sumitomo Pharma, and generic clozapine, as well as the typical antipsychotics haloperidol, chlorpromazine, thioridazine, and sulpiride (all of which are generic).

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 compounds less attractive.

We have no experience selling, marketing or distributing products, other than providing assistance to Novartis relating to the U.S. commercialization of Fanapt®, which may make commercializing our products and product candidates difficult.

At present, we have no marketing experience, other than providing assistance to Novartis relating to the U.S. commercialization of Fanapt®. Therefore, in order for us to commercialize Fanapt®, outside the U.S. and Canada, or our other compounds, including tasimelteon, we must either acquire or 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. For example, we rely completely on Novartis to market, sell and distribute Fanapt® in the U.S. and Canada.

For the commercialization of Fanapt® outside the U.S. and Canada or our other compounds, we may not be able to establish, other than those currently established, sales and distribution 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 partner. In the event that we attempt to acquire or develop our own in-house sales, marketing and distribution capabilities, factors that may inhibit our efforts to commercialize our products and product candidates 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 against companies with broader product lines; and

unforeseen costs associated with creating our own sales and marketing team or with entering into a partnering agreement with an independent sales and marketing organization.

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

Novartis began selling, marketing and distributing our first approved product, Fanapt®, in the U.S. in the first quarter of 2010 and we will depend heavily on the success of this product in the marketplace.

Our ability to generate revenue for the next few years will depend substantially on the success of Fanapt® and the sales of this product by Novartis in the U.S. and Canada. The ability of Fanapt® to generate revenue at the levels we expect will depend on many factors, including the following:

the extent and effectiveness of the development, sales and marketing and distribution support Fanapt® receives;

the amount of resources and efforts utilized by Novartis in relation to the commercialization 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 payers;

Table of Contents

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

the size of the market for Fanapt®;

successfully expanding and sustaining manufacturing 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®;

Novartis ability to obtain regulatory approval in Canada for Fanapt® and our or our partners ability to obtain regulatory approval for Fanapt® in countries outside the U.S. and Canada;

our ability to successfully develop and commercialize Fanapt®, including a long-acting injectable (or depot) formulation of Fanapt®, outside of the U.S. and Canada; and

the unfavorable outcome or other negative effects of any potential litigation relating to Fanapt®.

We entered into an amended and restated sublicense agreement with Novartis to commercialize Fanapt® in the U.S. and Canada. As such, we are not directly involved in the marketing or sales efforts for Fanapt® in the U.S. and Canada. Our revenues for the forseeable future depend substantially on royalties and milestone payments we may receive from Novartis. Pursuant to the amended and restated sublicense agreement with Novartis, we received an upfront payment of $200.0 million and are 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. Based on the current sales performance of Fanapt® in the U.S. and the decision by Novartis to cease development of the long-acting injectable (or depot) formulation of Fanapt®, we expect that some or all of these commercial and development milestones will not be achieved by Novartis. We also receive royalties, which, as a percentage of net sales, are in the low double-digits, on net sales of Fanapt® in the U.S. and Canada. Such royalties may not be significant and will depend on numerous factors, many of which we cannot control. We cannot control the amount and timing of resources that Novartis may devote to Fanapt®. If Novartis fails to successfully commercialize Fanapt® in the U.S. or fails to develop and commercialize Fanapt® in Canada, if Novartis efforts are not effective, or if Novartis focuses its efforts on other schizophrenia therapies or schizophrenia drug candidates, our business will be negatively affected. If Novartis does not successfully commercialize Fanapt® in the U.S. or Canada, we will receive limited revenues from them. Although we have developed and continue to develop additional products and product candidates for commercial introduction, we expect to be substantially dependent on sales from Fanapt® for the foreseeable future. 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 safety or efficacy issues, the introduction or greater acceptance of competing products or adverse regulatory or legislative developments, will have a material adverse effect on our financial condition and results of operations.

If our compounds are determined to be unsafe or ineffective in humans, whether commercially or in clinical trials, our business will be materially harmed.

Despite the FDA s approval of the NDA for Fanapt® in May 2009 and the positive results of our completed trials for Fanapt® and tasimelteon, we are uncertain whether either of these products will ultimately prove to be effective and safe in humans. Frequently, products that have shown promising results in clinical trials have suffered significant setbacks in later clinical trials or even after they are approved for commercial sale. Future uses of our compounds, whether in clinical trials or commercially, may reveal that the compound is ineffective, unacceptably toxic, has other undesirable side effects, is difficult to manufacture on a large scale, is uneconomical, infringes on proprietary rights of another party or is otherwise not fit for further use. If our compounds are determined to be unsafe or ineffective in humans, our business will be materially harmed.

Table of Contents

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

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

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

Clinical development efforts performed by us or our partners may not be successfully completed. Completion of clinical trials may take several years or more. The length of time can vary substantially with the type, complexity, novelty and intended use of the compounds and the size of the prospective patient population. The commencement and rate of completion of clinical trials for our compounds may be delayed by many factors, including:

- the inability to manufacture or obtain from third parties materials sufficient for use in pre-clinical studies and clinical trials;
- delays in beginning a clinical trial;
- delays in patient enrollment and variability in the number and types of patients available for clinical trials;
- difficulty in maintaining contact with patients after treatment, resulting in incomplete data;
- poor effectiveness of our compounds during clinical trials;
- unforeseen safety issues or side effects; and
- governmental or regulatory delays and changes in regulatory requirements and guidelines.

If we or our partners fail to complete successfully one or more clinical trials for our compounds, we or they may not receive the regulatory approvals needed to market that compound. Therefore, any failure or delay in commencing or completing these clinical trials would harm our business materially.

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

Undesirable side effects caused by our compounds could interrupt, delay or halt clinical trials and could result in the denial of regulatory approval by the FDA or other regulatory authorities for any or all targeted indications, and in turn prevent us or our partners from commercializing or continuing the commercialization of such compounds and generating revenues from their sale. We and our partners, as applicable, will continue to assess the side effect profile of our compounds in ongoing clinical development programs. However, we cannot predict whether the commercial use of our approved compounds (or our compounds in development, if and when they are approved for commercial use) will produce undesirable or unintended side effects that have not been evident in the use of, or in clinical trials conducted for,

such compounds to date. Additionally, incidents of product misuse may occur. These events, among others, could result in product recalls, product liability actions or withdrawals or additional regulatory controls, all of which could have a material adverse effect on our business, results of operations and financial condition.

Table of Contents

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

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

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

We have a history of operating losses, anticipate future losses and may never become profitable on a sustained basis.

We have been engaged in identifying and developing compounds since March 2003, which has required, and will continue to require, significant research and development expenditures.

As of December 31, 2012, we had an accumulated deficit of $291.1 million, and we cannot estimate with precision the extent of our future losses. Our ability to generate revenue and achieve profitability largely depends on Novartis and our ability to sell Fanapt®. Novartis launched Fanapt® in the U.S. in the first quarter of 2010 and sales to date have not met our expectations. Fanapt® may continue to not be as commercially successful as we expected, Novartis may not succeed in gaining additional market acceptance of Fanapt® in the U.S. or developing and commercializing Fanapt® in Canada, and we may not succeed in commercializing Fanapt® outside of the U.S. and Canada. In addition, we may not succeed in commercializing any other compounds. Tasimelteon is presently in development for Non-24 and will require significant resources prior to market approval. We may not be profitable even if our compounds are successfully commercialized. We may be unable to fully develop, obtain regulatory approval for, commercialize, manufacture, market, sell and derive revenue from our compounds in the timeframes we project, if at all, and our inability to do so would materially and adversely impact the market price of our common stock and our ability to raise capital and continue operations.

There can be no assurance that we will achieve sustained profitability. Our ability to achieve sustained profitability in the future depends, in part, upon:

- our and our partners ability to obtain and maintain regulatory approval for our compounds, both in the U.S. and in foreign countries;
- Novartis ability to successfully market and sell Fanapt® in the U.S. and Canada and achieve certain product development and sales milestones;
- our and our partners ability to successfully commercialize Fanapt® outside the U.S. and Canada;
- our ability to enter into and maintain agreements to develop and commercialize our products and product candidates;

our and our partners ability to develop, have manufactured and market our products and product candidates;

our and our partners ability to obtain adequate reimbursement coverage for our compounds from insurance companies, government programs and other third party payors; and

our ability to obtain additional research and development funding from collaborative partners or funding for our products and product candidates.

Table of Contents

In addition, the amount we spend will impact our profitability. Our spending will depend, in part, upon:

- the progress of our research and development programs for our products and product candidates, including clinical trials;
- the time and expense that will be required to pursue FDA and/or foreign regulatory approvals for our compounds and whether such approvals are obtained on a timely basis, if at all;
- the time and expense required to prosecute, enforce and/or challenge patent and other intellectual property rights;
- the cost of operating and maintaining development and research facilities;
- the cost of third party manufacturers;
- the number of product candidates we pursue;
- how competing technological and market developments affect our compounds;
- the cost of possible acquisitions of technologies, compounds, product rights or companies;
- the cost of obtaining licenses to use technology owned by others for proprietary products and otherwise;
- the costs and effects of potential litigation; and
- the costs associated with recruiting and compensating a highly skilled workforce in an environment where competition for such employees may be intense.

We may not achieve all or any of these goals and, thus, we cannot provide assurances that we will ever be profitable on a sustained basis or achieve significant revenues. Even if we do achieve some or all of these goals, we may not achieve significant or sustained commercial success.

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

In general, under Section 382 of the Internal Revenue Code of 1986, as amended (Code), a corporation that undergoes an ownership change is subject to limitations on its ability to utilize its pre-change net operating losses, or NOLs, and certain other tax assets to offset future taxable income. In general, an ownership change occurs if the aggregate stock ownership of certain stockholders increases by more than 50 percentage points over such stockholders lowest percentage ownership during the testing period (generally three years). Transactions involving our common stock, even those outside our control, such as purchases or sales by investors, within the testing period could result in an ownership change. A limitation on our ability to utilize some or all of our NOLs could have a material adverse effect on our results of operations and cash flows.

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

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

Table of Contents

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

If we lose our relationship with any one or more of these parties, we could experience a significant delay in both identifying another comparable provider and then contracting for its services. We may be unable to retain an alternative provider on reasonable terms, if at all. Even if we locate an alternative provider, it is likely that this provider may need additional time to respond to our needs and may not provide the same type or level of service as the original provider. In addition, any provider that we retain will be subject to current Good Laboratory Practices or cGLP, and similar foreign standards and we do not have control over compliance with these regulations by these providers. Consequently, if these practices and standards are not adhered to by these providers, the development and commercialization of our products or product candidates could be delayed.

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

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

We do not have long-term agreements with any of these third parties, and if they are unable or unwilling to perform for any reason, we may not be able to locate alternative acceptable manufacturers or formulators or enter into favorable agreements with them. Any inability to acquire sufficient quantities of our products or product candidates in a timely manner from these third parties could adversely affect sales of our products, delay clinical trials and prevent us from developing our products and product candidates in a cost-effective manner or on a timely basis. In addition, manufacturers of our products and product candidates are subject to cGMP and similar foreign standards and we do not have control over compliance with these regulations by our manufacturers. If one of our contract manufacturers fails to maintain compliance, the production of our products or product candidates could be interrupted, resulting in delays and additional costs. In addition, if the facilities of such manufacturers do not pass a pre-approval or post-approval plant inspection, the FDA will not grant approval and may institute restrictions on the marketing or sale of our products or product candidates.

