

Vanda Pharmaceuticals Inc.
Form 424B5
August 06, 2013
Table of Contents

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The information in this preliminary prospectus supplement and the accompanying prospectus is not complete and may be changed. A registration statement relating to these securities has been declared effective by the Securities and Exchange Commission. This preliminary prospectus supplement and the accompanying prospectus are not an offer to sell nor do they solicit an offer to buy these securities in any jurisdiction where the offer or sale is not permitted.

Subject to completion, dated August 6, 2013

PROSPECTUS SUPPLEMENT

(to Prospectus dated February 11, 2011)

Shares

Common Stock

We are offering _____ shares of our common stock. Our common stock is listed on The NASDAQ Global Market under the symbol VNDA. The last sale price of our common stock on August 5, 2013, as reported by The NASDAQ Global Market, was \$11.52 per share.

Investing in our common stock involves a high degree of risk. See Risk Factors beginning on page S-6 of this prospectus supplement and page 6 of the accompanying prospectus.

Neither the Securities and Exchange Commission nor any state securities commission has approved or disapproved of these securities or determined if this prospectus supplement or the accompanying prospectus is truthful or complete. Any representation to the contrary is a criminal offense.

	Per Share	Total
Public offering price	\$	\$
Underwriting discount	\$	\$
Proceeds, before expenses, to Vanda Pharmaceuticals Inc.	\$	\$

Delivery of the shares of common stock is expected to be made on or about August , 2013. We have granted the underwriters an option for a period of 30 days to purchase up to an additional shares of our common stock. If the underwriters exercise the option in full, the total underwriting discounts and commissions payable by us will be \$ and the total proceeds to us, before expenses, will be \$.

Joint Book-Running Managers

Lazard Capital Markets

Piper Jaffray & Co.

Prospectus Supplement dated August , 2013.

Table of Contents

TABLE OF CONTENTS

Prospectus Supplement

	Page
<u>ABOUT THIS PROSPECTUS SUPPLEMENT</u>	S-ii
<u>SUMMARY</u>	S-1
<u>THE OFFERING</u>	S-3
<u>SUMMARY CONSOLIDATED FINANCIAL DATA</u>	S-4
<u>RISK FACTORS</u>	S-6
<u>FORWARD-LOOKING STATEMENTS</u>	S-29
<u>USE OF PROCEEDS</u>	S-30
<u>DESCRIPTION OF SECURITIES</u>	S-31
<u>PRICE RANGE OF OUR COMMON STOCK</u>	S-32
<u>DIVIDEND POLICY</u>	S-32
<u>CAPITALIZATION</u>	S-33
<u>DILUTION</u>	S-35
<u>UNDERWRITING</u>	S-37
<u>INDEMNIFICATION</u>	S-41
<u>LEGAL MATTERS</u>	S-41
<u>EXPERTS</u>	S-41
<u>WHERE YOU CAN FIND MORE INFORMATION</u>	S-42
<u>INCORPORATION BY REFERENCE</u>	S-43

Prospectus

	Page
<u>ABOUT THIS PROSPECTUS</u>	1
<u>WHERE YOU CAN FIND MORE INFORMATION</u>	1
<u>INFORMATION INCORPORATED BY REFERENCE</u>	1
<u>SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS</u>	2
<u>THE COMPANY</u>	4
<u>OUR CORPORATE INFORMATION</u>	5
<u>RISK FACTORS</u>	6
<u>DESCRIPTION OF SECURITIES</u>	27
<u>USE OF PROCEEDS</u>	40
<u>RATIO OF FIXED CHARGES AND PREFERENCE DIVIDENDS TO EARNINGS</u>	40

<u>DIVIDEND POLICY</u>	40
<u>PLAN OF DISTRIBUTION</u>	40
<u>LEGAL MATTERS</u>	41
<u>EXPERTS</u>	41

Table of Contents

ABOUT THIS PROSPECTUS SUPPLEMENT

This document is in two parts. The first part is this prospectus supplement, which describes the terms of this offering of common stock and related matters. The second part is the accompanying prospectus, which gives more general information, some of which may not apply to this offering of common stock. To the extent the information contained in this prospectus supplement differs or varies from the information contained in the accompanying prospectus or any document incorporated by reference, the information in this prospectus supplement shall control.

All references in this prospectus supplement and the accompanying prospectus to Vanda, Vanda Pharmaceuticals, the Company, we, us, or our, similar references refer to Vanda Pharmaceuticals Inc. and its subsidiaries on a consolidated basis, except where the context otherwise requires or as otherwise indicated.

You should rely only on the information contained or incorporated by reference in this prospectus supplement, the accompanying prospectus and any free-writing prospectus that we authorize to be distributed to you. We have not, and the underwriters have not, authorized anyone to provide you with different information. This prospectus supplement and the accompanying prospectus are not an offer to sell, nor are they seeking an offer to buy, these securities in any state where the offer or sale is not permitted. The information in this prospectus supplement and the accompanying prospectus are complete and accurate as of the date the information is presented, but the information may have changed since that date.

Vanda is a trademark of Vanda Pharmaceuticals Inc. This prospectus may also include other registered and unregistered trademarks of Vanda Pharmaceuticals Inc. and other persons.

Table of Contents

SUMMARY

The following summary is qualified in its entirety by, and should be read together with, the more detailed information and financial statements and related notes thereto appearing elsewhere or incorporated by reference in this prospectus supplement and the accompanying prospectus. Before you decide to invest in our common stock, you should read the entire prospectus supplement and the accompanying prospectus carefully, including the risk factors and the financial statements and related notes incorporated by reference in this prospectus supplement and the accompanying prospectus.

Vanda Pharmaceuticals Inc.

Company Overview

Vanda Pharmaceuticals Inc. is a biopharmaceutical company focused on the development and commercialization of products for the treatment of central nervous system disorders. We commenced operations in 2003. Our product portfolio includes tasimelteon, a compound for the treatment of circadian rhythm sleep disorders, which is currently in clinical development for Non-24-Hour Disorder (Non-24) and for which a New Drug Application (NDA) is under review by the U.S. Food and Drug Administration (FDA), 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.

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. We held a pre-NDA meeting with the FDA's Division of Neurology Products in the first quarter of 2013 to discuss the regulatory filing path for an NDA for tasimelteon in the treatment of patients with Non-24. At the pre-NDA meeting, the FDA confirmed that the efficacy and safety data that we proposed to submit in the tasimelteon NDA for the treatment of Non-24 was adequate to support filing. The NDA supporting package that included data from clinical pharmacology, pre-clinical pharmacology program, chemistry and manufacturing was also deemed adequate to support filing. In May 2013, we submitted an NDA to the FDA for tasimelteon for the treatment of Non-24. In July 2013, we announced that the FDA accepted the filing and granted a priority review classification to its NDA for tasimelteon for the treatment of Non-24 in the totally blind. The FDA determined the action target date under the Prescription Drug User Fee Act (PDUFA-V) to be January 31, 2014. The FDA has also tentatively scheduled an advisory committee meeting to discuss the tasimelteon application on November 14, 2013. As a result of achieving this regulatory milestone, we will incur certain costs in the third quarter of 2013 including a \$3.0 million cash milestone obligation under our license agreement with Bristol-Meyers Squibb, a \$0.5 million cash milestone obligation under a regulatory consulting agreement and additional non-cash stock-based compensation expense of \$0.3 million for performance-based stock options and \$0.2 million for performance-based restricted stock unit awards. In January 2013, we 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 (HAM-D-17) after eight weeks of treatment as compared to placebo. As a result, all activities have been discontinued related to the MDD indication for tasimelteon. We incurred \$12.3 million in research and development costs for the six months ended June 30, 2013 directly attributable to our development of tasimelteon.

Table of Contents

In December 2012, the European Medicines Agency's (EMA) Committee for Medicinal Products for Human Use (CHMP) issued a negative opinion recommending against approval of Fanaptum (oral iloperidone tablets) for the treatment of schizophrenia in adult patients in the European Union. The CHMP was of the opinion that the benefits of Fanaptum did not outweigh its risks and recommended against marketing authorization. We initiated an appeal of this opinion and requested a re-examination of the decision by the CHMP, but withdrew our Marketing Authorization Application in the first quarter of 2013 because the additional clinical data requested by the CHMP will not be available in the timeframe allowed by the EMA's Centralized Procedure. We intend to reassess our European regulatory strategy for Fanaptum once the results from the Relapse Prevention Study in Patients with Schizophrenia (REPRIEVE) being conducted by Novartis, become available. We incurred \$0.3 million in research and development costs for the six months ended June 30, 2013 directly attributable to our development of Fanapt®.

In the second half of 2013, we plan to initiate a proof of concept study for VLY-686 in treatment resistant pruritus in atopic dermatitis. We incurred \$0.8 million in research and development costs for the six months ended June 30, 2013 directly attributable to our development of VLY-686.

Since we began 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 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 Risk Factors starting on page S-6 of this prospectus supplement.

Our founder and Chief Executive Officer, Mihael H. Polymeropoulos, M.D., started Vanda's operations early in 2003 after establishing and leading the Pharmacogenetics Department at Novartis. In acquiring and developing our 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 circadian rhythm sleep disorders 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.

Corporate Information

Vanda was incorporated in Delaware in 2002. Our principal executive offices are located at 2200 Pennsylvania Avenue N.W., Suite 300E, Washington D.C. 20037, and our telephone number is (202) 734-3400. Our website address is www.vandapharma.com. We do not incorporate the information on our website into this prospectus supplement and the accompanying prospectus and you should not consider it part of this prospectus supplement and the accompanying prospectus.

Table of Contents

THE OFFERING

Common stock we are offering	shares of common stock.
Option to purchase additional shares	We have granted the underwriters an option for a period of up to 30 days from the date of this prospectus supplement to purchase up to additional shares of common stock at the public offering price less the underwriting discounts and commissions to cover over-allotments, if any.
Offering price	\$ per share of common stock.
Common stock to be outstanding after this offering	shares (or shares if the underwriters exercise in full their option to purchase additional shares).
Use of proceeds	We intend to use the net proceeds from this offering for sales and marketing expenditures, which may include commercial launch activities for tasimelteon for the treatment of Non-24 following receipt of regulatory approval, if any, research and development activities and other general corporate purposes. We may also use a portion of the net proceeds to acquire or invest in businesses, products or technologies that we believe are complementary to our own, although we are not currently planning or negotiating any such transactions. See the section titled Use of Proceeds.
Risk Factors	You should read the Risk Factors section of this prospectus supplement and in the documents incorporated by reference in this prospectus supplement for a discussion of factors to consider before deciding to purchase shares of our common stock.
NASDAQ Global Market symbol	VNDA
The number of shares of common stock that will be outstanding immediately after this offering as shown above is based on 28,483,231 shares of common stock outstanding as of June 30, 2013 and excludes:	

670,744 shares of common stock issuable upon the exercise of outstanding options as of June 30, 2013 under our Second Amended and Restated Management Equity Plan (the 2004 Plan), with a weighted average exercise price of \$1.79 per share;

4,718,721 shares of common stock issuable upon the exercise of outstanding options as of June 30, 2013 under our 2006 Equity Incentive Plan (the 2006 Plan), with a weighted average exercise price of \$10.76 per share;

602,565 shares of common stock issuable upon the vesting of outstanding restricted stock units as of June 30, 2013; and

2,301,263 shares of common stock reserved for future issuance as of June 30, 2013 under our 2006 Plan.