Our manufacturing strategy presents the following additional risks:

- because most of our third-party manufacturers and formulators are located outside of the U.S., there may be difficulties in importing our products and product candidates or their components into the U.S. as a result of, among other things, FDA import inspections, incomplete or inaccurate import documentation or defective packaging; and

- because of the complex nature of our products and product candidates, our manufacturers may not be able to successfully manufacture our products and product candidates in a cost-effective and/or timely manner.

Table of Contents

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

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

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

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

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

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

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

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

Table of Contents

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

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

The risk that we may be sued on product liability claims is inherent in the development and sale of pharmaceutical products. For example, we face a risk of product liability exposure related to the testing of our products and product candidates in clinical trials and will face even greater risks upon commercialization by us or our partners of our compounds. We believe that we may be at a greater risk of product liability claims relative to other pharmaceutical companies because our compounds are intended to treat central nervous system disorders, and it is possible that we may be held liable for the behavior and actions of patients who use our compounds. These lawsuits may divert our management from pursuing our business strategy and may be costly to defend. In addition, if we are held liable in any of these lawsuits, we may incur substantial liabilities and we or our partners may be forced to limit or forego further commercialization of one or more of our compounds. Although we maintain product liability insurance, our aggregate coverage limit under this insurance is $10.0 million, and while we believe this amount of insurance is sufficient to cover our product liability exposure, these limits may not be high enough to fully cover potential liabilities. As our development activities and commercialization efforts progress and we and our partners sell our compounds, this coverage may be inadequate, we may be unable to obtain adequate coverage at an acceptable cost or we may be unable to get adequate coverage at all or our insurer may disclaim coverage as to a future claim. This could prevent the commercialization or limit the commercial potential of our compounds. Even if we are able to maintain insurance that we believe is adequate, our results of operations and financial condition may be materially adversely affected by a product liability claim. Uncertainties resulting from the initiation and continuation of products liability litigation or other proceedings could have a material adverse effect on our ability to compete in the marketplace. Product liability litigation and other related proceedings may also require significant management time.

Legislative or regulatory reform of the healthcare system in the U.S. and foreign jurisdictions may affect our or our partners ability to sell our products or partnered products profitably.

The continuing efforts of the U.S. and foreign governments, insurance companies, managed care organizations and other payors of health care services to contain or reduce health care costs may adversely affect our or our partners ability to set prices for our products or partnered products which we or our partners believe are fair, and our ability to generate revenues and achieve and maintain profitability.

Specifically, in both the U.S. and some foreign jurisdictions there have been a number of legislative and regulatory proposals to change the healthcare system in ways that could affect our or our partners ability to sell our products or partnered products profitably. In the U.S., the Medicare Prescription Drug Improvement and Modernization Act of 2003 reformed the way Medicare covered and provided reimbursement for pharmaceutical products. This legislation could decrease the coverage and price that we or our partners may receive for our products or partnered products. Other 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 or partnered products may not be considered cost effective, and coverage and reimbursement may not be available or sufficient to allow the sale of such products on a competitive and profitable basis. Further federal and state proposals and healthcare reforms are likely which could limit the prices that can be charged for the drugs we develop and may further limit our commercial opportunity. Our results of operations could be materially adversely affected by the Medicare prescription drug coverage legislation, by the possible effect of this legislation on amounts that private insurers will pay and by other healthcare reforms that may be enacted or adopted in the future.

The Patient Protection and Affordable Care Act of 2010, as amended by the Health Care and Education Reconciliation Act of 2010, or PPACA, is a sweeping measure intended to expand healthcare coverage within the U.S., primarily through the imposition of health insurance mandates on employers and individuals and expansion of the Medicaid program, and the establishment of health care exchanges. Several provisions of the new law,

Table of Contents

which have varying effective dates, may affect us, and will likely increase certain of our costs. For example, an increase in the Medicaid rebate rate from 15.1% to 23.1% was effective as of January 1, 2010, and the volume of rebated drugs was expanded to include beneficiaries in Medicaid managed care organizations effective as of March 23, 2010. The PPACA also imposes an annual fee on pharmaceutical manufacturers which began in 2011, based on the manufacturer s sale of branded pharmaceuticals and biologics (excluding orphan drugs); expands the 340B drug discount program (excluding orphan drugs) including the creation of new penalties for non-compliance; and includes a 50% discount on brand name drugs for Medicare Part D participants in the coverage gap, or doughnut hole . The law also revised the definition of average manufacturer price for reporting purposes (effective October 1, 2010), which could increase the amount of Medicaid drug rebates to states. Substantial new provisions affecting compliance also have been added, which may require us to modify our business practices with health care practitioners.

The reforms imposed by the new law will significantly impact the pharmaceutical industry; however, the full effects of the PPACA cannot be known until these provisions are implemented and the Centers for Medicare & Medicaid Services and other federal and state agencies issue applicable regulations or guidance. Moreover, in the coming years, additional changes could be made to governmental healthcare programs that could significantly impact the success of our products or product candidates. We will continue to evaluate the PPACA, as amended, the implementation of regulations or guidance related to various provisions of the PPACA by federal agencies, as well as trends and changes that may be encouraged by the legislation and that may potentially impact on our business over time. These developments could, however, have a material adverse effect on our business, financial condition and results of operations.

In some foreign countries, including major markets in the European Union and Japan, the pricing of prescription pharmaceuticals is subject to governmental control. In these countries, pricing negotiations with governmental authorities can take nine to twelve months or longer after the receipt of regulatory marketing approval for a product. To obtain reimbursement or pricing approval in some countries, we may be required to conduct a clinical trial that compares the cost-effectiveness of our product to other available therapies. Our business could be materially harmed if reimbursement of our products is unavailable or limited in scope or amount or if pricing is set at unsatisfactory levels.

Our business is subject to extensive governmental regulation and oversight and changes in laws could adversely affect our revenues and profitability.

Our business is subject to extensive government regulation and oversight. As a result, we may become subject to governmental actions which could materially and adversely affect our business, results of operations and financial condition, including:

- new laws, regulations or judicial decisions, or new interpretations of existing laws, regulations or decisions, related to patent protection and enforcement, health care availability, method of delivery and payment for health care products and services or our business operations generally;
- changes in the FDA and foreign regulatory approval processes that may delay or prevent the approval of new products and result in lost market opportunity;
- new laws, regulations and judicial decisions affecting pricing or marketing; and
- changes in the tax laws relating to our operations.

In addition, the Food and Drug Administration Amendments Act of 2007 or the FDAAA included new authorization for the FDA to require post-market safety monitoring, along with a clinical trials registry, and expanded authority for the FDA to impose civil monetary penalties on companies that fail to meet certain commitments. The amendments, among other things, require some new drug applicants to submit risk evaluation and minimization strategies to monitor and address potential safety issues for products upon approval, grant the FDA the authority to impose risk management measures for marketed products and to mandate labeling changes in certain circumstances, and establish new requirements for disclosing the results of clinical trials. Companies that violate the law are subject to substantial civil monetary penalties. Additional measures have also been enacted to address the perceived shortcomings in the FDA s handling of drug safety issues, and to limit

32

Table of Contents

pharmaceutical company sales and promotional practices. While the FDAAA has had, and is expected to have, a substantial effect on the pharmaceutical industry, the full extent of that effect is not yet known. As the FDA issues further regulations, guidance and interpretations relating to this legislation, the impact on the industry as well as our business will become clearer. The requirements and other changes that the FDAAA imposes may make it more difficult, and likely more costly, to obtain approval of new pharmaceutical products and to produce, market and distribute existing products. Our and our partners ability to commercialize approved products successfully may be hindered, and our business may be harmed as a result.

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

Our and our partners activities, including the sale and marketing of our products or partnered 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 of drugs and biologicals, such as us, 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.

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

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

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

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

affect our results of operations and could harm the market price of our stock.

Table of Contents

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

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

Our quarterly operating results may fluctuate significantly.

Our operating results will continue to be subject to quarterly fluctuations. The revenues we generate, if any, and our operating results will be affected by numerous factors, including:

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

the timing and recognition of stock-based compensation expense.

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

Risks related to intellectual property and other legal matters

Our rights to develop and commercialize our product and product candidates are subject in part to the terms and conditions of licenses or sublicenses granted to us by other pharmaceutical companies. With respect to tasimelteon, these terms and conditions include an option in favor of the licensor to reacquire rights to commercialize and develop this product in certain circumstances.

Tasimelteon is based in part on patents that we have licensed on an exclusive basis and other intellectual property licensed from Bristol-Myers Squibb Company (BMS). BMS holds certain rights with respect to

Table of Contents

tasimelteon in the license agreement. If we have not agreed to one or more partnering arrangements to develop and commercialize tasimelteon in certain significant markets with one or more third parties by a certain date, BMS has the option to exclusively develop and commercialize tasimelteon on its own on pre-determined financial terms, including milestone and royalty payments. BMS may terminate our license if we fail to meet certain milestones or if we otherwise breach our royalty or other obligations in the agreement. In the event that we terminate our license, or if BMS terminates our license due to our breach, all of our rights to tasimelteon (including any intellectual property we develop with respect to tasimelteon) will revert back to BMS or otherwise be licensed back to BMS on an exclusive basis. Any termination or reversion of our rights to develop or commercialize tasimelteon, including any reacquisition by BMS of our rights, may have a material adverse effect on our business.

Fanapt® (iloperidone) is based in part on patents and other intellectual property owned by sanofi-aventis and Novartis. Titan Pharmaceuticals, Inc. (Titan) holds an exclusive license from sanofi-aventis to the intellectual property owned by sanofi-aventis, and Titan has sublicensed its rights under such license on an exclusive basis to Novartis. We acquired exclusive rights to this and other intellectual property through a further sublicense from Novartis. The sublicense with Novartis was amended and restated in October of 2009 to provide Novartis with exclusive rights to commercialize Fanapt® in the U.S. and Canada and further develop and commercialize a long-acting injectable or depot formulation of Fanapt® in the U.S. and Canada. In October 2012, Novartis informed us that it had determined to cease development of the long-acting (or depot) formulation of Fanapt®. We retained exclusive rights to Fanapt® outside the U.S. and Canada and we have exclusive rights to use any of Novartis data for Fanapt® for developing and commercializing Fanapt® outside the U.S. and Canada. At Novartis option, we will enter into good faith discussions with Novartis relating to the co-commercialization of Fanapt® outside of the U.S. and Canada or, alternatively, Novartis will receive a royalty on net sales of Fanapt® outside of the U.S. and Canada. Novartis has chosen not to co-commercialize Fanapt® in Europe and certain other countries and will instead receive a royalty on net sales in those countries. These include, but are not limited to, the countries in the European Union, as well as Switzerland, Norway, Liechtenstein and Iceland. We may lose our rights to develop and commercialize Fanapt® outside the U.S. and Canada if we fail to comply with certain requirements in the amended and restated sublicense agreement regarding our financial condition, or if we fail to comply with certain diligence obligations regarding our development or commercialization activities or if we otherwise breach the amended and restated sublicense agreement and fail to cure such breach. Our rights to develop and commercialize Fanapt® outside the U.S. and Canada may be impaired if we do not cure breaches by Novartis of similar obligations contained in its sublicense agreement with Titan. Our loss of rights in Fanapt® to Novartis would have a material adverse effect on our business, financial condition and results of operations. In addition, if Novartis breaches the amended and restated sublicense agreement with respect to its commercialization activities in the U.S. or Canada, we may terminate Novartis commercialization rights in the applicable country. We would no longer receive royalty payments from Novartis in connection with such country in the event of such termination.