Unless otherwise indicated, all information in this prospectus assumes:

that the underwriters do not exercise their option to purchase up to additional shares of our common stock to cover over-allotments, if any; and

no options, restricted stock units, warrants, or shares of common stock were issued after June 30, 2013, and no outstanding options or warrants were exercised after June 30, 2013 and no outstanding restricted stock units vested after such date.

S-3

Table of Contents**SUMMARY CONSOLIDATED FINANCIAL DATA**

The following tables present our Summary Consolidated Statements of Operations data for the years ended December 31, 2010 through 2012 as well as for the six months ended June 30, 2012 and 2013 and consolidated balance sheet data as of June 30, 2013. You should read this information in conjunction with our consolidated financial statements, including the related notes, and Management's Discussion and Analysis of Financial Condition and Results of Operations in our Annual Report on Form 10-K for the year ended December 31, 2012 and our Quarterly Report on Form 10-Q for the quarter ended June 30, 2013. Our historical results are not necessarily indicative of the results that may be expected in the future.

Consolidated Statement of Operations Data: <i>(in thousands, except for share and per share amounts)</i>	Year Ended December 31,			Six Months Ended June 30,	
	2010	2011 (Audited)	2012	2012 (Unaudited)	2013 (Unaudited)
Revenues:					
Licensing agreement	\$ 26,789	\$ 26,789	\$ 26,789	\$ 13,284	\$ 13,284
Royalty revenue	3,141	4,481	5,938	3,235	3,103
Product sales	5,290				
Grant revenue	489				
Total revenues	35,709	31,270	32,727	16,519	16,387
Operating expenses:					
Cost of sales	2,891		129		
Research and development	12,338	28,996	45,446	24,670	13,942
General and administrative	10,147	11,486	13,882	7,510	9,032
Intangible asset amortization	1,495	1,495	1,495	741	741
Total operating expenses	26,871	41,977	60,952	32,921	23,715
Income (loss) from operations	8,838	(10,707)	(28,225)	(16,402)	(7,328)
Other income	431	461	561	433	76
Income (loss) before tax benefit	9,269	(10,246)	(27,664)	(15,969)	(7,252)
Tax provision (benefit)	2,077	(444)			
Net income (loss)	\$ 7,192	\$ (9,802)	\$ (27,664)	\$ (15,969)	\$ (7,252)
Net income (loss) per share:					
Basic	0.26	(0.35)	(0.98)	(0.57)	(0.26)
Diluted	0.25	(0.35)	(0.98)	(0.57)	(0.26)
Shares used in calculation of net income					
(loss) per share:					
Basic	27,916,388	28,106,831	28,228,409	28,226,743	28,361,340
Diluted	27,534,617	28,106,831	28,228,409	28,226,743	28,361,340

Table of Contents

The following table presents selected consolidated balance sheet data as of June 30, 2013 on an actual basis and on an as adjusted basis to reflect the assumed sale of 4,000,000 shares of our common stock in this offering at an assumed public offering price of \$11.52 per share (the last reported sales price of our common stock on The NASDAQ Global Market on August 5, 2013), after deducting underwriting discounts and commissions and estimated offering expenses payable by us.

Consolidated Balance Sheet Data: <i>(in thousands, except for share and per share amounts)</i>	June 30, 2013 Actual (Unaudited)	June 30, 2013 As Adjusted (Unaudited)
ASSETS		
Current assets:		
Cash and cash equivalents	\$ 103,633	\$ 146,148
Accounts receivable	1,641	1,641
Prepaid expenses and other current assets	2,651	2,651
Restricted cash, current	430	430
Total current assets	108,355	150,870
Property and equipment, net	2,208	2,208
Intangible asset, net	5,791	5,791
Restricted cash, non-current	600	600
Total assets	\$ 116,954	\$ 159,469
LIABILITIES AND STOCKHOLDERS EQUITY		
Current liabilities:		
Accounts payable	\$ 1,167	\$ 1,167
Accrued liabilities	3,770	3,770
Deferred rent, current	209	209
Deferred revenue, current	26,789	26,789
Total current liabilities	31,935	31,935
Deferred rent, non-current	3,002	3,002
Deferred revenue, non-current	76,991	76,991
Total liabilities	\$ 111,928	\$ 111,928
Stockholders equity:		
Preferred stock, \$0.001 par value; 20,000,000 shares authorized and none issued and outstanding		
Common stock, \$0.001 par value; 150,000,000 shares authorized and 28,483,231 shares issued and outstanding, actual; 32,483,231 shares issued and outstanding, as adjusted	28	32
Additional paid-in capital	303,357	345,868
Accumulated deficit	(298,359)	(298,359)
Total stockholders equity	5,026	47,541
Total liabilities and stockholders equity	\$ 116,954	\$ 159,469

Table of Contents

RISK FACTORS

An investment in our common stock involves a high degree of risk. You should carefully consider the risks described under **Risk Factors** in our most recent Annual Report on Form 10-K and Quarterly Reports on Form 10-Q, and all of the other information contained in this prospectus supplement and the accompanying prospectus, and incorporated by reference into this prospectus supplement and the accompanying prospectus, including our financial statements and related notes, before investing in our common stock. If any of the possible events described below or in those sections actually occur, our business, business prospects, cash flow, results of operations or financial condition could be harmed, the trading price of our common stock could decline, and you might lose all or part of your investment in our common stock. Additional risks and uncertainties not presently known to us or that we currently deem immaterial may also impair our operations and results.

Risks related to our business and industry

If the FDA does not approve the NDA that we submitted for tasimelteon for the treatment of Non-24, 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 (RESET study). In addition, we have two ongoing open-label safety studies for tasimelteon in treatment of Non-24. We met with the U.S. Food and Drug Administration (FDA) in the first quarter of 2013 for a pre-NDA meeting on tasimelteon in the treatment of patients with Non-24 and submitted a New Drug Application (NDA) with the FDA in May 2013. In July 2013, we announced that the FDA accepted the filing and granted a priority review classification to our NDA and that the FDA tentatively scheduled an advisory committee meeting to discuss the NDA. Any adverse developments or results or perceived adverse developments or results with respect to our regulatory submission, the advisory committee meeting 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 manufacturing processes or facilities used for the program; and

the FDA determining that the Phase III program in Non-24 raises safety concerns or does not demonstrate adequate efficacy.

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

Table of Contents

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-V) 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.

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

S-7

Table of Contents

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, but subsequently withdrew our marketing authorization application because the additional clinical data requested by the CHMP will not be available in the timeframe allowed by the EMA's Centralized Procedure. We intend to reassess our European regulatory strategy for Fanaptum once the results from the Relapse Prevention Study in Patients with Schizophrenia (REPRIEVE) being conducted by Novartis, become available. Even if the results of the REPRIEVE study are positive, however, we may determine not pursue foreign regulatory approvals for Fanaptum or, if we do, we still may not be able to obtain such approval.

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 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.

Table of Contents

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 June 30, 2013, our total cash and cash equivalents and marketable securities were \$103.6 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.

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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 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.

S-9

Table of Contents

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 Non-24, 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 Daiippon 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 Daiippon 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.

Table of Contents

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;

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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;

S-11

Table of Contents

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 foreseeable 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.

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.

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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

S-12

Table of Contents

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.

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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;

S-13

Table of Contents

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 partner's or the compound's 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. If the NDA for tasimelteon is approved, the commercial launch for tasimelteon will require substantial additional expenditures.

As of June 30, 2013, we had an accumulated deficit of \$298.4 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

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

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;

S-14

Table of Contents

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

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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.

S-15

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

Table of Contents

research scientists. Competition for qualified personnel is intense, and the process of hiring and integrating such qualified personnel is often lengthy. We may be unable to recruit such personnel on a timely basis, if at all, which would negatively impact our development and commercialization programs.

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

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

Table of Contents

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, 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.

Table of Contents

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 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;

Table of Contents

acquisitions;

strategic alliances;

licensing agreements; and

co-promotion and similar agreements.

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

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

Although we have no experience in acquiring businesses, we may acquire businesses or assets that complement or augment our existing business. If we acquire businesses with promising 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.

S-21

Table of Contents**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 tasimelteon in the license agreement. 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

Table of Contents

secrets. As of June 30, 2013, excluding in-licensed patents and patent applications, we had 24 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. Our patent applications may be challenged or fail to result in issued patents and our existing or future patents may be too narrow to prevent third parties from developing or designing around these patents. In addition, we generally rely on trade secret protection and confidentiality agreements to protect certain proprietary know-how that is not patentable, for processes for which patents are difficult to enforce and for any other elements of our drug development processes that involve proprietary know-how, information and technology that is not covered by patent applications. While we require all of our employees, consultants, advisors and any third parties who have access to our proprietary know-how, information and technology to enter into confidentiality agreements, we cannot be certain that this know-how, information and technology will not be disclosed or that competitors will not otherwise gain access to our trade secrets or independently develop substantially equivalent information and techniques. Further, the laws of some foreign countries do not protect proprietary rights to the same extent as the laws of the U.S. As a result, we may encounter significant problems in protecting and defending our intellectual property both in the U.S. and abroad. If we are unable to protect or defend the intellectual property related to our technologies, we will not be able to establish or maintain a competitive advantage in our market.

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 patent 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,

Table of Contents

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

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

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 the offering and 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 January 1, 2013 and June 30, 2013, the high and low sale prices of our common stock as reported on The NASDAQ Global Market varied between \$3.57 and \$13.30. 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.

Table of Contents

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;

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;

the publication of negative research or articles about our company, our business or our compounds by industry analysts or others;

publicity regarding actual or potential transactions involving us; and

economic, political and other external factors beyond our control.

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

We have been the subject of litigation in the past and may be subject to litigation in the future. In the past, following periods of volatility in the market price of their stock, many companies, including us, have been the subjects of securities class action litigation. Any such litigation can result in substantial costs and diversion of management's attention and resources and could harm our stock price, business results of operations and financial condition. As a result of these factors, holders of our common stock might be unable to sell their shares at or above the price they paid for such shares. On June 24, 2013, a securities class action complaint was filed in the United States District Court for the District of Columbia, naming the Company and certain of our officers as defendants seeking to assert violations of Section 10(b) and 20(a) of the Securities Exchange Act of 1934 and Rule 10b-5 promulgated thereunder, in connection with allegedly false and misleading statements and alleged omissions regarding our Phase III trial results for tasimelteon and other disclosures between December 18, 2012 and June 18, 2013. A similar complaint was filed on July 8, 2013. Our management believes that we have meritorious defenses and intends to defend these lawsuits vigorously. We do not anticipate that this litigation will have a material adverse effect on our business, results of operations or financial condition. However, the lawsuits are subject to inherent uncertainties, the actual cost may be significant, and we may not prevail. We believe we are entitled to coverage under our relevant insurance policies, subject to a retention, but coverage could be denied or prove to be insufficient.

S-25

Table of Contents

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 June 30, 2013, there were a total of 5,992,030 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.

Our management will have broad discretion over the use of the proceeds we receive in this offering and might not apply the proceeds in ways that increase the value of your investment.

Our management will have broad discretion to use the net proceeds from this offering, and you will be relying on the judgment of our management regarding the application of these proceeds. They might not apply the net proceeds of this offering in ways that increase the value of your investment. Our management might not be able to yield a significant return, if any, on any investment of these net proceeds. You will not have the opportunity to influence our decisions on how to use the proceeds.

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.

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.

You will experience immediate and substantial dilution.

The offering price per share in this offering may exceed the net tangible book value per share of our common stock outstanding prior to this offering. Assuming that an aggregate of 4,000,000 shares of our common stock are sold at the assumed offering price of \$11.52 per share (the last reported sale price of our common stock on The

Table of Contents

NASDAQ Global Market on August 5, 2013), for aggregate gross proceeds of approximately \$46.1 million, and after deducting underwriting discounts and commissions and estimated aggregate offering expenses payable by us, you will experience immediate dilution of \$10.23 per share, representing the difference between our as adjusted net tangible book value per share as of June 30, 2013 after giving effect to this offering and the assumed offering price. In addition, we are not restricted from issuing additional securities in the future, including shares of common stock, securities that are convertible into or exchangeable for, or that represent the right to receive, common stock or substantially similar securities. The issuance of these securities may cause further dilution to our stockholders. The exercise of outstanding stock options and the vesting of outstanding restricted stock units may also result in further dilution of your investment. See the section entitled "Dilution" on page S-35 below for a more detailed illustration of the dilution you may incur if you participate in this offering.

You may experience future dilution as a result of future equity offerings.

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

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;

Table of Contents

do not provide for cumulative voting in the election of directors, which would allow holders of less than a majority of the stock to elect some directors;

establish a classified board of directors, as a result of which the successors to the directors whose terms have expired will be elected to serve from the time of election and qualification until the third annual meeting following their election;

require that directors only be removed from office for cause;

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

limit who may call special meetings of stockholders;

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

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

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.

Prolonged economic uncertainties or downturns, as well as 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. These economic conditions, and uncertainty as to the general direction of the macroeconomic environment, are beyond our control and may make any necessary debt or equity financing more difficult, more costly, and more dilutive. While we believe we have adequate capital resources to meet current working capital and capital expenditure requirements, 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 negative trends in the general economy in the U.S. or other jurisdictions in which we may do business, 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.

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. During challenging and uncertain economic times and in tight credit markets, there may be a disruption or delay in the performance of our third party contractors, suppliers or partners. If such third parties are unable to satisfy their commitments to us, our business and results of operations would be adversely affected.

Table of Contents

FORWARD-LOOKING STATEMENTS

This prospectus supplement, the accompanying prospectus and the documents incorporated by reference in these documents contain forward-looking statements. Words such as, but not limited to, believe, expect, anticipate, estimate, intend, plan, project, target, would, and could, or the negative of these terms and similar expressions or words, identify forward-looking statements. Forward-looking statements are based upon current expectations 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 failure to obtain, or any delay in obtaining, regulatory approval for our products or product candidates, particularly tasimelteon for the treatment of Non-24-Hour Disorder (Non-24), or to comply with ongoing regulatory requirements;

our ability to successfully commercialize tasimelteon following the receipt of regulatory approval, if any;

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

our failure to develop or obtain sales, marketing and distribution resources and expertise or to otherwise manage our growth;

a lack of acceptance of our products, product candidates or partnered product in the marketplace, or a failure to become or remain profitable;

a loss of rights to develop and commercialize our products, product candidates or partnered products under our license and sublicense agreements;

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 product to be demonstrably safe and effective;

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

our failure to identify or obtain rights to new products or product candidates;

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

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

the cost and effects of current or potential litigation; 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.

In addition, you should refer to the section of this prospectus supplement entitled "Risk Factors" as well as the documents we have incorporated by reference for a discussion of other important factors that may cause our actual results to differ materially from those expressed or implied by our forward-looking statements. As a result of these factors, we cannot assure you that the forward-looking statements in this prospectus supplement will prove to be accurate. Furthermore, if our forward-looking statements prove to be inaccurate, the inaccuracy may be material. In light of the significant uncertainties in these forward-looking statements, you should not regard these statements as a representation or warranty by us or any other person that we will achieve our objectives and plans in any specified time frame, or at all.

S-29

Table of Contents

USE OF PROCEEDS

We estimate that the net proceeds from the assumed sale of 4,000,000 shares of our common stock in this offering will be approximately \$42.5 million, or approximately \$49.0 million if the underwriters exercise in full their option to purchase additional shares of common stock, based on an assumed public offering price of \$11.52 per share (the last reported sales price of our common stock on The NASDAQ Global Market on August 5, 2013), after deducting the underwriting discounts and commissions and estimated offering expenses payable by us.

We intend to use the net proceeds from this offering for sales and marketing expenditures, which may include commercial launch activities for tasimelteon for the treatment of Non-24 following receipt of regulatory approval, if any, research and development activities and other general corporate purposes. We may also use a portion of the net proceeds to acquire or invest in businesses, products or technologies that we believe are complementary to our own, although we are not currently planning or negotiating any such transactions. We have not yet determined the amount of net proceeds to be used specifically for any of the foregoing purposes. Accordingly, our management will have significant discretion and flexibility in applying the net proceeds from the sale of these securities. Pending any use, as described above, we intend to invest the net proceeds in high-quality, short-term, interest-bearing securities.

S-30

Table of Contents

DESCRIPTION OF SECURITIES

Capital Stock

We are authorized to issue 150,000,000 shares of common stock, \$0.001 par value per share, and 20,000,000 shares of preferred stock, \$0.001 par value per share.

The transfer agent for our common stock is American Stock Transfer & Trust Company, LLC.

For more information regarding our capital stock, including a summary of the rights of our common stock and preferred stock, please read the information discussed under the heading *Description of Securities* beginning on page 27 of the accompanying prospectus dated February 11, 2011.

S-31

Table of Contents**PRICE RANGE OF OUR COMMON STOCK**

Our common stock is traded on The NASDAQ Global Market under the symbol VNDA. The following table summarizes the high and low closing sales prices for our common stock as reported by The NASDAQ Global Market for the period indicated:

	High	Low
2011		
First Quarter	\$ 9.98	\$ 6.81
Second Quarter	8.05	6.84
Third Quarter	7.54	4.95
Fourth Quarter	6.00	4.36
2012		
First Quarter	\$ 5.46	\$ 4.47
Second Quarter	4.78	4.02
Third Quarter	4.50	3.91
Fourth Quarter	4.16	3.03
2013		
First Quarter	\$ 4.37	\$ 3.68
Second Quarter	13.00	3.93
Third Quarter (through August 5, 2013)	12.07	8.05

The last reported sale price for our common stock on The NASDAQ Global Market on August 5, 2013 was \$11.52.

DIVIDEND POLICY

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.

Table of Contents**CAPITALIZATION**

The following table sets forth our cash, cash equivalents and capitalization as of June 30, 2013,

on an actual basis; and

on an as adjusted basis to give effect to the assumed issuance and sale by us of 4,000,000 shares of common stock in this offering, and the receipt of the net proceeds from the assumed sale of these shares, at an assumed public offering price of \$11.52 (the last reported sales price of our common stock on The NASDAQ Global Market on August 5, 2013), after deducting underwriting discounts and commissions and estimated offering expenses payable by us.

You should read this table in conjunction with the sections titled "Management's Discussion and Analysis of Financial Condition and Results of Operations" and our consolidated financial statements and related notes appearing in our most recent Annual Report on Form 10-K and Quarterly Reports on Form 10-Q, which are incorporated by reference in this prospectus supplement and the accompanying prospectus.

Consolidated Balance Sheet Data: <i>(in thousands, except for share and per share amounts)</i>	June 30, 2013 Actual (Unaudited)	June 30, 2013 As Adjusted (Unaudited)
ASSETS		
Current assets:		
Cash and cash equivalents	\$ 103,633	\$ 146,148
Accounts receivable	1,641	1,641
Prepaid expenses and other current assets	2,651	2,651
Restricted cash, current	430	430
Total current assets	108,355	150,870
Property and equipment, net	2,208	2,208
Intangible asset, net	5,791	5,791
Restricted cash, non-current	600	600
Total assets	\$ 116,954	\$ 159,469
LIABILITIES AND STOCKHOLDERS' EQUITY		
Current liabilities:		
Accounts payable	\$ 1,167	\$ 1,167
Accrued liabilities	3,770	3,770
Deferred rent, current	209	209
Deferred revenue, current	26,789	26,789
Total current liabilities	31,935	31,935
Deferred rent, non-current	3,002	3,002
Deferred revenue, non-current	76,991	76,991
Total liabilities	\$ 111,928	\$ 111,928
Stockholders' equity:		
Preferred stock, \$0.001 par value; 20,000,000 shares authorized and none issued and outstanding		
Common stock, \$0.001 par value; 150,000,000 shares authorized and 28,483,231 shares issued and outstanding, actual; 32,483,231 shares issued and outstanding, as adjusted	28	32
Additional paid-in capital	303,357	345,868
Accumulated deficit	(298,359)	(298,359)

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Total stockholders' equity	5,026	47,541
Total liabilities and stockholders' equity	\$ 116,954	\$ 159,469

S-33

Table of Contents

The number of shares in the table above excludes:

670,744 shares of common stock issuable upon the exercise of outstanding options as of June 30, 2013 under our Second Amended and Restated Management Equity Plan (the 2004 Plan), with a weighted average exercise price of \$1.79 per share;

4,718,721 shares of common stock issuable upon the exercise of outstanding options as of June 30, 2013 under our 2006 Equity Incentive Plan (the 2006 Plan), with a weighted average exercise price of \$10.76 per share;

602,565 shares of common stock issuable upon the vesting of outstanding restricted stock units as of June 30, 2013; and

2,301,263 shares of common stock reserved for future issuance as of June 30, 2013 under our 2006 Plan.

S-34

Table of Contents**DILUTION**

If you purchase our common stock in this offering, your ownership interest will be diluted to the extent of the difference between the public offering price per share of common stock and the pro forma net tangible book value per share of our common stock after this offering. Net tangible book value per share is determined by dividing the number of outstanding shares of our common stock into our total tangible assets (total assets less intangible assets) less total liabilities. As of June 30, 2013, we had a historical net tangible book value of our common stock of \$(0.8) million, or approximately \$(0.03) per share.

Investors participating in this offering will incur immediate, substantial dilution. After giving effect to the assumed sale of 4,000,000 shares of common stock in this offering at an assumed public offering price of \$11.52 per share (the last reported sales price of our common stock on The NASDAQ Global Market on August 5, 2013), after deducting underwriting discounts and commissions and estimated offering expenses payable by us, our net tangible book value as of June 30, 2013 would have been approximately \$41.7 million, or approximately \$1.29 per share of common stock. This represents an immediate increase in net tangible book value of approximately \$1.32 per share to existing stockholders, and an immediate dilution of approximately \$10.23 per share to investors participating in this offering.