VLY-686 is based in part on patents that we have licensed on an exclusive basis and other intellectual property licensed from Lilly. Lilly may terminate our license if we fail to use our commercially reasonable efforts to develop and commercialize VLY-686 or if we materially breach the agreement and fail to cure that breach. In the event that we terminate our license, or if Lilly terminates our license for the reasons stated above, all of our rights to VLY-686 (including any intellectual property we develop with respect to VLY-686) will revert back to Lilly, subject to payment by Lilly to us of a royalty on net sales of products that contain VLY-686.

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

In addition to the rights we have licensed from Novartis, BMS and Lilly relating to our compounds, we rely upon intellectual property we own relating to these compounds, including patents, patent applications and trade secrets. As of December 31, 2012, excluding in-licensed patents and patent applications, we had 29 patent and patent application families, most of which have been filed in key markets including the U.S., and one pending Patent Cooperation Treaty application, relating to Fanapt® and tasimelteon. In addition, we had five other patent applications relating to compounds not presently in clinical studies. Our patent applications may be challenged or

Table of Contents

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

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

The United States Drug Price Competition and Patent Term Restoration Act of 1984, more commonly known as the Hatch-Waxman Act, provides for an extension of patent term for drugs for a period of up to five years to compensate for time spent in development. Assuming we gain a five-year patent term restoration for tasimelteon, and that we continue to have rights under our license agreement with respect to this product, we would have exclusive rights to tasimelteon s U.S. new chemical entity patent (the primary patent covering the compound as a new composition of matter) until 2022. In August 2011, the U.S. Patent and Trademark Office issued a certificate of extension under the Hatch-Waxman Act, extending by five years the term of sanofi-aventis new chemical entity patent relating to Fanapt® to November 2016. Fanapt® will also be eligible for 6 months of additional protection for successfully completing studies in the pediatric population potentially extending the term of the new chemical entity parent in the U.S. until May 2017. The patent for the microsphere long-acting injectable (or depot) formulation of Fanapt® expires in 2024 in the U.S. and 2022 in most of the major markets in Europe. The pending patent application for the aqueous microcrystals long acting injectable (or depot) formulation of Fanapt® will expire in 2023 in the U.S. The patent for the aqueous microcrystals long acting injectable (or depot) formulation of Fanapt® will expire in 2023 in most of the major markets in Europe. A directive in the European Union provides that companies that receive regulatory approval for a new compound will have a 10-year period of market exclusivity for that compound (with the possibility of a further one-year extension) in most countries in Europe, beginning on the date of such European regulatory approval, regardless of when the European new chemical entity patent covering such compound expires. A generic version of the approved drug may not be marketed or sold in Europe during such market exclusivity period. This directive is of material importance with respect to Fanapt®, since the European new chemical entity patent for Fanapt® has expired.

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

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

Our commercial success depends in part on our not infringing the patents and proprietary rights of third parties. Third parties may assert that we are employing their proprietary technology without authorization. In addition, third parties may obtain patents in the future and claim that use of our technologies infringes upon these patents. Furthermore, parties making claims against us may obtain injunctive or other equitable relief, which could effectively block our ability to develop and commercialize one or more of our products. Defense of these claims, regardless of their merit, would divert substantial financial and employee resources from our business. In

Table of Contents

the event of a successful claim of infringement against us, we may have to pay substantial damages, obtain one or more licenses from third parties or pay royalties. In addition, even in the absence of litigation, we may need to obtain additional licenses from third parties to advance our research or allow commercialization of our products. We may fail to obtain any of these licenses at a reasonable cost or on reasonable terms, if at all. In that event, we would be unable to develop and commercialize further one or more of our products.

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

If we use hazardous and biological materials in a manner that causes injury or violates applicable law, we may be liable for damages.

Our research, development and commercialization activities involve the controlled use of potentially hazardous substances, including toxic chemical and biological materials. Although our goal is for our safety procedures for handling and disposing of such materials to comply with state and federal standards, there will always be the risk of contamination, injury or other damages resulting from these hazardous substances. If we were to become liable for an accident, or if we or our partners or manufacturers were to suffer an extended facility shutdown, we could incur significant costs, damages and penalties that could materially harm our business, results of operations and financial condition.

In addition, our operations produce hazardous waste products. While third parties are responsible for disposal of our hazardous waste, we could be liable under environmental laws for any required cleanup of sites at which our waste is disposed. Federal, state, foreign and local laws and regulations govern the use, manufacture, storage, handling and disposal of these hazardous materials. If we fail to comply with these laws and regulations at any time, or if they change, we may be subject to criminal sanctions and substantial civil liabilities, which may adversely affect our business.

Even if we continue to comply with all applicable laws and regulations regarding hazardous materials, we cannot eliminate the risk of accidental contamination or discharge and our resultant liability for any injuries or other damages caused by these accidents. Although we maintain pollution liability insurance, our coverage limit under this insurance is $2.0 million, and while we believe this amount and type of insurance is sufficient to cover risks typically associated with our handling of materials, the insurance may not cover all environmental liabilities, and these limits may not be high enough to cover potential liabilities for these damages fully. The amount of uninsured liabilities may exceed our financial resources and materially harm our business.

Risks related to our common stock

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

The realization of any of the risks described in these risk factors or other unforeseen risks could have a dramatic and adverse effect on the market price of our common stock. Between December 31, 2011 and December 31, 2012, the high and low sale prices of our common stock as reported on the NASDAQ Global Market varied between $2.92 and $5.47. Additionally, market prices for securities of biotechnology and pharmaceutical companies, including ours, have historically been very volatile. The market for these securities has from time to time experienced significant price and volume fluctuations for reasons that were unrelated to the operating performance of any one company.

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

- publicity regarding actual or potential testing or trial results relating to products under development by us or our competitors;
- the outcome of regulatory review relating to products under development by us or our competitors;

Table of Contents

regulatory developments in the U.S. and foreign countries;

developments concerning any collaboration or other strategic transaction we may undertake;

announcements of patent issuances or denials, technological innovations or new commercial products by us or our competitors;

termination or delay of development or commercialization program(s) by our partners;

safety issues with our products or those of our competitors;

our partners ability to successfully commercialize our partnered products;

our ability to successfully execute our commercialization strategies;

announcements of technological innovations or new therapeutic products or methods by us or others;

actual or anticipated variations in our quarterly operating results;

changes in estimates of our financial results or recommendations by securities analysts or failure to meet such financial expectations;

changes in government regulations or policies;

changes in patent legislation or patent decisions or adverse changes to patent law;

additions or departures of key personnel or members of our board of directors;

publicity regarding actual or potential transactions involving us; or

economic, political and other external factors beyond our control.

As a result of these factors, holders of our common stock might be unable to sell their shares at or above the price they paid for such shares.

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

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

In addition to our outstanding common stock, as of December 31, 2012, there were a total of 6,243,008 shares of common stock that we have registered and that we are obligated to issue upon the exercise of currently outstanding options and settlement of restricted stock unit awards granted under our Second Amended and Restated Management Equity Plan and 2006 Equity Incentive Plan. Upon the exercise of these options or settlement of the shares underlying these restricted stock units, as the case may be, in accordance with their respective terms, these shares may be resold freely, subject to restrictions imposed on our affiliates under Rule 144. If significant sales of these shares occur in short periods of time, these sales could reduce the market price of our common stock. Any reduction in the trading price of our common stock could impede our ability to raise capital on attractive terms, if at all.

If we fail to maintain the requirements for continued listing on the NASDAQ Global Market, our common stock could be delisted from trading, which would adversely affect the liquidity of our common stock and our ability to raise additional capital.

Our common stock is currently listed for quotation on the NASDAQ Global Market. We are required to meet specified listing criteria in order to maintain our listing on the NASDAQ Global Market. If we fail to satisfy the NASDAQ Global Market s continued listing requirements, our common stock could be delisted from the NASDAQ Global Market, in which case we may transfer to the NASDAQ Capital Market, which generally has lower financial requirements for initial listing or, if we fail to meet its listing requirements, the over-the-counter bulletin board. Any potential delisting of our common stock from the NASDAQ Global Market would make it more difficult for our stockholders to sell our stock in the public market and would likely result in decreased liquidity and increased volatility for our common stock.

Table of Contents

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

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

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

Proxy contests have been waged against many companies in the biopharmaceutical industry, including us, over the last few years. If faced with a proxy contest or other type of shareholder activism, we may not be able to respond successfully to the contest or dispute, which would be disruptive to our business. Even if we are successful, our business could be adversely affected by a proxy contest or shareholder dispute involving us or our partners because:

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

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

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

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

- authorize the issuance of blank check preferred stock that could be issued by our board of directors to thwart a takeover attempt;
- do not provide for cumulative voting in the election of directors, which would allow holders of less than a majority of the stock to elect some directors;
- establish a classified board of directors, as a result of which the successors to the directors whose terms have expired will be elected to serve from the time of election and qualification until the third annual meeting following their election;
- require that directors only be removed from office for cause;

provide that vacancies on the board of directors, including newly-created directorships, may be filled only by a majority vote of directors then in office;

limit who may call special meetings of stockholders;

prohibit stockholder action by written consent, requiring all actions to be taken at a meeting of the stockholders; and

Table of Contents

establish advance notice requirements for nominating candidates for election to the board of directors or for proposing matters that can be acted upon by stockholders at stockholder meetings.

Moreover, in September 2008, our board of directors adopted a rights agreement, the provisions of which could result in significant dilution of the proportionate ownership of a potential acquirer and, accordingly, could discourage, delay or prevent a change in our management or control over us.

Unstable market, credit and financial conditions may exacerbate certain risks affecting our business and have serious adverse consequences on our business.

The global economic downturn and market instability has made the business climate more volatile and more costly. Our general business strategy may be adversely affected by unpredictable and unstable market conditions. If the equity and credit markets deteriorate further, or do not improve, it may make any necessary debt or equity financing more difficult, more costly, and more dilutive. While we believe we have adequate capital resources to meet current working capital and capital expenditure requirements, a lingering economic downturn or significant increase in our expenses could require additional financing on less than attractive rates or on terms that are excessively dilutive to existing stockholders. Failure to secure any necessary financing in a timely manner and on favorable terms could have a material adverse effect on our stock price and could require us to delay or abandon clinical development plans.