The following table illustrates this per share dilution:

Assumed public offering price per share		\$ 11.52
Historical net tangible book value per share as of June 30, 2013	\$ (0.03)	
Increase in net tangible book value per share after this offering	\$ 1.32	
Net tangible book value per share after this offering		\$ 1.29
Dilution per share to investors participating in this offering		\$ 10.23

Each \$1.00 increase (decrease) in the assumed public offering price of \$11.52 per share would increase (decrease) our pro forma consolidated net tangible book value, as adjusted, after this offering by \$3.8 million and the dilution per share to investors participating in this offering by \$0.89, in each case assuming the number of shares offered by us, as set forth on the cover page of this prospectus, remains the same and after deducting the underwriting discount and commissions and estimated offering expenses payable by us.

We may also increase or decrease the number of shares we are offering. An increase of 1,000,000 shares in the number of shares offered by us would increase our as adjusted net tangible book value after this offering by approximately \$10.8 million, or \$0.28 per share, and the dilution per share to new investors would be approximately \$9.95 per share, assuming that the assumed public offering price remains the same and after deducting the underwriting discount and commissions and estimated offering expenses payable by us.

Similarly, a decrease of 1,000,000 shares in the number of shares offered by us would decrease our as adjusted net tangible book value after this offering by approximately \$10.8 million, or \$0.31 per share, and the dilution per share to new investors would be approximately \$10.54 per share, assuming that the assumed public offering price remains the same, without deducting the estimated underwriting discounts and commissions, but after deducting estimated offering expenses payable by us.

If the underwriters exercise in full their option to purchase 600,000 additional shares of common stock at the assumed public offering price of \$11.52 per share, the pro forma as adjusted net tangible book value after this offering would be approximately \$1.46 per share, representing an increase in net tangible book value of approximately \$1.49 per share to existing stockholders and immediate dilution in net tangible book value of approximately \$10.06 per share to investors purchasing our common stock in this offering at the public offering price.

The information discussed above is illustrative only and will adjust based on the actual public offering price and other terms of this offering determined at pricing.

Table of Contents

The above discussion and tables also excludes:

670,744 shares of common stock issuable upon the exercise of outstanding options as of June 30, 2013 under the 2004 Plan, with a weighted average exercise price of \$1.79 per share;

4,718,721 shares of common stock issuable upon the exercise of outstanding options as of June 30, 2013 under the 2006 Plan, with a weighted average exercise price of \$10.76 per share;

602,565 shares of common stock issuable upon the vesting of outstanding restricted stock units as of June 30, 2013; and

2,301,263 shares of common stock reserved for future issuance as of June 30, 2013 under our 2006 Plan.

To the extent that any of these options are exercised, new options are issued under our equity incentive plans and subsequently exercised or we issue additional shares of common stock in the future, there will be further dilution to investors participating in this offering.

Table of Contents

UNDERWRITING

Under the terms and subject to the conditions in an underwriting agreement dated the date of this prospectus supplement, the underwriters named below, for whom Lazard Capital Markets and Piper Jaffray & Co. are acting as the representatives, have severally agreed to purchase, and we have agreed to sell to them, the number of shares of our common stock at the public offering price, less the underwriting discounts and commissions, as set forth on the cover page of this prospectus supplement as indicated below:

Underwriter	Number of Shares
Lazard Capital Markets LLC	
Piper Jaffray & Co.	
Total	

The underwriters are offering the shares of common stock subject to their acceptance of the shares from us and subject to prior sale. The underwriting agreement provides that the obligations of the underwriters to pay for and accept delivery of the shares of common stock offered by this prospectus supplement are subject to the approval of certain legal matters by their counsel and to other conditions. The underwriters are obligated to take and pay for all of the shares of common stock offered by this prospectus supplement if any such shares are taken.

The underwriters have an option to buy up to additional shares of common stock from us to cover sales of shares by the underwriters which exceed the number of shares specified in the table above. The underwriters may exercise this option at any time and from time to time during the 30-day period from the date of this prospectus supplement. If any additional shares of common stock are purchased, the underwriters will offer the additional shares on the same terms as those on which the shares are being offered.

The underwriters initially propose to offer the shares of common stock directly to the public at the public offering price listed on the cover page of this prospectus supplement. After the initial offering of the shares of common stock, the offering price and other selling terms may from time to time be varied by the underwriters.

The underwriting agreement provides that the obligations of the underwriters are subject to certain conditions precedent, including the absence of any material adverse change in our business and the receipt of customary legal opinions, letters and certificates.

Commissions and Discounts

The following table summarizes the public offering price, underwriting discounts and commissions and proceeds before expenses to us assuming both no exercise and full exercise of the underwriters' option to purchase additional shares:

	Per Share	Without Over- Allotment	Total With Over- Allotment
Public offering price	\$	\$	\$
Underwriting discounts and commissions			
Proceeds, before expenses, to us			

We estimate that the total expenses of this offering, including registration, filing and listing fees, printing fees, and legal and accounting expenses, but excluding the underwriting discounts and commissions, will be approximately \$. We have agreed to reimburse the underwriters for certain legal fees and expenses up to \$.

Table of Contents

The relationship between Lazard Frères & Co. LLC and Lazard Capital Markets LLC is governed by a business alliance agreement between their respective parent companies. Pursuant to such agreement, Lazard Frères & Co. LLC referred this transaction to Lazard Capital Markets LLC and will receive a referral fee from Lazard Capital Markets LLC in connection therewith; however, such referral fee is not in addition to the fee paid by us to Lazard Capital Markets LLC described above.

Indemnification

We and the underwriters have agreed to indemnify each other, and we have also agreed to indemnify the underwriters against certain liabilities, including certain liabilities under the Securities Act of 1933, as amended, and liabilities arising from breaches of representations and warranties contained in the underwriting agreement. We have also agreed to contribute to payments the underwriters may be required to make in respect of such liabilities.

No Sales of Similar Securities

We and each of our executive officers and directors, subject to certain exceptions, have agreed with the underwriters not to dispose of or hedge any of our shares of common stock or securities convertible into or exercisable or exchangeable for common stock for ninety (90) days after the date of this prospectus supplement without first obtaining the written consent of the representative. The exceptions to the lock-up for executive officers and directors are: transfers of beneficially owned shares, common stock or securities convertible into or exercisable or exchangeable for common stock (i) as a bona fide gift or gifts, (ii) to any trust for the direct or indirect benefit of the undersigned or the immediate family of the undersigned or (iii) by will or intestacy to the executive officer s or director s, as applicable, legal representative, heir or legatee; provided that each donee, distributee or transferee shall execute and deliver to Lazard Capital Markets a lock-up letter for the balance of the lock-up period in the form required. The exceptions to the lock-up for us are: (a) our sale of shares in this offering; and (b) the issuance of restricted common stock or options to acquire common stock pursuant to our existing benefit plans, qualified equity incentive plans or other compensation plans. The 90-day lock-up period during which we and our executive officers and directors are restricted from engaging in transactions in our common stock or securities convertible into or exercisable or exchangeable for common stock is subject to extension such that, in the event that either (i) during the last 17 days of the lock-up period, we issue an earnings or financial results release or material news or a material event relating to us occurs, or (ii) prior to the expiration of the lock-up period, we announce that we will release earnings or financial results during the 16-day period beginning on the last day of the lock-up period, then in either case the expiration of the lock-up period will be extended until the expiration of the 18-day period beginning on the issuance of the earnings or financial results release or the occurrence of the material news or material event, as applicable, unless the representative waives, in writing, such an extension.

Price Stabilization, Short Positions

In order to facilitate the offering of our common stock, the underwriters may engage in transactions that stabilize, maintain or otherwise affect the price of our common stock. Specifically, the underwriters may sell more shares than they are obligated to purchase under the underwriting agreement, creating a short position. The underwriters must close out any short position by purchasing shares in the open market. A short position may be created if the underwriters are concerned that there may be downward pressure on the price of the common stock in the open market after pricing that could adversely affect investors who purchased in this offering. As an additional means of facilitating this offering, the underwriters may bid for, and purchase, shares of our common stock in the open market to stabilize the price of the common stock. These activities may raise or maintain the market price of our common stock above independent market levels or prevent or slow a decline in the market price of our common stock. The underwriters are not required to engage in these activities, and may end any of these activities at any time.

Table of Contents

A prospectus in electronic format may be made available on websites maintained by the underwriters. The representative may agree to allocate a number of shares of common stock to other underwriters for sale to their online brokerage account holders. Internet distributions will be allocated by the underwriters on the same basis as other allocations.

United Kingdom

This document is only being distributed to and is only directed at (i) persons who are outside the United Kingdom or (ii) to investment professionals falling within Article 19(5) of the Financial Services and Markets Act 2000 (Financial Promotion) Order 2005 (the Order) or (iii) high net worth entities, and other persons to whom it may lawfully be communicated, falling within Article 49(2)(a) to (e) of the Order (all such persons together being referred to as relevant persons). The shares of common stock are only available to, and any invitation, offer or agreement to subscribe, purchase or otherwise acquire such common stock will be engaged in only with, relevant persons. Any person who is not a relevant person should not act or rely on this document or any of its contents.

Each underwriter has represented and agreed that:

(a) it has only communicated or caused to be communicated and will only communicate or cause to be communicated an invitation or inducement to engage in investment activity (within the meaning of Section 21 of the Financial Services and Markets Act 2000 or FSMA) received by it in connection with the issue or sale of the shares in circumstances in which Section 21(1) of the FSMA does not apply to us, and

(b) it has complied with, and will comply with all applicable provisions of FSMA with respect to anything done by it in relation to the shares in, from or otherwise involving the United Kingdom.

European Economic Area

To the extent that the offer of the common stock is made in any Member State of the European Economic Area that has implemented the Prospectus Directive before the date of publication of a prospectus in relation to the common stock which has been approved by the competent authority in the Member State in accordance with the Prospectus Directive (or, where appropriate, published in accordance with the Prospectus Directive and notified to the competent authority in the Member State in accordance with the Prospectus Directive), the offer (including any offer pursuant to this document) is only addressed to qualified investors in that Member State within the meaning of the Prospectus Directive or has been or will be made otherwise in circumstances that do not require us to publish a prospectus pursuant to the Prospectus Directive.

In relation to each Member State of the European Economic Area which has implemented the Prospectus Directive (each, a Relevant Member State), each underwriter has represented and agreed that with effect from and including the date on which the Prospectus Directive is implemented in that Relevant Member State (the Relevant Implementation Date) it has not made and will not make an offer of shares to the public in that Relevant Member State prior to the publication of a prospectus in relation to the shares which has been approved by the competent authority in that Relevant Member State or, where appropriate, approved in another Relevant Member State and notified to the competent authority in that Relevant Member State, all in accordance with the Prospectus Directive, except that it may, with effect from and including the Relevant Implementation Date, make an offer of shares to the public in that Relevant Member State at any time:

(a) to legal entities which are authorized or regulated to operate in the financial markets or, if not so authorized or regulated, whose corporate purpose is solely to invest in securities,

(b) to any legal entity which has two or more of (1) an average of at least 250 employees during the last financial year; (2) a total balance sheet of more than 43,000,000 and (3) an annual net turnover of more than 50,000,000, as shown in its last annual or consolidated accounts, or

Table of Contents

(c) in any other circumstances which do not require the publication by us of a prospectus pursuant to Article 3 of the Prospectus Directive. For the purposes of this provision, the expression an offer of shares to the public in relation to any shares in any Relevant Member State means the communication in any form and by any means of sufficient information on the terms of the offer and the shares to be offered so as to enable an investor to decide to purchase or subscribe the shares, as the same may be varied in that Relevant Member State by any measure implementing the Prospectus Directive in that Relevant Member State and the expression Prospectus Directive means Directive 2003/71/EC and includes any relevant implementing measure in each Relevant Member State.

The EEA selling restriction is in addition to any other selling restrictions set out below. In relation to each Relevant Member State, each purchaser of shares of common stock (other than the underwriters) will be deemed to have represented, acknowledged and agreed that it will not make an offer of shares of common stock to the public in any Relevant Member State, except that it may, with effect from and including the date on which the Prospectus Directive is implemented in the Relevant Member State, make an offer of shares of common stock to the public in that Relevant Member State at any time in any circumstances which do not require the publication by us of a prospectus pursuant to Article 3 of the Prospectus Directive, provided that such purchaser agrees that it has not and will not make an offer of any shares of common stock in reliance or purported reliance on Article 3(2)(b) of the Prospectus Directive. For the purposes of this provision, the expression an offer of shares to the public in relation to any shares of common stock in any Relevant Member State has the same meaning as in the preceding paragraph.

Switzerland

This document does not constitute a prospectus within the meaning of Art. 652a of the Swiss Code of Obligations. The shares of common stock may not be sold directly or indirectly in or into Switzerland except in a manner which will not result in a public offering within the meaning of the Swiss Code of Obligations. Neither this document nor any other offering materials relating to the shares of common stock may be distributed, published or otherwise made available in Switzerland except in a manner which will not constitute a public offer of the shares of common stock in Switzerland.

Listing on The NASDAQ Global Market

Our common shares are traded on The NASDAQ Global Market under the symbol VNDA. The transfer agent for our common stock is American Stock Transfer & Trust Company.

Table of Contents

INDEMNIFICATION

Insofar as indemnification for liabilities arising under the Securities Act of 1933, as amended, may be permitted to directors, officers and controlling persons of the Company pursuant to the foregoing provisions, or otherwise, the Company has been advised that in the opinion of the SEC such indemnification is against public policy as expressed in the Act and is, therefore, unenforceable.

LEGAL MATTERS

The validity of the shares of common stock being offered by this prospectus will be passed upon for us by Gunderson Dettmer Stough Villeneuve Franklin & Hachigian, LLP, Waltham, Massachusetts. Certain intellectual property matters will be passed upon for us by Hoffman Warnick LLC. The underwriters are being represented by Proskauer Rose LLP.

EXPERTS

The financial statements and management's assessment of the effectiveness of internal control over financial reporting (which is included in Management's Report on Internal Control over Financial Reporting) incorporated in this prospectus supplement by reference to the Company's Annual Report on Form 10-K for the year ended December 31, 2012 have been so incorporated in reliance on the reports of PricewaterhouseCoopers LLP, an independent registered public accounting firm, given on the authority of said firm as experts in auditing and accounting.

S-41

Table of Contents

WHERE YOU CAN FIND MORE INFORMATION

We have filed with the SEC a registration statement on Form S-3 (File No. 333-171963), of which this prospectus supplement and the accompanying prospectus are a part, under the Securities Act, to register the shares of common stock offered by this prospectus supplement. However, this prospectus supplement and the accompanying prospectus do not contain all of the information contained in the registration statement and the exhibits and schedules to the registration statement. We encourage you to carefully read the registration statement and the exhibits and schedules to the registration statement.

We file annual, quarterly and special reports, proxy statements and other information with the Securities and Exchange Commission (SEC). Our SEC filings are available to the public over the Internet at the SEC's web site at <http://www.sec.gov>. You may also read and copy any document we file with the SEC at its public reference facilities at 100 F Street, N.E., Washington, D.C. 20549. You can also obtain copies of the documents at prescribed rates by writing to the Public Reference Section of the SEC at 100 F Street, N.E., Washington, D.C. 20549. Please call the SEC at 1-800-SEC-0330 for further information on the operation of the public reference facilities. Our SEC filings are also available at the office of The NASDAQ Global Market. For further information on obtaining copies of our public filings at The NASDAQ Global Market, you should call 212-401-8700.

S-42

Table of Contents

INCORPORATION OF CERTAIN INFORMATION BY REFERENCE

We incorporate by reference into this prospectus supplement the information we file with the SEC, which means that we can disclose important information to you by referring you to those documents. The information incorporated by reference is an important part of this prospectus supplement and information that we file subsequently with the SEC will automatically update this prospectus supplement. We incorporate by reference the documents listed below and any filings we make with the SEC under Sections 13(a), 13(c), 14, or 15(d) of the Securities Exchange Act of 1934 after initial filing of the registration statement that contains this prospectus and prior to the time that we sell all the securities offered by this prospectus (in each case, except for the information furnished under Item 2.02 or Item 7.01 in any current report on Form 8-K and Form 8-K/A):

our annual report on Form 10-K for the fiscal year ended December 31, 2012;

our quarterly reports on Form 10-Q for the quarters ended March 31, 2013 and June 30, 2013;

our definitive proxy statement on Schedule 14A, filed on April 26, 2013 (excluding those portions that are not incorporated by reference into our annual report on Form 10-K for the fiscal year ended December 31, 2012);

the description of our common stock contained in our Registration Statement on Form 8-A filed on March 28, 2006;

the description of the Rights to Purchase Series A Junior Participating Preferred Stock contained in our registration statement on Form 8-A on September 25, 2008, as amended on December 22, 2009; and

our current reports on Form 8-K filed on January 23, 2013, January 31, 2013, March 14, 2013, March 25, 2013, April 29, 2013, June 21, 2013, July 30, 2013 and August 6, 2013.

You may request a copy of these filings (other than an exhibit to a filing unless that exhibit is specifically incorporated by reference into that filing) at no cost, by writing to or telephoning us at the following address:

Vanda Pharmaceuticals Inc.

2200 Pennsylvania Avenue N.W., Suite 300E

Washington, D.C. 20037

(202) 734-3400

Attn: Investor Relations

Table of Contents

PROSPECTUS

\$50,000,000

Preferred Stock

Common Stock

Debt Securities

Warrants

From time to time, we may offer and sell shares of preferred stock, common stock, debt securities or warrants to purchase preferred stock, common stock or any combination of these securities, either separately or in units, in one or more offerings in amounts, at prices and on terms that we will determine at the time of the offering. The debt securities and warrants may be convertible into or exercisable or exchangeable for preferred stock, common stock or debt securities and the preferred stock may be convertible into or exchangeable for common stock. The aggregate initial offering price of all securities sold by us under this prospectus will not exceed \$50,000,000.

Each time we offer securities, we will provide you with specific terms of the securities offered in supplements to this prospectus. The prospectus supplement may also add, update or change information contained in this prospectus. You should read this prospectus, the information incorporated by reference in this prospectus, any applicable prospectus supplement and the additional information described below under the heading "Where You Can Find More Information" carefully before you invest in any securities.

The securities offered by this prospectus may be sold directly by us to investors, through agents designated from time to time or to or through underwriters or dealers. We will set forth the names of any underwriters or agents in an accompanying prospectus supplement. For additional information on the methods of sale, you should refer to the section entitled "Plan of Distribution." The price to the public of such securities and the net proceeds we expect to receive from such sale will also be set forth in a prospectus supplement.

Our common stock is listed on The NASDAQ Global Market under the symbol "VNDA". The last reported sale price of our common stock on January 28, 2011 was \$8.01 per share.

INVESTING IN OUR SECURITIES INVOLVES A HIGH DEGREE OF RISKS. SEE "RISK FACTORS" ON PAGE 6 OF THIS PROSPECTUS AND IN THE OTHER DOCUMENTS INCORPORATED BY REFERENCE IN THIS PROSPECTUS AND THE APPLICABLE PROSPECTUS SUPPLEMENT TO READ ABOUT FACTORS YOU SHOULD CONSIDER BEFORE BUYING OUR SECURITIES.

Neither the Securities and Exchange Commission nor any state securities commission has approved or disapproved of these securities or determined if this prospectus or the accompanying prospectus supplement is truthful or complete. Any representation to the contrary is a criminal offense.

The date of this prospectus is February 11, 2011.

Table of Contents

TABLE OF CONTENTS

	Page
<u>ABOUT THIS PROSPECTUS</u>	1
<u>WHERE YOU CAN FIND MORE INFORMATION</u>	1
<u>INFORMATION INCORPORATED BY REFERENCE</u>	1
<u>SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS</u>	2
<u>THE COMPANY</u>	4
<u>OUR CORPORATE INFORMATION</u>	5
<u>RISK FACTORS</u>	6
<u>DESCRIPTION OF SECURITIES</u>	27
<u>USE OF PROCEEDS</u>	40
<u>RATIO OF FIXED CHARGES AND PREFERENCE DIVIDENDS TO EARNINGS</u>	40
<u>DIVIDEND POLICY</u>	40
<u>PLAN OF DISTRIBUTION</u>	40
<u>LEGAL MATTERS</u>	41
<u>EXPERTS</u>	41

You should rely only on the information contained or incorporated by reference in this prospectus or any applicable prospectus supplement. We have not authorized anyone to provide you with information in addition to or different from that contained in this prospectus or any applicable prospectus supplement. We will be offering to sell, and seeking offers to buy, the shares only in jurisdictions where offers and sales are permitted. You should not assume that the information in this prospectus or any applicable prospectus supplement is accurate as of any date other than the date on the front of those documents.

Unless the context otherwise requires, throughout this prospectus and any applicable prospectus supplement, the words "Vanda," "we," "us," "the registrant" or the "company" refer to Vanda Pharmaceuticals Inc.; the term "securities" refers collectively to our preferred stock, common stock, debt securities or warrants to purchase preferred stock, common stock or debt securities, or any combination of the foregoing securities.

Table of Contents

ABOUT THIS PROSPECTUS

This prospectus is part of a registration statement that we filed with the Securities and Exchange Commission, or the SEC, using a shelf registration process. Using this process, we may, from time to time, sell any combination of the securities described in this prospectus in one or more offering transactions up to a total dollar amount of \$50,000,000. This prospectus provides you with a general description of the securities we may offer. Each time we sell any securities under this prospectus, we will provide a prospectus supplement that will contain more specific information about the specific terms of that particular offering. Each such prospectus supplement may also add, update or change information contained in this prospectus or in documents we have incorporated by reference into this prospectus. To the extent that any statements that we make in a prospectus supplement are inconsistent with statements made in this prospectus, the statements made in this prospectus will be deemed modified or superseded by those made in the prospectus supplement. This prospectus, together with the applicable prospectus supplements and the documents incorporated by reference into this prospectus, includes all material information relating to the offering of the securities described in this prospectus. The information contained in this prospectus is accurate only as of the date of this prospectus, regardless of the time of delivery of this prospectus or any sales of securities. To obtain additional information that may be important to you, you should read the exhibits filed by us with the registration statement of which this prospectus is a part or our other filings with the SEC. You should read this prospectus, any applicable prospectus supplement and the additional information described below under **Where You Can Find More Information** before making any investment decision with respect to the securities offered hereby.