Sales of our products and partnered products will be dependent, in large part, on reimbursement from government health administration authorities, private health insurers, distribution partners and other organizations. As a result of the current credit and financial market conditions, these organizations may be unable to satisfy their reimbursement obligations or may delay payment. In addition, federal and state health authorities may reduce Medicare and Medicaid reimbursements, and private insurers may increase their scrutiny of claims. A reduction in the availability or extent of reimbursement could negatively affect our or our partners product sales and revenue. Customers may also reduce spending during times of economic uncertainty.

In addition, we rely on third parties for several important aspects of our business. For example, we depend upon Novartis for Fanapt® royalty revenue, we use third party contract research organizations for many of our clinical trials, and we rely upon several single source providers of raw materials and contract manufacturers for the manufacture of our products and product candidates. Due to the recent tightening of global credit and the continued deterioration in the financial markets, there may be a disruption or delay in the performance of our third party contractors, suppliers or partners. If such third parties are unable to satisfy their commitments to us, our business would be adversely affected.

ITEM 1B. UNRESOLVED STAFF COMMENTS

Not applicable.

ITEM 2. PROPERTIES

In the second quarter of 2012, we relocated our headquarters to 21,400 square feet of leased office space at 2200 Pennsylvania Avenue NW, Washington, D.C. 20037. Management believes that our current facility is suitable for and adequate to meet our anticipated needs.

ITEM 3. LEGAL PROCEEDINGS

The Company is not a party to any material pending legal proceedings, and management is not aware of any contemplated proceedings by any governmental authority against the Company.

ITEM 4. MINE SAFETY DISCLOSURES

Not applicable.

Table of Contents

PART II

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

Our common stock is quoted on The NASDAQ Global Market under the symbol VNDA. The following table sets forth, for the periods indicated, the range of high and low sale prices of our common stock as reported on The NASDAQ Global Market:

Year Ended December 31, 2012	High	Low
First quarter	$ 5.47	$ 4.40
Second quarter	4.82	3.93
Third quarter	4.64	3.90
Fourth quarter	4.42	2.92

Year Ended December 31, 2011	High	Low
First quarter	$ 10.17	$ 6.61
Second quarter	8.45	6.75
Third quarter	7.80	4.89
Fourth quarter	6.06	4.33

As of February 15, 2013, there were 10 holders of record of our common stock.

Dividends

The Company has not paid dividends to its stockholders (other than a dividend of preferred share purchase rights which was declared in September 2008) since its inception and does not plan to pay dividends in the foreseeable future. The Company currently intends to retain earnings, if any, to finance the growth of the Company.

Table of Contents

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

The following graph shows the cumulative five-year total return on our common stock relative to the cumulative total returns of the NASDAQ Composite Index and the NASDAQ Biotechnology Index. An investment of $100 (with reinvestment of dividends) is assumed to have been made in our common stock and in each of the indexes on December 31, 2007 and its relative performance is tracked through December 31, 2012. The comparisons in the table are required by the SEC and are not intended to forecast or be indicative of possible future performance of the Company s common stock. We have not paid dividends to our stockholders since the inception (other than a dividend of preferred share purchase rights which was declared in September 2008) and do not plan to pay dividends in the foreseeable future. The following graph and related information is being furnished solely to accompany this annual report on Form 10-K pursuant to Item 201(e) of Regulation S-K and shall not be deemed soliciting materials or to be filed with the SEC (other than as provided in Item 201), nor shall such information be incorporated by reference into any of our filings under the Securities Act of 1933 or the Securities Exchange Act of 1934, whether made before or after the date hereof, and irrespective of any general incorporation language in any such filing.

ITEM 6. SELECTED CONSOLIDATED FINANCIAL DATA

The consolidated statements of operations data for the years ended December 31, 2012, 2011 and 2010 and the consolidated balance sheet data as of December 31, 2012 and 2011 are each derived from our audited consolidated financial statements included in this annual report on Form 10-K. The consolidated statements of operations data for the years ended December 31, 2009 and 2008, and the consolidated balance sheet data as of December 31, 2010, 2009 and 2008 are each derived from our audited consolidated financial statements not included herein. Our historical results for any prior period are not necessarily indicative of results to be expected in any future period.

Table of Contents

The following data should be read together with our consolidated financial statements and accompanying notes and the section entitled Management s Discussion and Analysis of Financial Condition and Results of Operations included in this annual report on Form 10-K.

(in thousands, except for share and per share amounts)	Year Ended December 31, 2012	2011	2010	2009	2008
Statements of operations data					
Revenue	$ 32,727	$ 31,720	$ 35,709	$ 4,548	$
Operating expenses:					
Cost of sales	129		2,891	1,915	
Research and development	45,446	28,996	12,338	13,874	23,936
General and administrative	13,882	11,486	10,147	23,724	28,909
Intangible asset amortization	1,495	1,495	1,495	983	
Total operating expenses	60,952	41,977	26,871	40,496	52,845
Income (loss) from operations	(28,225)	(10,707)	8,838	(35,948)	(52,845)
Other income	561	461	431	89	1,781
Income (loss) before tax provision	(27,664)	(10,246)	9,269	(35,859)	(51,064)
Tax provision (benefit)		(444)	2,077		
Net income (loss)	$ (27,664)	$ (9,802)	$ 7,192	$ (35,859)	$ (51,064)
Net income (loss) per share:					
Basic	$ (0.98)	$ (0.35)	$ 0.26	$ (1.33)	$ (1.92)
Diluted	$ (0.98)	$ (0.35)	$ 0.25	$ (1.33)	$ (1.92)
Shares used in calculations of net income (loss) per share:					
Basic	28,228,409	28,106,831	27,916,388	27,015,271	26,650,126
Diluted	28,228,409	28,106,831	28,534,617	27,015,271	26,650,126

	December 31, 2012	2011	2010	2009	2008
Balance sheet data					
Cash and cash equivalents	$ 88,772	$ 87,923	$ 42,559	$ 205,295	$ 39,079
Marketable securities, current	31,631	60,961	155,478		7,379
Marketable securities, non-current		19,012			
Working capital	93,705	121,882	169,546	181,417	44,335
Total assets	135,448	182,618	213,101	225,714	49,934
Total liabilities	125,543	149,144	175,370	202,683	3,914
Accumulated deficit	(291,107)	(263,443)	(253,641)	(260,833)	(224,974)
Total stockholders equity	9,905	33,474	37,731	23,031	46,020

Table of Contents

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

You should read the following discussion and analysis of our financial condition and results of operations together with Selected Consolidated Financial Data and our consolidated financial statements and related notes appearing in this annual report on Form 10-K. Some of the information contained in this discussion and analysis or set forth elsewhere in this annual report on Form 10-K include historical information and other information with respect to our plans and strategy for our business and contain forward-looking statements that involve risks, uncertainties and assumptions. Our actual results may differ materially from those anticipated in these forward-looking statements as a result of certain factors, including but not limited to those set forth under the Risk Factors section of this report and elsewhere in this annual report on Form 10-K.

Overview

We are a biopharmaceutical company focused on the development and commercialization of products for the treatment of central nervous system disorders. We believe that each of our products and partnered products will address a large market with significant unmet medical needs by offering advantages over currently available therapies. Our product portfolio includes Fanapt® (iloperidone), a compound for the treatment of schizophrenia, the oral formulation of which is currently being marketed and sold in the U.S. by Novartis Pharma AG (Novartis), tasimelteon, a compound for the treatment of circadian rhythm sleep disorders (CRSD), which is currently in clinical development for the treatment of Non-24, and VLY-686, a small molecule neurokinin-1 receptor (NK-1R) antagonist.

In December 2012 and January 2013, we announced positive results for two Phase III studies for tasimelteon in the treatment of Non-24-Hour Disorder (Non-24). The SET Phase III study demonstrated that tasimelteon was able to entrain the master body clock as measured by melatonin and cortisol circadian rhythms. Tasimelteon was also shown to significantly improve clinical symptoms across a number of sleep and wake measures. These results provided robust evidence of direct and clinically meaningful benefits to patients with Non-24. The RESET Phase III study demonstrated the maintenance effect of 20 milligrams (mg) of tasimelteon to entrain melatonin and cortisol circadian rhythms in individuals with Non-24. Patients treated with tasimelteon maintained their clinical benefits while patients receiving placebo showed significant deterioration in measures of nighttime sleep, daytime naps and timing of sleep. The tasimelteon Non-24 program continues towards its goal of a projected mid-2013 New Drug Application (NDA) filing with the U.S. Food and Drug Administration (FDA). We will meet with the FDA in the first quarter of 2013 for a pre-NDA meeting on tasimelteon in the treatment of patients with Non-24. In January 2013, Vanda reported top-line results of the Phase IIb/III clinical study (MAGELLAN) in Major Depressive Disorder (MDD), investigating the efficacy and safety of tasimelteon as a monotherapy in the treatment of patients with MDD. The clinical study did not meet the primary endpoint of change from baseline in the Hamilton Depression Scale (HAMD-17) after 8 weeks of treatment as compared to placebo. As a result, all activities have been discontinued related to the MDD indication for tasimelteon. We incurred $40.9 million in research and development costs in 2012 directly attributable to our development of tasimelteon.

Pursuant to the amended and restated sublicense agreement with Novartis, we received an upfront payment of $200.0 million in 2009 and are 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. Based on the current sales performance of Fanapt® in the U.S. and the decision by Novartis to cease development of the long-acting injectable (or depot) formulation of Fanapt®, we expect that some or all of these commercial and development milestones will not be achieved by Novartis. We also receive royalties, which, as a percentage of net sales, are in the low double-digits, on net sales of Fanapt® in the U.S. and Canada. We retain exclusive rights to Fanapt® outside the U.S. and Canada and we have exclusive rights to use any of Novartis data for Fanapt® for developing and commercializing Fanapt® outside the U.S. and Canada. We incurred $1.5 million in research and development costs in 2012 directly attributable to our development of Fanapt®.

Since we began our operations in 2003, we have devoted substantially all of our resources to the in-licensing and clinical development of our compounds. Our ability to generate additional revenues largely depends upon our ability, alone or with others, to complete the development of our products or product candidates to obtain the

Table of Contents

regulatory approvals for and manufacture, market and sell our products and product candidates and on Novartis ability to successfully commercialize Fanapt® in the U.S. The results of our operations will vary significantly from year-to-year and quarter-to-quarter and depend on a number of factors, including risks related to our business, risks related to our industry, and other risks which are detailed in Item 1A of Part I of this annual report on Form 10-K, entitled Risk Factors .

Revenues. Our revenues are derived primarily from our amended and restated sublicense agreement with Novartis and include an upfront payment, product sales and future milestone and royalty payments. Revenue is considered both realizable and earned when the following four conditions are met: (i) persuasive evidence of an arrangement exists, (ii) the arrangement fee is fixed or determinable, (iii) delivery or performance has occurred and (iv) collectability is reasonably assured. Revenue related to the $200.0 million upfront payment is being recognized ratably on a straight-line basis from the date the amended and restated sublicense agreement became effective (November 2009) through the expected life of the U.S. patent for Fanapt® which we expect to last until May 2017. This includes the Hatch-Waxman extension that extends patent protection for drug compounds for a period of five years to compensate for time spent in development and a six-month pediatric term extension. Fanapt® has qualified for the full five-year patent term Hatch-Waxman extension and we expect that Fanapt® will be eligible for six months of pediatric exclusivity. We recognize revenue from Fanapt® royalties and commercial and development milestones from Novartis when realizable and product revenue upon delivery of our products to Novartis.