WHERE YOU CAN FIND MORE INFORMATION

We have filed with the SEC a registration statement on Form S-3 under the Securities Act with respect to the securities offered by this prospectus. This prospectus, which is part of the registration statement, omits certain information, exhibits, schedules and undertakings set forth in the registration statement, as permitted by the SEC. For further information pertaining to us and the securities offered in this prospectus, reference is made to that registration statement and the exhibits and schedules to the registration statement. Statements contained in this prospectus as to the contents or provisions of any documents referred to in this prospectus are not necessarily complete, and in each instance where a copy of the document has been filed as an exhibit to the registration statement, reference is made to the exhibit for a more complete description of the matters involved.

We file annual, quarterly and current reports, proxy statements and other information with the SEC. Our SEC filings can be read and copied at the SEC's Public Reference Room at 100 F Street, N.E., 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 that file electronically with the SEC, including us.

Our common stock is listed on the NASDAQ Global Market under the symbol **VNDA**. General information about our company, including our Annual Report on Form 10-K, Quarterly Reports on Form 10-Q and Current Reports on Form 8-K, as well as any amendments and exhibits to those reports, are available free of charge through our website at www.vandapharma.com as soon as reasonably practicable after we file them with, or furnish them to, the SEC. Information on, or that can be accessed through, our website is not incorporated into this prospectus or other securities filings and is not a part of these filings.

INCORPORATION OF CERTAIN INFORMATION BY REFERENCE

The SEC allows us to incorporate by reference into this prospectus the information we file with it, which means that we can disclose important information to you by referring you to those documents. The information we incorporate by reference is an important part of this prospectus, and later information that we file with the

Table of Contents

SEC will automatically update and supersede some of this information. We incorporate by reference the documents listed below and any future filings we make with the SEC under Section 13(a), 13(c), 14 or 15(d) of the Securities Exchange Act of 1934, as amended (the Exchange Act) (other than Current Reports on Form 8-K containing only information furnished under Item 2.02 or Item 7.01 of Form 8-K, unless otherwise indicated therein), including filings made after the date of the initial registration statement, until we sell all of the shares covered by this prospectus or the sale of shares by us pursuant to this prospectus is terminated. The documents we incorporate by reference are:

our Annual Report on Form 10-K for the year ended December 31, 2009;

our Quarterly Reports on Form 10-Q for the quarters ended March 31, 2010, June 30, 2010 and September 30, 2010;

our Proxy Statement on Schedule 14A filed with the SEC on April 28, 2010;

our Current Reports on Form 8-K filed on January 11, 2010, March 10, 2010, March 25, 2010, April 19, 2010, April 20, 2010, June 7, 2010, July 1, 2010, July 9, 2010, November 12, 2010 and December 17, 2010 in each case only to the extent filed and not furnished;

the description of our common stock contained in our registration statement on Form 8-A (File No. 000-51863) filed under the Exchange Act on March 28, 2006, including any amendment or reports filed for the purpose of updating such descriptions; and

the description of the Rights to Purchase Series A Junior Participating Preferred Stock contained in our registration statement on Form 8-A (File No. 001-34186) filed under the Exchange Act on September 25, 2008, including any amendment or report filed for the purpose of updating such description.

Any statement contained in a document incorporated or deemed to be incorporated by reference into this prospectus will be deemed to be modified or superseded for purposes of this prospectus to the extent that a statement contained in this prospectus or any other subsequently filed document that is deemed to be incorporated by reference into this prospectus modifies or supersedes the statement. Any statement so modified or superseded will not be deemed, except as so modified or superseded, to constitute a part of this prospectus.

We will provide each person to whom a prospectus is delivered a copy of all of the information that has been incorporated by reference in this prospectus but not delivered with the prospectus. You may obtain copies of these filings, at no cost, through the Investor Relations section of our website (www.vandapharma.com) and you may request a copy of these filings (other than an exhibit to any filing unless we have specifically incorporated that exhibit by reference into the filing), at no cost, by writing or telephoning us at the following address:

Corporate Secretary

Vanda Pharmaceuticals Inc.

9605 Medical Center Drive, Suite 300

Rockville, Maryland 20850

(240) 599-4500

Information on, or that can be accessed through, our website is not incorporated into this prospectus or other securities filings and is not a part of these filings.

SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS

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This prospectus, any applicable prospectus supplement and the documents incorporated by reference contain forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995. Various

Table of Contents

statements in this prospectus, and any prospectus supplement, may be forward-looking statements, under the securities laws. Words such as, but not limited to, believe, expect, anticipate, estimate, intend, plan, targets, likely, will, would, and could, and similar expressions are 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 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 clinical trials;

a failure of our products, product candidates or partnered products to be demonstrably safe and effective;

our failure to obtain regulatory approval for our products or product candidates or to comply with ongoing regulatory requirements;

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 costs and expenses;

our inability to obtain the capital necessary to fund additional research and development activities;

our failure to identify or obtain rights to new products or product candidates;

our failure to develop or obtain sales, marketing and distribution resources and expertise or to otherwise manage our growth;

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

losses incurred from product liability claims made against us; and

a loss of rights to develop and commercialize our products or product candidates under our license and sublicense agreements.

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.

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We encourage you to read the discussion and analysis of our financial condition and our condensed consolidated financial statements contained in or incorporated by reference in this prospectus, and any prospectus supplement. We also encourage you to read the statements under "Risk Factors" and other sections of this prospectus, which contains a more complete discussion of the risks and uncertainties associated with our business. In addition to the risks described above and in the section entitled "Risk Factors" of this prospectus, other unknown or unpredictable factors also could affect our results. 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.

Table of Contents**THE COMPANY**

We are a biopharmaceutical company focused on the development and commercialization of products for 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). We have developed Fanapt®, and will continue to develop it outside the U.S. and Canada, to treat schizophrenia. On May 6, 2009, the United States Food and Drug Administration (FDA) granted U.S. marketing approval of Fanapt® for the acute treatment of schizophrenia in adults. On October 12, 2009, we entered into an amended and restated sublicense agreement with Novartis. We had originally entered into a sublicense agreement with Novartis on June 4, 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. On January 11, 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®. 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. 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. In addition, we are no longer required to make any future milestone payments with respect to sales of Fanapt® or any future royalty payments with respect to 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. On February 23, 2010, the U.S. Patent and Trademark Office (PTO) issued a notice of allowance for our patent application for the microsphere long acting injectable (or depot) formulation of Fanapt®. On August 3, 2010, the PTO informed us that the patent has been issued with a patent term adjustment of 605 days, extending the patent expiration date to June 27, 2023. Subsequently, on October 28, 2010, the PTO informed us that it has granted an additional patent term adjustment of 59 days, making the total extension 664 days and making the patent expiration date August 25, 2023. We continue to explore the regulatory path and commercial opportunity for Fanapt® oral formulation outside of the U.S. and Canada. On November 1, 2010, the Therapeutic Goods Administration of Australia's Department of Health and Ageing, accepted for evaluation our application for marketing approval.

As a result of the FDA's approval of the new drug application (NDA) for Fanapt®, we met a milestone under the original sublicense agreement which required us to make a milestone payment of \$12.0 million to Novartis. The \$12.0 million was capitalized and will be amortized over the remaining life of the U.S. patent for Fanapt®.

Tasimelteon. Tasimelteon is an oral compound in development for sleep and mood disorders, including Circadian Rhythm Sleep Disorders (CRSD). The compound binds selectively to the brain's melatonin receptors, which are thought to govern the body's natural sleep/wake cycle. Compounds that bind selectively to these receptors are thought to be able to help treat sleep disorders, and additionally are believed to offer potential benefits in mood disorders. We announced positive top-line results from our Phase III trial of tasimelteon in transient insomnia in November 2006. In June 2008, we announced positive top-line results from the Phase III trial of tasimelteon in chronic primary insomnia. The trial was a randomized, double-blind, and placebo-controlled study with 324 patients. The trial measured time to fall asleep and sleep maintenance, as well as next-day performance. On January 19, 2010, the FDA granted orphan drug designation status for tasimelteon in a specific CRSD, Non-24-Hour

Table of Contents

Sleep/Wake Disorder (N24HSWD) in blind individuals with no 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. We initiated two clinical trials to pursue FDA approval of tasimelteon for the treatment of N24HSWD in blind individuals with no light perception in the third quarter of 2010. The first trial is a randomized, double-blind, placebo-controlled study with a planned enrollment of approximately 160 patients with N24HSWD. The trial has a six month treatment period and includes measures of both nighttime and daytime sleep, as well as laboratory measures of the synchronization between the internal body clock and the 24-hour environmental light/dark cycle. We also initiated a one-year safety study of tasimelteon for the treatment of N24HSWD. This trial is an open-label safety study with a planned enrollment of approximately 140 patients with N24HSWD. We plan to conduct additional clinical trials over the next one to two years to support the use of tasimelteon as a circadian regulator and the submission of a NDA to the FDA and a marketing authorization application to the European Medicines Agency (EMA). The application for orphan designation from the EMA is pending. Tasimelteon is also ready for Phase II trials for the treatment of depression. Given the range of potential indications for tasimelteon, we may pursue one or more partnerships for the development and commercialization of tasimelteon worldwide.

OUR CORPORATE INFORMATION

We were incorporated in Delaware in November 2002. Vanda commenced its operations in 2003. Our principal executive offices are located at 9605 Medical Center Drive, Suite 300, Rockville, Maryland, 20850 and our telephone number is (240) 599-4500. Our website address is www.vandapharma.com. The information on, or that can be accessed through, our website is not part of this prospectus.

Vanda is a trademark of Vanda Pharmaceuticals Inc. This prospectus may also include other registered and unregistered trademarks of Vanda Pharmaceuticals Inc. and other persons.

Throughout this prospectus, 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 and tasimelteon 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.

Table of Contents

RISK FACTORS

An investment in our securities involves a high degree of risk. You should carefully consider the following information, together with the other information contained in this prospectus, any applicable prospectus supplement and other documents that are incorporated by reference into this prospectus and any applicable prospectus supplement, including the section entitled "Risk Factors" in our most recent annual report on Form 10-K as revised and supplemented by our most recent quarterly report on Form 10-Q, each of which are on file with the SEC and are incorporated herein by reference, and which may be amended, supplemented or superseded from time to time by other reports we file with the SEC in the future before buying our securities. These risks are not the only risks facing Vanda. Additional risks and uncertainties not currently known to us or that we currently deem to be immaterial also may materially adversely affect our business, financial condition and/or operating results. If any of these 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

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 ability of patients to be able to afford Fanapt[®] or obtain health care coverage that covers Fanapt[®] in the current uncertain economic climate

acceptance of, and ongoing satisfaction, with Fanapt[®] by the medical community, patients receiving therapy and third party payers

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

the extent and effectiveness of the sales and marketing and distribution support Fanapt[®] receives

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

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

Novartis' ability to successfully develop and commercialize a long-acting injectable (or depot) formulation of Fanapt® in the U.S. and Canada

Novartis' ability to expand the indications for which Fanapt® can be marketed in the U.S.

Novartis' ability to obtain regulatory approval in Canada for Fanapt® and our 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

the unfavorable outcome of any potential litigation relating to Fanapt®

Table of Contents

We entered into an amended and restated sublicense agreement with Novartis to commercialize Fanapt® in the U.S. and Canada and to further develop and commercialize a long-acting injectable (or depot) formulation of Fanapt® in the U.S. and Canada. As such, we will not be involved in the marketing or sales efforts for Fanapt® in the U.S. and Canada. Our future revenues 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, which may or may not be achieved or met. 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. We cannot control the amount and timing of resources that Novartis may devote to Fanapt® or the depot formulation of Fanapt®. If Novartis fails to successfully commercialize Fanapt® in the U.S., fails to develop and commercialize Fanapt® in Canada or further develop a long-acting injectable (or depot) formulation of Fanapt®, 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 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 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® 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 product 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.

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, and it may be difficult to design efficacy studies for our compounds in new indications.

Table of Contents

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. 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.

We and our partners face heavy government regulation. FDA regulatory approval of our compounds is uncertain and we and our partners are 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

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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

Table of Contents

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 of our compounds. Other than Fanapt® in the U.S., which is being marketed and sold by Novartis, we have not received regulatory approval to market any of our compounds in any jurisdiction.

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 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.

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 may be required to obtain separate regulatory approvals and to comply with numerous and

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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. We have no experience obtaining any such foreign approvals. Additionally, the foreign regulatory approval process may include all of the risks associated with obtaining FDA approval. For all of these reasons, we 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 may

Table of Contents

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.

Our compounds may cause undesirable side effects or have other properties that could delay or prevent 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.

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 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.

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 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 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.

Table of Contents

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 2010 and beyond. As of September 30, 2010, our total cash and cash equivalents and marketable securities were approximately \$202.1 million. Our long term capital requirements are expected to depend on many factors, including, among others:

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 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) clearance

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 receive royalty payments and hope to receive milestone payments relating to Fanapt® in connection with our amended and restated sublicense agreement with Novartis. However, if Fanapt® is not as commercially successful as we expect and we do not receive such payments, 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, given the current global economic climate, we may have more difficulty raising funds than we would during a period of economic stability, and we may not be able to raise additional funds on acceptable terms, or at all. If we are unable to secure sufficient capital to fund our 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 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 September 30, 2010, we

Table of Contents

had accumulated net losses of approximately \$256 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®. Although Novartis launched Fanapt® in the U.S. in the first quarter of 2010, it is too early to determine whether or not Fanapt® will be a commercial success. Fanapt® may not be as commercially successful as we expect, Novartis may not succeed in gaining 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. We cannot assure you that we will 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 ability to successfully commercialize Fanapt® outside the U.S. and Canada

our ability to enter into agreements to develop and commercialize our products and product candidates

our 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

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

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

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 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

Table of Contents

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.

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.

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

Table of Contents

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

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.

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 our 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 affect our or our partners' ability to generate revenues from the sale of such products or partnered products.

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

Table of Contents

FDA approval or commercializing superior products or other competing products before we do. Technological developments or the FDA's 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 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).

For tasimelteon in the treatment of insomnia, Rozerem[™] (ramelteon) by Takeda Pharmaceuticals Company Limited, hypnotics such as Ambien[®] (zolpidem) by sanofi-aventis (including Ambien CR[®]), Lunesta[®] (eszopiclone) by Sepracor Inc. and Sonata[®] (zaleplon) by King Pharmaceuticals, 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[®].

For tasimelteon in the treatment of depression, antidepressants such as Paxil[®] (paroxetine) by GlaxoSmithKline (GSK), Zoloft[®] (sertraline) by Pfizer, Prozac[®] (fluoxetine) by Eli Lilly, Lexapro (escitalopram) by Lundbeck A/S /Forest Pharmaceuticals Inc., Viibryd (vilazodone HCL) by Clinical Data Inc. and Effexor[®] (venlafaxine) by Wyeth as well as other compounds such as Wellbutrin[®] (bupropion) by GSK, Cymbalta[®] (duloxetine) by Eli Lilly, and Valdoxan (agomelatine) by Novartis and Les Laboratoires Servier.

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 and no internal capability to do so, which may make commercializing our products and product candidates difficult.

At present, we have no marketing experience or sales capabilities. Therefore, in order for us to commercialize Fanapt[®] outside the U.S. and Canada or our other compounds, 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 and our future revenues are materially dependent on the success of the efforts of Novartis.

For the commercialization of Fanapt[®] outside the U.S. and Canada or our other compounds, we may not be able to establish sales and distribution partnerships on acceptable terms or at all, and if we do enter into a distribution arrangement, our success will be materially dependent upon the performance of our partner. In the

Table of Contents

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.

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. 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

Table of Contents

management resources. In addition, we depend on our ability to attract and retain other highly skilled personnel, including research scientists. Competition for qualified personnel is intense, and the process of hiring and integrating such qualified personnel is often lengthy. We may be unable to recruit such personnel on a timely basis, if at all, which would negatively impact our development and commercialization programs.

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

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

Table of Contents

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. Several provisions of the new law, 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% is effective as of January 1, 2010, and the volume of rebated drugs has been 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 beginning 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 revises the definition of "average manufacturer price" for reporting purposes (effective October 1, 2010), which could increase the amount of the Company's Medicaid drug rebates to states, once the provision is effective. 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.

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 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

Table of Contents

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 pharmaceutical company sales and promotional practices. While we expect the FDAAA to have a substantial effect on the pharmaceutical industry, the extent of that effect is not yet known. As the FDA issues regulations, guidance and interpretations relating to the new 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 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.

Table of Contents

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

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

mergers

acquisitions

strategic alliances

licensing agreements and

co-promotion and similar agreements

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

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

Although we have no experience in acquiring businesses, we may acquire businesses 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. 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 of royalties or milestone payments, if any, from the sales of Fanapt®

regulatory developments affecting our compounds or those of our competitors

product sales

cost of product sales

marketing and other expenses

manufacturing or supply issues and

any intellectual property infringement lawsuit in which we may become involved

Table of Contents

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.

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. We retained exclusive rights to Fanapt® outside the U.S. and Canada and we will 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, although we are not aware of any such breach by Novartis. Our loss of rights in Fanapt® to Novartis would have a material adverse effect on our business. 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.

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 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.

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 and BMS relating to our compounds, we rely upon intellectual property we own relating to these compounds, including patents, patent applications and trade

Table of Contents

secrets. As of September 30, 2010, we had twenty pending Patent Cooperation Treaty applications, fourteen of which have already been entered into the national stage in the U.S. and other countries, relating to our compounds in clinical development. In addition, we have one patent and three patent applications that have been filed in the U.S. Our patent applications may be challenged or fail to result in issued patents and our existing or future patents may be too narrow to prevent third parties from developing or designing around these patents. In addition, we generally rely on trade secret protection and confidentiality agreements to protect certain proprietary know-how that is not patentable, for processes for which patents are difficult to enforce and for any other elements of our drug development processes that involve proprietary know-how, information and technology that is not covered by patent applications. While we require all of our employees, consultants, advisors and any third parties who have access to our proprietary know-how, information and technology to enter into confidentiality agreements, we cannot be certain that this know-how, information and technology will not be disclosed or that competitors will not otherwise gain access to our trade secrets or independently develop substantially equivalent information and techniques. Further, the laws of some foreign countries do not protect proprietary rights to the same extent as the laws of the U.S. As a result, we may encounter significant problems in protecting and defending our intellectual property both in the U.S. and abroad. If we are unable to protect or defend the intellectual property related to our technologies, we will not be able to establish or maintain a competitive advantage in our market.

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 materially 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 tasimelepton, and that we continue to have rights under our license agreement with respect to this product, we would have exclusive rights to tasimelepton's U.S. new chemical entity patent (the primary patent covering the compound as a new composition of matter) until 2022. During the second quarter of 2009, we submitted to the PTO our application to extend the term of our patent relating to Fanapt® under the Hatch-Waxman Act. As of this time, the PTO has preliminarily determined that the patent is eligible for patent term restoration under the Hatch-Waxman Act. Assuming we gain a five-year extension for Fanapt®, pursuant to the terms and conditions of our amended and restated sublicense agreement, Novartis would have the benefit of exclusive rights to the new chemical entity patent until 2016, with the possibility of a further six months of pediatric exclusivity. 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 may be of particular importance with respect to Fanapt®, since the European new chemical entity patent for Fanapt® will expire prior to the end of this 10-year period of market exclusivity. 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

Table of Contents

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

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

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 we believe that our safety procedures for handling and disposing of such materials 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 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 the offering and ownership of our securities

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, 2009 and December 31, 2010, the high and low sale prices of our common stock as reported on the NASDAQ Global Market varied between \$12.62 and \$6.04. 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.

Table of Contents

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

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 or patent decisions

changes in patent legislation 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 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. Additionally, a small number of early investors in our company have rights, subject to certain conditions, to require us to file registration statements to permit the resale of their shares in the public market or to include their shares in registration statements that we may file for ourselves or other stockholders.

In addition to our outstanding common stock, as of December 31, 2010, there were a total of 4,377,794 shares of common stock that we have registered and that we are obligated to issue upon the exercise of currently outstanding options and vesting of restricted stock unit awards granted under our Second Amended and Restated Management Equity Plan and 2006 Equity Incentive Plan. Upon the exercise or settlement of these options or 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.

Table of Contents

Our management will have broad discretion over the use of the proceeds we receive in this offering and might not apply the proceeds in ways that increase the value of your investment.

Our management will have broad discretion to use the net proceeds from any offerings under this prospectus, and you will be relying on the judgment of our management regarding the application of these proceeds. They might not apply the net proceeds of this offering in ways that increase the value of your investment. Unless otherwise indicated in an accompanying prospectus supplement, we expect to use the net proceeds from this offering for general corporate purposes. We have not allocated these net proceeds for any specific purposes. Our management might not be able to yield a significant return, if any, on any investment of these net proceeds. You will not have the opportunity to influence our decisions on how to use the proceeds.

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 securities 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 another proxy contest, we may not be able to respond successfully to the contest, which would be disruptive to our business. Even if we are successful, our business could be adversely affected by a proxy contest 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

Table of Contents

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

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, on September 25, 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 recent 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 current 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 both royalty revenue and the further clinical development of Fanapt[®], 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.

Table of Contents

DESCRIPTION OF SECURITIES

PREFERRED STOCK

We currently have authorized 20,000,000 shares of preferred stock, par value \$0.001, the rights and preferences of which may be established from time to time by our board of directors. As of the date of this prospectus, our board of directors has designated 30,000 of the shares of authorized preferred stock as Series A Junior Participating Preferred Stock in connection with our stockholder rights plan, which is described in greater detail under Rights Plan.

Under Delaware law and our amended and restated certificate of incorporation, our board of directors is authorized, without stockholder approval, to issue shares of preferred stock from time to time in one or more series. Subject to limitations prescribed by Delaware law and our amended and restated certificate of incorporation and by-laws, the board of directors can determine the number of shares constituting each series of preferred stock and the designation, preferences, voting powers, qualifications, and special or relative rights or privileges of that series. These may include provisions concerning voting, redemption, dividends, dissolution or the distribution of assets, conversion or exchange, and other subjects or matters as may be fixed by resolution of the board or an authorized committee of the board. The preferred stock offered by this prospectus will, when issued, be fully paid and nonassessable.