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

We incurred research and development expenses in the aggregate of $45.4 million in 2012 including employee stock-based compensation expense of $1.4 million. We expect to incur significant research and development expenses as we continue to develop our products and product candidates. We expect to incur licensing costs in the future that could be substantial, as we continue our efforts to develop our products, product candidates and partnered products and to evaluate potential in-license product candidates or compounds.

Table of Contents

The following table summarizes our product development initiatives for 2012, 2011 and 2010, respectively. Included in this table are the research and development expenses recognized in connection with the clinical development of Fanapt®, tasimelteon and VLY-686.

	Year Ended December 31,		
(in thousands)	**2012**	**2011**	**2010**
Direct project costs(1)			
Tasimelteon	$ 40,939	$ 24,810	$ 8,329
Fanapt®	1,494	2,197	2,708
VLY-686	1,144		
Total direct product costs	43,577	27,007	11,037
Indirect project costs(1)			
Facility	1,280	1,507	609
Depreciation	354	259	184
Other indirect overhead costs	235	223	508
Total indirect expenses	1,869	1,989	1,301
Total research and development expenses	$ 45,446	$ 28,996	$ 12,338

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

General and administrative expenses. General and administrative expenses consist primarily of salaries, other related costs for personnel, including employee stock-based compensation, related to executive, finance, accounting, information technology, marketing, and human resource functions. Other costs include facility costs not otherwise included in research and development expenses and fees for legal, accounting and other professional services. General and administrative expenses also include third party expenses incurred to support business development, marketing and other business activities related to Fanapt®. We incurred general and administrative expenses of $13.9 million in 2012, including employee stock-based compensation expense of $2.7 million.

Other income. Other income consists of interest income earned on our cash and cash equivalents, marketable securities and restricted cash and non-recurring income (expense) transactions that are outside of our normal business operations.

Critical Accounting Policies

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

A summary of our significant accounting policies appears in the notes to our audited consolidated financial statements for the year ended December 31, 2012 included in this annual report on Form 10-K. However, we believe that the following accounting policies are important to understanding and evaluating our reported financial results, and we have accordingly included them in this discussion.

Accrued liabilities. As part of the process of preparing financial statements we are required to estimate accrued liabilities. The estimation of accrued liabilities involves identifying services that have been performed on

Table of Contents

our behalf, and then estimating the level of service performed and the associated cost incurred for such services as of each balance sheet date in the financial statements. Accrued liabilities include professional service fees, such as lawyers and accountants, contract service fees, such as those under contracts with clinical monitors, data management organizations and investigators in conjunction with clinical trials, fees to contract manufacturers in conjunction with the production of clinical materials, and fees for marketing and other commercialization activities. Pursuant to our assessment of the services that have been performed on clinical trials and other contracts, we recognize these expenses as the services are provided. Our assessments include, but are not limited to: (i) an evaluation by the project manager of the work that has been completed during the period, (ii) measurement of progress prepared internally and/or provided by the third-party service provider, (iii) analyses of data that justify the progress, and (iv) our judgment. In the event that we do not identify certain costs that have begun to be incurred or we under- or over-estimate the level of services performed or the costs of such services, our reported expenses for such period would be too low or too high.

Milestone payments are accrued when it is deemed probable that the milestone event will be achieved. Upon FDA acceptance of an NDA filing for tasimelteon, the Company would be obligated to make milestone payments of $0.5 million under regulatory consulting agreements and $3.8 million under licensing agreements, respectively.

Revenue Recognition. Our revenues are derived primarily from our amended and restated sublicense agreement with Novartis and include an upfront payment, product revenue and future milestone and royalty revenues. Revenue related to the upfront payment is being recognized ratably from the date the amended and restated sublicense agreement became effective (November 2009) through the expected life of the U.S. patent for Fanapt®, which we expect to last until May 2017. This includes the Hatch-Waxman extension that extends patent protection for drug compounds for a period of five years to compensate for time spent in development and a six-month pediatric term extension. Fanapt® has qualified for the full five-year patent term Hatch-Waxman extension and we expect that Fanapt® will be eligible for six months of pediatric exclusivity. We recognize revenue related to Fanapt® royalties and commercial and development milestones as they are realizable and earned, and product revenue upon delivery of our products to Novartis. Our revenues have also been derived from grant revenue which is recognized when it is received.

Employee stock-based compensation. We use the Black-Scholes-Merton option pricing model to determine the fair value of stock options. The determination of the fair value of stock options on the date of grant using an option pricing model is affected by our stock price as well as assumptions regarding a number of complex and subjective variables. These variables include the expected stock price volatility over the expected term of the awards, actual and projected employee stock option exercise behaviors, risk-free interest rate and expected dividends. Expected volatility rates are based on the historical volatility of our publicly traded common stock and other factors. The weighted average expected term of stock options granted is based on the simplified method as the options meet the plain vanilla criteria required by authoritative guidance. Significant changes in the market price of the Company s common stock in recent years has made historical data less reliable for the purpose of estimating future vesting, exercise, and employment behavior. The simplified method provided a more reasonable approach for estimating the weighted average expected term for options granted in 2012.

The risk-free interest rates are based on the U.S. Treasury yield for a period consistent with the expected term of the option in effect at the time of the grant. We have not paid dividends to our stockholders since our inception (other than a dividend of preferred share purchase rights which was declared in September 2008) and do not plan to pay dividends in the foreseeable future. Employee stock-based compensation expense for a period is also affected by the expected forfeiture rate for the respective option grants. If our estimates of the fair value of these equity instruments or expected forfeitures are too high or too low, it would have the effect of overstating or understating expenses.

Table of Contents

Employee stock-based compensation expense related to stock-based awards for the years ended December 31, 2012, 2011 and 2010, was comprised of the following:

	Year Ended December 31,		
(in thousands)	**2012**	**2011**	**2010**
Research and development	$ 1,356	$ 2,450	$ 2,536
General and administrative	2,718	3,036	2,271
Total employee stock-based compensation expense	$ 4,074	$ 5,486	$ 4,807

The research and development portion of employee stock-based compensation expense for 2012 was impacted by the termination of our Chief Medical Officer in the third quarter of 2012 and the resulting reversal of employee stock-based compensation expense resulting from the cancellation of certain of his outstanding equity awards.

Income taxes. On a periodic basis, we evaluate the realizability of our deferred tax assets and liabilities and will adjust such amounts in light of changing facts and circumstances, including but not limited to future projections of taxable income, the reversal of deferred tax liabilities, tax legislation, rulings by relevant tax authorities and tax planning strategies. Settlement of filing positions that may be challenged by tax authorities could impact our income taxes in the year of resolution.

In assessing the realizability of deferred tax assets, we consider whether it is more likely than not that some portion or all of the deferred tax assets will not be realized. The ultimate realization of deferred tax assets is dependent upon the generation of future taxable income during the period in which those temporary differences becomes deductible or the net operating losses (NOLs) and credit carryforwards can be utilized. When considering the reversal of the valuation allowance, we consider the level of past and future taxable income, the reversal of deferred tax liabilities, the utilization of the carryforwards and other factors. Revisions to the estimated net realizable value of the deferred tax asset could cause our provision for income taxes to vary significantly from period to period.

Deferred tax assets are reduced by a valuation allowance when, in the opinion of management, it is more likely than not that some portion or all of the deferred tax assets will not be realized. The fact that we have historically generated NOLs serves as strong evidence that it is more likely than not that deferred tax assets will not be realized in the future. Therefore, we have a full valuation allowance against all deferred tax assets as of December 31, 2012.

Recent Accounting Pronouncements

There are no new accounting pronouncements that have had or that we expect will have a material effect on our consolidated financial statements.

Results of Operations

We anticipate that our results of operations will fluctuate for the foreseeable future due to several factors, including any possible payments made or received pursuant to license or collaboration agreements, progress of our research and development efforts, the timing and outcome of clinical trials and related possible regulatory approvals and our and our partners ability to successfully commercialize our products, product candidates and partnered products. Our limited operating history makes predictions of future operations difficult or impossible. Since our inception, we have incurred significant losses. As of December 31, 2012, we had an accumulated deficit of $291.1 million.

Year ended December 31, 2012 compared to year ended December 31, 2011

Revenues. Revenues were $32.7 million for the year ended December 31, 2012 compared to revenues of $31.3 million for the year ended December 31, 2011. Revenues for the year ended December 31, 2012 included $26.8 million recognized from Novartis related to straight-line recognition of upfront license fees and $5.9

Table of Contents

million in royalty revenue based on 2012 net sales of Fanapt®. Revenues for the year ended December 31, 2011 included $26.8 million recognized from Novartis related to straight-line recognition of upfront license fees and $4.5 million in royalty revenue based on 2011 net sales of Fanapt®.

Intangible asset amortization. Intangible asset amortization was $1.5 million for both the year ended December 31, 2012 and the year ended December 31, 2011. Intangible amortization relates to the capitalized intangible asset of $12.0 million resulting from the Fanapt® milestone payment to Novartis in May 2009.

Research and development expenses. Research and development expenses increased by $16.4 million, or 56.7%, to $45.4 million for the year ended December 31, 2012 compared to $29.0 million for the year ended December 31, 2011.

The following table discloses the components of research and development expenses reflecting all of our project expenses for the years ended December 31, 2012 and 2011:

	Year Ended December 31,	
(in thousands)	**2012**	**2011**
Direct project costs:		
Clinical trials	$ 28,296	$ 14,440
Contract research and development manufacturing, consulting, materials and other direct costs	9,047	5,987
Salaries, benefits and related costs	4,878	4,130
Employee stock-based compensation expense	1,356	2,450
Total direct costs	43,577	27,007
Indirect project costs	1,869	1,989
Total	$ 45,446	$ 28,996

Direct costs increased by $16.6 million, or 61.4%, to $43.6 million for the year ended December 31, 2012 compared to $27.0 million for the year ended December 31, 2011 primarily as a result of increases in clinical trial costs, contract research and development, consulting, materials and other direct costs and salaries, benefits and related costs partially offset by lower stock-based compensation. Clinical trials costs increased by $13.9 million, or 96.0%, to $28.3 million for the year ended December 31, 2012 compared to $14.4 million for the year ended December 31, 2011 primarily due to costs related to the tasimelteon trials for the treatment of Non-24 in blind individuals without light perception and the tasimelteon trial for the treatment of MDD. Contract research and development, consulting, materials and other direct costs increased by $3.1 million, or 51.1%, to $9.0 million for the year ended December 31, 2012 compared to $6.0 million for the year ended December 31, 2011 primarily due to costs related to the tasimelteon Non-24 and MDD trials, costs related to the preparation of a future tasimelteon New Drug Application (NDA) filing with the FDA and the $1.0 initial license fee associated with VLY-686. Salaries, benefits and related costs increased by $0.7 million, or 18.1%, to $4.9 million for the year ended December 31, 2012 compared to $4.1 million for the year ended December 31, 2011 due to new employees hired in 2011 and 2012 and the termination of our Chief Medical Officer in the third quarter of 2012 and the severance costs associated with his termination. Employee stock-based compensation expense decreased by $1.1 million, or 44.7%, to $1.4 million for the year ended December 31, 2012 compared to $2.5 million for the year ended December 31, 2011 due to the termination of our Chief Medical Officer in the third quarter of 2012 and the reversal of employee stock-based compensation expense resulting from the cancellation of certain of his outstanding equity awards and a reduction in the amortization of employee stock-based compensation expense from the lower fair value of equity awards granted during 2011 and 2012 compared to equity awards granted in prior periods.

General and administrative expenses. General and administrative expenses increased by $2.4 million, or 20.9%, to $13.9 million for the year ended December 31, 2012 compared to $11.5 million for the year ended December 31, 2011.

Table of Contents

The following table discloses the components of our general and administrative expenses for the years ended December 31, 2012 and 2011:

	Year Ended December 31,	
(in thousands)	**2012**	**2011**
Salaries, benefits and related costs	$ 3,247	$ 2,065
Employee stock-based compensation expense	2,718	3,036
Marketing, legal, accounting and other professional services	4,777	3,575
Other expenses	3,140	2,810
Total	$ 13,882	$ 11,486

Salaries, benefits and related costs increased by $1.2 million, or 57.2%, to $3.2 million for the year ended December 31, 2012 compared to $2.1 million for the year ended December 31, 2011 primarily due to the hiring of an executive in the fourth quarter of 2011 and other new hires in 2011 and 2012. Marketing, legal, accounting and other professional expenses increased by $1.2 million, or 33.6%, to $4.8 million for the year ended December 31, 2012 compared to $3.6 million for the year ended December 31, 2011 primarily due to increased legal costs associated with developing Fanapt® outside the U.S. and Canada and increased market development expenses associated with tasimelteon. Other expenses included lease exit costs and related accelerated depreciation in 2012 and a lease termination penalty in 2011 relating to our former headquarters lease in Rockville, Maryland.

Other income. Other income increased $0.1 million, or 21.7%, to $0.6 million for the year ended December 31, 2012 compared to $0.5 million for the year ended December 31, 2011 primarily as a result of a legal settlement related to a lawsuit filed against one of our stockholders partially offset by lower interest income. While we did not participate in the lawsuit proceedings, we received a portion of the settlement.

Tax provision (benefit). The tax benefit for the year ended December 31, 2012 was fully offset by a tax valuation allowance resulting from our assessment that it is more likely than not that our deferred tax assets will not be realized. The ultimate realization of deferred tax assets is dependent upon the generation of future taxable income during the period in which NOLs and credit carryforwards can be utilized. The benefit for income taxes of $0.4 million for the year ended December 31, 2011 is the result of the approval for a change in accounting method from the Internal Revenue Service (IRS).

Year ended December 31, 2011 compared to year ended December 31, 2010

Revenues. Revenues were $31.3 million for the year ended December 31, 2011 compared to revenues of $35.7 million for the year ended December 31, 2010. Revenues for the year ended December 31, 2011 included $26.8 million recognized from Novartis related to straight-line recognition of upfront license fees and $4.5 million in royalty revenue based on 2011 sales of Fanapt®. Revenues for the year ended December 31, 2010 included $26.8 million recognized from Novartis related to straight-line recognition of upfront license fees, $3.1 million in royalty revenue based on 2010 sales of Fanapt®, $5.3 million for Fanapt® product sales to Novartis and grant revenue of $0.5 million for qualified research and development investments under the Internal Revenue Service s Therapeutic Discovery Project Credit Program. For the year ended December 31, 2011, there were no sales of products to Novartis and no grant revenue.

Cost of sales. There were no sales of products for the year ended December 31, 2011 compared to cost of sales of $2.9 million for the year ended December 31, 2010.

Intangible asset amortization. Intangible asset amortization was $1.5 million for both the year ended December 31, 2011 and the year ended December 31, 2010. The amortization is the result of the capitalized intangible asset related to the $12.0 million milestone payment to Novartis in May 2009.

Research and development expenses. Research and development expenses increased by $16.7 million, or 135.0%, to $29.0 million for the year ended December 31, 2011 compared to $12.3 million for the year ended December 31, 2010.

Table of Contents

The following table discloses the components of research and development expenses reflecting all of our project expenses for the years ended December 31, 2011 and 2010:

(in thousands)	Year Ended December 31, 2011	2010
Direct project costs:		
Clinical trials	$ 14,440	$ 2,542
Contract research and development manufacturing, consulting, materials and other direct costs	5,987	2,976
Salaries, benefits and related costs	4,130	2,983
Employee stock-based compensation expense	2,450	2,536
Total direct costs	27,007	11,037
Indirect project costs	1,989	1,301
Total	$ 28,996	$ 12,338

Direct costs increased by $16.0, or 144.7%, to $27.0 million for the year ended December 31, 2011 compared to $11.0 million for the year ended December 31, 2010 primarily as a result of higher clinical trial expenses, manufacturing costs and salary and benefit expenses, partially offset by lower stock-based compensation expenses. Clinical trials expense increased by $11.9 million, or 468.1%, to $14.4 million for the year ended December 31, 2011 compared to $2.5 million for the year ended December 31, 2010 primarily due to the costs associated with four Phase III clinical trials for tasimelteon in Non-24 in blind individuals without light perception, which were initiated in 2010 and 2011, and one Phase IIb/III clinical trial for tasimelteon in MDD, which was initiated in the third quarter of 2011. Contract research and development manufacturing, consulting, materials and other direct costs increased by $3.0 million, or 101.2%, to $6.0 million for the year ended December 31, 2011 compared to $3.0 million for the year ended December 31, 2010 primarily as a result of increased manufacturing costs for tasimelteon in 2011 and increased regulatory consulting expenses related to tasimelteon in 2011. Salary and benefit expenses increased by $1.1 million, or 38.5%, to $4.1 million for the year ended December 31, 2011 compared to $3.0 million for the year ended December 31, 2010 primarily due to new employees hired in 2011 to support the tasimelteon trials in Non-24 and MDD. Indirect costs increased by $0.7 million, or 52.9%, to $2.0 million for the year ended December 31, 2011 compared to $1.3 million for the year ended December 31, 2010 primarily as a result of the lease termination penalty recognized in the fourth quarter of 2011.

General and administrative expenses. General and administrative expenses increased by $1.3 million, or 13.2%, to $11.5 million for the year ended December 31, 2011 from $10.1 million for the year ended December 31, 2010.

The following table discloses the components of our general and administrative expenses for the years ended December 31, 2011 and 2010:

(in thousands)	Year Ended December 31, 2011	2010
Salaries, benefits and related costs	$ 2,065	$ 1,745
Employee stock-based compensation expense	3,036	2,271
Marketing, legal, accounting and other professional services	3,575	3,611
Other expenses	2,810	2,520
Total	$ 11,486	$ 10,147

Salaries, benefits and related costs increased by $0.3 million, or 18.3%, to $2.1 million for the year ended December 31, 2011 compared to $1.7 million for the year ended December 31, 2010 as a result of executive

Table of Contents

hirings made in the fourth quarter of 2010 and 2011. Employee stock-based compensation expense increased by $0.8 million, or 33.7%, to $3.0 million for the year ended December 31, 2011 compared $2.3 million for the year ended December 31, 2010 as a result of executive hirings made in the fourth quarter of 2010 and 2011. Other expenses increased by $0.3, or 11.6%, to $2.8 million for the year ended December 31, 2011 compared to $2.5 million for the year ended December 31, 2010 primarily due to the lease termination penalty recognized in the fourth quarter of 2011.

Other income. Other income increased $0.1 million, or 7.0%, to $0.5 million for the year ended December 31, 2011 from $0.4 million for the year ended December 31, 2010 due to a higher rate of return on investments.

Tax provision (benefit). The benefit for income taxes of $0.4 million for the year ended December 31, 2011 is a result of the approval for a change in accounting method from the IRS. Our effective tax rate of (4.3%) for the year ended December 31, 2011 was favorably impacted by the approval for a change in accounting method from the IRS. In addition, our tax rate was favorably impacted by the research and development and orphan drug credits.

Intangible Asset

The following is a summary of our intangible asset as of December 31, 2012:

		December 31, 2012		
(in thousands)	Estimated Useful Life (Years)	Gross Carrying Amount	Accumulated Amortization	Net Carrying Amount
Fanapt®	8	$ 12,000	$ 5,468	$ 6,532

In May 2009, we announced that the FDA had approved the NDA for Fanapt®. As a result of the FDA s approval of the NDA, we met a milestone under our original sublicense agreement with Novartis which required us to make a payment of $12.0 million to Novartis. The $12.0 million was capitalized and is being amortized over the remaining life of the U.S. patent for Fanapt®, which we expect to last until May 2017. This includes the Hatch-Waxman extension that provides patent protection for drug compounds for a period of five years to compensate for time spent in development and a six-month pediatric term extension. Fanapt® has qualified for the full five-year patent term Hatch-Waxman extension and we expect that Fanapt® will be eligible for six months of pediatric exclusivity. This term is our best estimate of the life of the patent; if, however, the pediatric extension is not granted, the intangible asset will be amortized over a shorter period.

We capitalized and began amortizing the asset immediately following the FDA approval of the NDA for Fanapt®. The intangible asset is being amortized over its estimated useful economic life using the straight-line method. Amortization expense was $1.5 million for the years ended December 31, 2012, 2011 and 2010, respectively.

The following table summarizes our intangible asset amortization schedule as of December 31, 2012:

(in thousands)	Total	2013	2014	2015	2016	After 2016
Intangible asset	$ 6,532	$ 1,495	$ 1,495	$ 1,495	$ 1,495	$ 552

Table of Contents

Deferred Revenue

The following is a summary of changes in total deferred revenue for the years ended December 31, 2012, 2011 and 2010:

(in thousands)	Balance at Beginning of Year	Reductions from Licensing Revenue Recognized	Balance at End of Year
Year ended:			
December 31, 2012	$ 143,853	$ 26,789	$ 117,064
December 31, 2011	170,642	26,789	143,853
December 31, 2010	197,431	26,789	170,642

We entered into an amended and restated sublicense agreement with Novartis in October 2009, pursuant to which Novartis has the right to commercialize and develop Fanapt® in the U.S. and Canada. Under the amended and restated sublicense agreement, we received an upfront payment of $200.0 million in December 2009. We established a Joint Steering Committee (JSC) with Novartis following the effective date of the amended and restated sublicense agreement. We concluded that the JSC constitutes a deliverable under the amended and restated sublicense agreement and that revenue related to the upfront payment will be recognized ratably over the term of the JSC; however, the delivery or performance has no term as the exact length of the JSC is undefined. As a result, we deemed the performance period of the JSC to be the life of the U.S. patent for Fanapt®, which we expect to last until May 2017. This includes the Hatch-Waxman extension that provides patent protection for drug compounds for a period of five years to compensate for time spent in development and a six-month pediatric term extension. Fanapt® has qualified for the full five-year patent term Hatch-Waxman extension and we expect that Fanapt® will be eligible for six months of pediatric exclusivity. This term is our best estimate of the life of the patent. Revenue related to the upfront payment will be recognized ratably from the date the amended and restated sublicense agreement became effective (November 2009) through the expected life of the U.S. patent for Fanapt® (May 2017). For each of the years ended December 31, 2012, 2011 and 2010, we recognized revenue of $26.8 million for the license agreement.

Liquidity and Capital Resources

As of December 31, 2012, our total cash and cash equivalents and marketable securities were $120.4 million compared to $167.9 million at December 31, 2011. Our cash and cash equivalents are deposits in operating accounts and highly liquid investments with an original maturity of 90 days or less at date of purchase and consist of time deposits, investments in money market funds with commercial banks and financial institutions, and commercial paper of high-quality corporate issuers. Our marketable securities consist of investments in government sponsored enterprises and commercial paper.

Table of Contents

As of December 31, 2012 and 2011, our liquidity resources are summarized as follows:

(in thousands)	As of December 31, 2012	2011
Cash and cash equivalents		
Cash and cash equivalents	$ 88,772	$ 87,923
Marketable securities, current		
U.S. Treasury and government agencies	14,442	23,755
Corporate debt	17,189	37,206
Marketable securities, current	31,631	60,961
Marketable securities, non-current		
U.S. Treasury and government agencies		19,012
Marketable securities, non-current		19,012
Total	$ 120,403	$ 167,896

As of December 31, 2012, we maintained all of our cash and cash equivalents in two financial institutions. Deposits held with these institutions may exceed the amount of insurance provided on such deposits, but we do not anticipate any losses with respect to such deposits.

We expect to continue to incur substantial expenses relating to our research and development efforts, as we focus on clinical trials and manufacturing required for the development of our products. The duration and cost of clinical trials are a function of numerous factors such as the number of patients to be enrolled in the trial, the amount of time it takes to enroll them, the length of time they must be treated and observed, and the number of clinical sites and countries for the trial. In addition, orphan clinical trials create an additional challenge due to the limited number of available patients afflicted with the disease.

We must receive regulatory approval to launch any of our products commercially. In order to receive such approval, the appropriate regulatory agency must conclude that our clinical data establish safety and efficacy and that our products and the manufacturing facilities meet all applicable regulatory requirements. We cannot be certain that we will establish sufficient safety and efficacy data to receive regulatory approval for any of our compounds or that our compounds and the manufacturing facilities will meet all applicable regulatory requirements.

Because of the uncertainties discussed above, the costs to advance our research and development projects are difficult to estimate and may vary significantly. We expect that our existing funds will be sufficient to fund our currently planned operations. Our future capital requirements and the adequacy of our available funds will depend on many factors, primarily including the scope and costs of our clinical development programs, the scope and costs of our manufacturing and process development activities, the magnitude of our discovery and preclinical development programs and the level of our pre-commercial launch activities. There can be no assurance that any additional financing required in the future will be available on acceptable terms, if at all.

Cash flow

The following table summarizes our cash flows for the years ended December 31, 2012, 2011 and 2010.

(in thousands)	Year Ended December 31, 2012	2011	2010
Net cash provided by (used in):			
Operating activities	$ (44,917)	$ (28,410)	$ (10,898)
Investing activities	45,754	73,749	(155,622)
Financing activities	12	25	3,784

Net change in cash and cash equivalents	$ 849	$ 45,364	$ (162,736)

Table of Contents

Year ended December 31, 2012 compared to year ended December 31, 2011

Net cash used in operations was $44.9 million for the year ended December 31, 2012 compared to $28.4 million for the year ended December 31, 2011. The increase in net cash used in operations for the year ended December 31, 2012 as compared to the year ended December 31, 2011 was primarily due to the costs associated with four Phase III clinical trials for tasimelteon in Non-24 in blind individuals without light perception, which were initiated in 2010 and 2011, and one Phase IIb/III clinical trial for tasimelteon in MDD, which was initiated in the third quarter of 2011. Adjustments to reconcile net loss to net cash used in operating activities for the year ended December 31, 2012 included non-cash charges for depreciation and amortization of $2.7 million, employee and non-employee stock-based compensation expense of $4.1 million, landlord contributions for tenant improvements of $1.8 million, a net increase of $0.9 million in prepaid expenses and other assets, accounts receivable, inventory, accounts payable, accrued liabilities and other liabilities and a decrease in deferred revenue of $26.8 million. Net cash provided by investing activities for the year ended December 31, 2012 was $45.8 million and consisted of net maturities, sales and purchases of marketable securities of $47.8 million and purchases of property and equipment of $2.0 million.

Year ended December 31, 2011 compared to year ended December 31, 2010

Net cash used in operations was $28.4 million for the year ended December 31, 2011 and $10.9 million for the year ended December 31, 2010. The increase in net cash used in operations for the year ended December 31, 2011 as compared to the year ended December 31, 2010 was primarily due to the costs associated with four Phase III clinical trials for tasimelteon in Non-24 in blind individuals without light perception, which were initiated in 2010 and 2011, and one Phase IIb/III clinical trial for tasimelteon in MDD, which was initiated in the third quarter of 2011. Adjustments to reconcile net loss to net cash used in operating activities for the year ended December 31, 2011 included non-cash charges for depreciation and amortization of $2.9 million, stock-based compensation of $5.5 million, decreases in deferred tax benefits of $1.8 million, decreases in accrued income taxes of $2.3 million, increases in prepaid expenses and other assets, accounts receivable, accounts payable, accrued liabilities and other liabilities of $0.3 million and a decrease in deferred revenue of $26.8 million. Net cash provided by investing activities for the year ended December 31, 2011 was $73.7 million and consisted of net maturities, sales and purchases of marketable securities of $74.6 million, purchases of property and equipment of $0.3 million and change in restricted cash of $0.6 million. Net cash provided from financing activities for the year ended December 31, 2011 was $0.03 million consisting of proceeds from the exercise of stock options.

Off-balance sheet arrangements

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

Contractual obligations and commitments

The following is a summary of our non-cancellable long-term contractual cash obligations as of December 31, 2012:

		Cash payments due by period					
***(in thousands)*(1)(2)(3)**	**Total**	**2013**	**2014**	**2015**	**2016**	**2017**	**After 2017**
Operating leases	$ 12,003	$ 1,312	$ 1,052	$ 1,079	$ 1,106	$ 1,133	$ 6,321

(1) This table does not include various agreements that we have entered into for services with third party vendors, including agreements to conduct clinical trials, to manufacture product candidates, and for consulting and other contracted services due to the cancelable nature of the services. We accrued the costs of these agreements based on estimates of work completed to date.

(2) This table does not include milestone payments that could be due under our agreement with a regulatory consultant we have engaged to assist in our efforts to prepare, file and obtain FDA approval of an NDA for tasimelteon. As part of the engagement and subject to certain conditions, we could be obligated to make

Table of Contents

milestone payments upon the achievement of certain milestones, including $0.5 million in the event that the tasimelteon NDA is accepted for filing by the FDA and $2.0 million in the event that the tasimelteon NDA is approved by the FDA.

(3) This table does not include milestone payments that could be due under our license agreements. Under our license agreement with Bristol-Myers Squibb (BMS) for the exclusive rights to develop and commercialize tasimelteon, we would be obligated to make future milestone payments to BMS and Massachusetts General Hospital (MGH) of less than $40.0 million in the aggregate (the majority of which are tied to sales milestones). In the event that a tasimelteon NDA is accepted for filing by the FDA, we will incur milestone obligations of $3.8 million. Under our license agreement with Eli Lilly and Company for the exclusive rights to develop and commercialize VLY-686, we could be obligated to make future milestone payments of up to $4.0 million for pre-NDA approval milestones and up to $95.0 million for future regulatory approval and sales milestones.

Operating leases

Our commitments related to operating leases represent the minimum annual payments for the operating lease for our headquarters located in Washington, D.C., which expires in 2023 and the lease exit liability for our former headquarters located in Rockville, Maryland, up to the lease termination date of June 30, 2013.

In July 2011, we entered into an office lease with Square 54 Office Owner LLC (the Landlord) for our current headquarters, consisting of 21,400 square feet at 2200 Pennsylvania Avenue, N.W. in Washington, D.C. (the Lease). Under the Lease, rent payments are abated for the first 12 months. The Landlord provided us with a cash contribution of $1.9 million for tenant improvements during the year ended December 31, 2012. Subject to the prior rights of other tenants in the building, we have the right to renew the Lease for five years following the expiration of its original term. We also have the right to sublease or assign all or a portion of the premises, subject to standard conditions. The Lease may be terminated early by us or the Landlord upon certain conditions.

ITEM 7A. QUALITATIVE AND QUANTITATIVE DISCLOSURES ABOUT MARKET RISK

Interest rates

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

Marketable securities

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

Effects of inflation

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

ITEM 8. FINANCIAL STATEMENTS AND SUPPLEMENTARY DATA

The consolidated financial statements and related financial statement schedules required to be filed are listed in the Index to Consolidated Financial Statements and are incorporated herein.

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

None.

Table of Contents

ITEM 9A. CONTROLS AND PROCEDURES

Conclusion Regarding the Effectiveness of Disclosure Controls and Procedures

Under the supervision and with the participation of our management, including the Chief Executive Officer and Chief Financial Officer, we evaluated the effectiveness of the design and operation of our disclosure controls and procedures (as defined in Rules 13a-15(e) and 15d-15(e) under the Securities and Exchange Act of 1934 (Exchange Act)) as of December 31, 2012. Based upon that evaluation, our Chief Executive Officer and Chief Financial Officer concluded that our disclosure controls and procedures are effective as of December 31, 2012, the end of the period covered by this annual report, to ensure that the information required to be disclosed by us in the reports that we file or submit under the Exchange Act is recorded, processed, summarized and reported within the time periods specified in the Securities and Exchange Commission s rules and forms, and that such information is accumulated and communicated to our management, including our Chief Executive Officer and Chief Financial Officer, as appropriate to allow timely decisions regarding required disclosures.

Management s Report on Internal Control Over Financial Reporting

Our management is responsible for establishing and maintaining an adequate system of internal control over financial reporting, as defined in the Exchange Act Rule 13a-15(f). Management conducted an assessment of our internal control over financial reporting based on the framework established by the Committee of Sponsoring Organizations of the Treadway Commission in *Internal Control Integrated Framework.* Based on the assessment, management concluded that, as of December 31, 2012, our internal control over financial reporting was effective.

The effectiveness of our internal control over financial reporting as of December 31, 2012 has been audited by PricewaterhouseCoopers LLP, an independent registered public accounting firm, as stated in their report included in this annual report on Form 10-K.

Changes in Internal Control over Financial Reporting

There has been no change in our internal controls over financial reporting (as defined in Rules 13a-15(f) and 15d-15(f) of the Exchange Act) during the fourth quarter of 2012 that has materially affected, or is reasonably likely to materially affect, our internal control over financial reporting.

ITEM 9B. OTHER INFORMATION

None.

PART III

ITEM 10. DIRECTORS, EXECUTIVE OFFICERS AND CORPORATE GOVERNANCE

Information required under this item will be contained in our Proxy Statement for the Annual Meeting of Stockholders to be filed with the SEC within 120 days after the end of the fiscal year ended December 31, 2012, under the captions Election of Directors, Executive Officers, Corporate Governance , and Section 16(a) Beneficial Ownership Reporting Compliance and is incorporated herein by reference pursuant to General Instruction G (3) to Form 10-K.

ITEM 11. EXECUTIVE COMPENSATION

Information required under this item will be contained in our Proxy Statement for the Annual Meeting of Stockholders to be filed with the SEC within 120 days after the end of the fiscal year ended December 31, 2012, under the captions Corporate Governance and Executive Compensation, and is incorporated herein by reference pursuant to General Instruction G(3) to Form 10-K, except that information required by Item 407(e)(5) of Regulation S-K will be deemed furnished in this Form 10-K and will not be deemed incorporated by reference into any filing under the Securities Act of 1933 or the Securities Exchange Act of 1934, except to the extent that we specifically incorporate it by reference into such filing.

57

Table of Contents

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

In addition to the information set forth under the caption Securities Authorized for Issuance Under Equity Compensation Plans below, the information required under this item will be contained in our Proxy Statement for the Annual Meeting of Stockholders to be filed with the SEC within 120 days after the end of the fiscal year ended December 31, 2012, under the caption Security Ownership by Certain Beneficial Owners and Management and is incorporated herein by reference pursuant to General Instruction G(3) to Form 10-K.

Securities Authorized for Issuance Under Equity Compensation Plans

The following table provides certain information regarding our equity compensation plans in effect as of December 31, 2012:

Equity Compensation Plan Information

Plan Category	Number of Securities to be Issued Upon Exercise of Outstanding Options, Warrants and Rights (a)	Weighted-Average Exercise Price of Outstanding Options, Warrants and Rights (b)	Number of Securities Remaining Available for Issuance Under Equity Compensation Plans (Excluding Securities Reflected in Column (a)) (c)
Equity compensation plans approved by security holders	6,243,008	$ 9.74	1,161,688
Equity compensation plans not approved by security holders			
Total	6,243,008	$ 9.74	1,161,688

(a) Includes 5,537,632 shares issuable upon exercise of outstanding options and 705,376 shares issuable upon settlement of RSUs under the 2006 Equity Incentive Plan and Second Amended and Restated Management Equity Plan.

(b) Does not take into account RSUs which have no exercise price.

(c) On January 1 of each year, the number of shares reserved under the 2006 Equity Incentive Plan is automatically increased by 4% of the total number of shares of common stock that are outstanding at that time, or, if less, by 1,500,000 shares (or such lesser number as may be approved by the Company s Board of Directors).

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

Information required under this item will be contained in our Proxy Statement for the Annual Meeting of Stockholders to be filed with the SEC within 120 days after the end of the fiscal year ended December 31, 2012, under the caption Corporate Governance and is incorporated herein by reference pursuant to General Instruction G(3) to Form 10-K.

ITEM 14. PRINCIPAL ACCOUNTANT FEES AND SERVICES

Information required under this item will be contained in our Proxy Statement for the Annual Meeting of Stockholders to be filed with the SEC within 120 days after the end of the fiscal year ended December 31, 2012, under the caption Ratification of Selection of Independent Registered Public Accounting Firm and is incorporated herein by reference pursuant to General Instruction G (3) to Form 10-K.

58

Table of Contents

PART IV

ITEM 15. EXHIBITS AND FINANCIAL STATEMENTS SCHEDULES

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

The Exhibits are listed in the Exhibit Index.

Table of Contents

Signatures

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

Vanda Pharmaceuticals Inc.

February 26, 2013 By: /s/ Mihael H. Polymeropoulos, M.D.
Mihael H. Polymeropoulos, M.D.
President and Chief Executive Officer

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

Name	Title	Date
/s/ Mihael H. Polymeropoulos, M.D. Mihael H. Polymeropoulos, M.D.	President and Chief Executive Officer and Director (principal executive officer)	February 26, 2013
/s/ James P. Kelly James P. Kelly	Senior Vice President, Chief Financial Officer, Secretary and Treasurer (principal financial officer and principal accounting officer)	February 26, 2013
/s/ Howard Pien Howard Pien	Chairman of the Board and Director	February 26, 2013
/s/ Michael Cola Michael Cola	Director	February 26, 2013
/s/ Richard W. Dugan Richard W. Dugan	Director	February 26, 2013
/s/ Steven K. Galson, M.D. Steven K. Galson, M.D.	Director	February 26, 2013
/s/ Vincent J. Milano Vincent J. Milano	Director	February 26, 2013
/s/ H. Thomas Watkins H. Thomas Watkins	Director	February 26, 2013

Table of Contents

Vanda Pharmaceuticals Inc.

Index to Consolidated Financial Statements

Table of Contents

Report of Independent Registered Public Accounting Firm

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

In our opinion, the accompanying consolidated balance sheets and the related consolidated statements of operations, of comprehensive income (loss), of changes in stockholders equity, and of cash flows present fairly, in all material respects, the financial position of Vanda Pharmaceuticals Inc. and Subsidiary (collectively, the Company) at December 31, 2012 and 2011, and the results of their operations and their cash flows for each of the three years in the period ended December 31, 2012, in conformity with accounting principles generally accepted in the United States of America. Also in our opinion, the Company maintained, in all material respects, effective internal control over financial reporting as of December 31, 2012, based on criteria established in *Internal Control Integrated Framework* issued by the Committee of Sponsoring Organizations of the Treadway Commission (COSO). The Company s management is responsible for these financial statements, for maintaining effective internal control over financial reporting and for its assessment of the effectiveness of internal control over financial reporting, included in Management s Report on Internal Control Over Financial Reporting appearing under Item 9A. Our responsibility is to express opinions on these financial statements and on the Company s internal control over financial reporting based on our integrated audits. We conducted our audits in accordance with the standards of the Public Company Accounting Oversight Board (United States). Those standards require that we plan and perform the audits to obtain reasonable assurance about whether the financial statements are free of material misstatement and whether effective internal control over financial reporting was maintained in all material respects. Our audits of the financial statements included examining, on a test basis, evidence supporting the amounts and disclosures in the financial statements, assessing the accounting principles used and significant estimates made by management, and evaluating the overall financial statement presentation. Our audit of internal control over financial reporting included obtaining an understanding of internal control over financial reporting, assessing the risk that a material weakness exists, and testing and evaluating the design and operating effectiveness of internal control based on the assessed risk. Our audits also included performing such other procedures as we considered necessary in the circumstances. We believe that our audits provide a reasonable basis for our opinions.

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

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

/s/ PricewaterhouseCoopers LLP

Baltimore, Maryland

February 25, 2013

Table of Contents

Vanda Pharmaceuticals Inc.

Consolidated Balance Sheets

(in thousands, except for share and per share amounts)	December 31, 2012	2011
Assets		
Current assets		
Cash and cash equivalents	$ 88,772	$ 87,923
Marketable securities, current	31,631	60,961
Accounts receivable	1,168	1,618
Inventory	57	
Prepaid expenses and other current assets	3,910	2,999
Restricted cash, current	430	
Total current assets	125,968	153,501
Marketable securities, non-current		19,012
Property and equipment, net	2,348	964
Other assets, non-current		84
Intangible asset, net	6,532	8,027
Restricted cash, non-current	600	1,030
Total assets	$ 135,448	$ 182,618
Liabilities and Stockholders Equity		
Current liabilities		
Accounts payable	$ 287	$ 996
Accrued liabilities	5,187	3,381
Deferred rent, current		453
Deferred revenues, current	26,789	26,789
Total current liabilities	32,263	31,619
Deferred rent, non-current	3,005	461
Deferred revenues, non-current	90,275	117,064
Total liabilities	125,543	149,144
Commitments and contingencies (Note 10)		
Stockholders equity		
Preferred stock, $0.001 par value; 20,000,000 shares authorized, and no shares issued or outstanding		
Common stock, $0.001 par value; 150,000,000 shares authorized; 28,241,743 and 28,117,026 shares issued and outstanding at December 31, 2012 and 2011, respectively	28	28
Additional paid-in capital	300,974	296,868
Accumulated other comprehensive income	10	21
Accumulated deficit	(291,107)	(263,443)
Total stockholders equity	9,905	33,474
Total liabilities and stockholders equity	$ 135,448	$ 182,618

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

63

Table of Contents

Vanda Pharmaceuticals Inc.

Consolidated Statements of Operations

(in thousands, except for share and per share amounts)	Year Ended December 31, 2012	2011	2010
Revenue:			
Licensing agreement	$ 26,789	$ 26,789	$ 26,789
Royalty revenue	5,938	4,481	3,141
Product sales			5,290
Grant revenue			489
Total revenue	32,727	31,270	35,709
Operating expenses:			
Cost of sales	129		2,891
Research and development	45,446	28,996	12,338
General and administrative	13,882	11,486	10,147
Intangible asset amortization	1,495	1,495	1,495
Total operating expenses	60,952	41,977	26,871
Income (loss) from operations	(28,225)	(10,707)	8,838
Other income	561	461	431
Income (loss) before tax provision	(27,664)	(10,246)	9,269
Tax provision (benefit)		(444)	2,077
Net income (loss)	$ (27,664)	$ (9,802)	$ 7,192
Net income (loss) per share:			
Basic	$ (0.98)	$ (0.35)	$ 0.26
Diluted	$ (0.98)	$ (0.35)	$ 0.25
Shares used in calculations of net income (loss) per share:			
Basic	28,228,409	28,106,831	27,916,388
Diluted	28,228,409	28,106,831	28,534,617

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

Table of Contents

Vanda Pharmaceuticals Inc.

Consolidated Statements of Comprehensive Income (Loss)

(in thousands)	Year Ended December 31, 2012	2011	2010
Net income (loss)	$ (27,664)	$ (9,802)	$ 7,192
Other comprehensive income (loss):			
Change in net unrealized gain (loss) on marketable securities	(11)	19	2
Tax provision on other comprehensive income (loss)			
Other comprehensive income (loss), net of tax	(11)	19	2
Comprehensive income (loss)	$ (27,675)	$ (9,783)	$ 7,194

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

Table of Contents

Vanda Pharmaceuticals Inc.

Statements of Changes in Stockholders Equity

(in thousands, except for share amounts)	Common Stock Shares	Common Stock Par Value	Additional Paid-In Capital	Accumulated Other Comprehensive Income (Loss)	Accumulated Deficit	Total
Balances at December 31, 2009	27,568,595	$ 28	$ 283,836	$	$ (260,833)	$ 23,031
Issuance of common stock from the exercise of stock options and settlement of restricted stock units	472,784		892			892
Employee and non-employee stock-based compensation			4,982			4,982
Excess tax benefits from exercise of stock options			1,632			1,632
Net income					7,192	7,192
Other comprehensive income, net of tax				2		2
Balances at December 31, 2010	28,041,379	28	291,342	2	(253,641)	37,731
Issuance of common stock from the exercise of stock options and settlement of restricted stock units	75,647		25			25
Employee and non-employee stock-based compensation			5,501			