Our board of directors could authorize the issuance of shares of preferred stock with terms and conditions which could have the effect of discouraging a takeover or other transaction which holders of some, or a majority, of our common stock might believe to be in their best interests or in which holders of some, or a majority, of our common stock might receive a premium for their shares over the then market price of those shares.

If we offer a specific series of preferred stock under this prospectus, we will describe the terms of the preferred stock in the prospectus supplement for such offering and will file a copy of the certificate establishing the terms of the preferred stock with the SEC. To the extent required, this description will include:

the title and stated value;

the number of shares offered, the liquidation preference per share, and the purchase price;

the dividend rate(s), period(s), and/or payment date(s), or method(s) of calculation for such dividends;

whether dividends will be cumulative or non-cumulative and, if cumulative, the date from which dividends will accumulate;

the procedures for any auction and remarketing, if any;

the provisions for a sinking fund, if any;

any listing of the preferred stock on any securities exchange or market;

whether the preferred stock will be convertible into Vanda common stock, and, if applicable, the conversion price (or how it will be calculated) and conversion period;

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whether the preferred stock will be exchangeable into debt securities, and, if applicable, the exchange price (or how it will be calculated) and exchange period;

voting rights, if any, of the preferred stock;

a discussion of any material and/or special U.S. federal income tax considerations applicable to the preferred stock;

the relative ranking and preferences of the preferred stock as to dividend rights and rights upon liquidation, dissolution, or winding up of the affairs of Vanda; and

any material limitations on issuance of any class or series of preferred stock ranking senior to or on a parity with the series of preferred stock as to dividend rights and rights upon liquidation, dissolution, or winding up of Vanda.

Table of Contents

Transfer Agent and Registrar. The transfer agent and registrar for any series or class of preferred stock will be set forth in the applicable prospectus supplement.

COMMON STOCK

We currently have authorized 150,000,000 shares of common stock, par value \$0.001 per share. As of January 24, 2011, there were 28,041,379 shares of common stock outstanding held of record by 12 stockholders. Holders of our common stock have no preemptive rights and no right to convert their common stock into any other securities. There are no redemption or sinking fund provisions applicable to the common stock. All outstanding shares of our common stock are fully paid and nonassessable.

The following summary of the terms of our common stock is subject to and qualified in its entirety by reference to our amended and restated certificate of incorporation and by-laws, copies of which are on file with the SEC as exhibits to previous SEC filings. Please refer to the section entitled *Where You Can Find More Information* for directions on obtaining these documents.

Voting Rights. The holders of our common stock are entitled to one vote for each share held of record on all matters submitted to a vote of stockholders, including, without limitation, the election of our board of directors. Our stockholders have no right to cumulate their votes in the election of directors.

Dividends. Subject to preferences that may apply to shares of preferred stock outstanding at the time, the holders of our common stock are entitled to receive ratably those dividends declared from time to time by the board of directors.

Rights Upon Liquidation. Subject to preferences that may apply to shares of preferred stock outstanding at the time, in the event of liquidation, dissolution or winding up, holders of our common stock are entitled to share ratably in assets remaining after payment of liabilities.

Anti-Takeover Effects of Our Amended and Restated Certificate of Incorporation, Bylaws and Delaware Law. Some provisions of Delaware law and our amended and restated certificate of incorporation and bylaws could make the following transactions more difficult: our acquisition by means of a tender offer; our acquisition by means of a proxy contest or otherwise; or removal of our incumbent officers and directors.

Section 203 of the Delaware General Corporation Law is applicable to takeovers of Delaware corporations. Subject to exceptions enumerated in Section 203, Section 203 provides that a corporation shall not engage in any business combination with any interested stockholder for a three-year period following the date that the stockholder becomes an interested stockholder unless:

prior to that date, the board of directors of the corporation approved either the business combination or the transaction that resulted in the stockholder becoming an interested stockholder;

upon consummation of the transaction that resulted in the stockholder becoming an interested stockholder, the interested stockholder owned at least 85% of the voting stock of the corporation outstanding at the time the transaction commenced, though some shares may be excluded from the calculation; and

on or subsequent to that date, the business combination is approved by the board of directors of the corporation and by the affirmative votes of holders of at least two-thirds of the outstanding voting stock that is not owned by the interested stockholder. Except as specified in Section 203, an interested stockholder is generally defined to include any person who, together with any affiliates or associates of that person, beneficially owns, directly or indirectly, 15% or more of the outstanding voting stock of the corporation, or is an affiliate or associate of the corporation and was the owner of 15% or more of the outstanding voting stock of the corporation, any time within three years

Table of Contents

immediately prior to the relevant date. Under certain circumstances, Section 203 makes it more difficult for an interested stockholder to effect various business combinations with a corporation for a three-year period, although the stockholders may elect not to be governed by this section, by adopting an amendment to the certificate of incorporation or by-laws, effective 12 months after adoption. Our amended and restated certificate of incorporation and by-laws do not opt out from the restrictions imposed under Section 203. We anticipate that the provisions of Section 203 may encourage companies interested in acquiring us to negotiate in advance with the board because the stockholder approval requirement would be avoided if a majority of the directors then in office excluding an interested stockholder approve either the business combination or the transaction that resulted in the stockholder becoming an interested stockholder. These provisions may have the effect of deterring hostile takeovers or delaying changes in control, which could depress the market price of our common stock and deprive stockholders of opportunities to realize a premium on shares of common stock held by them.

In addition to our board of directors' ability to issue shares of preferred stock, our amended and restated certificate of incorporation and by-laws contain provisions that may discourage, delay or prevent a change in our management or control over us that stockholders may consider favorable. Our amended and restated certificate of incorporation and bylaws:

authorize the issuance of blank check preferred stock that could be issued by our board of directors to thwart a takeover attempt;

do not provide for cumulative voting in the election of directors, which would allow holders of less than a majority of the stock to elect some directors;

establish a classified board of directors, as a result of which the successors to the directors whose terms have expired will be elected to serve from the time of election and qualification until the third annual meeting following their election;

require that directors only be removed from office for cause;

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

limit who may call special meetings of stockholders;

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

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

Rights Plan. Our board of directors adopted a Rights Plan (the "Plan") as set forth in the Rights Agreement, dated as of September 25, 2008, between us and American Stock Transfer & Trust Company, as Rights Agent (as amended, the "Rights Agreement"). A series of our preferred stock, designated as Series A Junior Participating Preferred Stock, par value \$0.001 per share, was created in accordance with the Rights Agreement. The Plan is designed to deter coercive takeover tactics, including the accumulation of shares in the open market or through private transactions, and to prevent an acquirer from gaining control of us without offering a fair and adequate price and terms to all of our stockholders. As such, the Plan enhances our board of directors' ability to protect stockholder interests and ensure that stockholders receive fair and equal treatment in the event any proposed takeover of Vanda is made in the future. Pursuant to the Rights Agreement, our board of directors declared a dividend distribution of one preferred stock purchase right for each outstanding share of our common stock. The preferred stock purchase rights are attached to, and trade with, our common stock. The purchase rights are currently exercisable upon the occurrence of certain triggering events described in the Rights Agreement.

Transfer Agent and Registrar. The transfer agent and registrar for our common stock is American Stock Transfer & Trust Company.

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Listing. Our common stock is listed on the NASDAQ Global Market under the symbol VNDA.

Table of Contents

DEBT SECURITIES

We may issue, from time to time, debt securities in one or more series that will consist of either senior debt or subordinated debt under one or more trust indentures to be executed by us and a specified trustee. The terms of the debt securities will include those stated in the indenture and those made a part of the indenture (before any supplements) by reference to the Trust Indenture Act of 1939. The indentures will be qualified under the Trust Indenture Act. Debt securities, whether senior or subordinated, may be issued as convertible debt securities or exchangeable debt securities.

The following description sets forth certain anticipated general terms and provisions of the debt securities to which any prospectus supplement may relate. The particular terms of the debt securities offered by any prospectus supplement (which terms may be different than those stated below) and the extent, if any, to which such general provisions may apply to the debt securities so offered will be described in the prospectus supplement relating to such debt securities. Accordingly, for a description of the terms of a particular issue of debt securities, investors should review both the prospectus supplement relating thereto and the following description. Forms of the senior indenture (as discussed herein) and the subordinated indenture (as discussed herein) are included as exhibits to the registration statement of which this prospectus is a part.

General

The debt securities will be our direct obligations and may be either senior debt securities or subordinated debt securities. The indebtedness represented by subordinated securities will be subordinated in right of payment to the prior payment in full of our senior debt (as defined in the applicable indenture). Senior securities and subordinated securities will be issued pursuant to separate indentures (respectively, a senior indenture and a subordinated indenture), in each case between us and a trustee.

Except as set forth in the applicable indenture and described in a prospectus supplement relating thereto, the debt securities may be issued without limit as to aggregate principal amount, in one or more series, secured or unsecured, in each case as established from time to time in or pursuant to authority granted by a resolution of our board of directors or as established in the applicable indenture. All debt securities of one series need not be issued at the time and, unless otherwise provided, a series may be reopened, without the consent of the holders of the debt securities of such series, for issuance of additional debt securities of such series. The applicable indenture may provide that we may issue debt securities in any currency or currency unit designated by us. Except for any limitations on consolidation, merger and sale of all or substantially all of our assets that may be contained in the applicable indenture, the terms of such indenture will not contain any covenants or other provisions designed to afford holders of any debt securities protection with respect to our operations, financial condition or transactions involving us.

The prospectus supplement relating to any series of debt securities being offered will contain the specific terms thereof, including, without limitation:

the title of such debt securities and whether such debt securities are senior securities or subordinated securities and the terms of any such subordination;

the aggregate principal amount of such debt securities and any limit on such aggregate principal amount;

the percentage of the principal amount at which such debt securities will be issued and, if other than the principal amount thereof, the portion of the principal amount thereof payable upon declaration of acceleration of the maturity thereof, or (if applicable) the portion of the principal amount of such debt securities which is convertible into common stock or preferred stock, or the method by which any such portion shall be determined;

the date or dates, or the method for determining the date or dates, on which the principal of such debt securities will be payable;

Table of Contents

the rate or rates (which may be fixed or variable), or the method by which the rate or rates shall be determined, at which such debt securities will bear interest, if any;

the date or dates, or the method for determining such date or dates, from which any interest will accrue, the interest payment dates on which any such interest will be payable, the regular record dates for such interest payment dates, or the method by which any such date shall be determined, the person to whom such interest shall be payable, and the basis upon which interest shall be calculated if other than that of a 360-day year of twelve 30-day months;

the right, if any, to extend the interest payment periods and the duration of the extensions;

the place or places where the principal of (and premium, if any) and interest, if any, on such debt securities will be payable, such debt securities may be surrendered for conversion or registration of transfer or exchange and notices or demands to or upon us in respect of such debt securities and the applicable indenture may be served;

the period or periods within which, the price or prices at which and the terms and conditions upon which such debt securities may be redeemed, as a whole or in part, at our option, if we have such an option;

our obligation, if any, to redeem, repay or purchase such debt securities pursuant to any sinking fund or analogous provision or at the option of a holder thereof, and the period or periods within which, the price or prices at which and the terms and conditions upon which such debt securities will be redeemed, repaid or purchased, as a whole or in part, pursuant to such obligation;

if other than U.S. dollars, the currency or currencies in which such debt securities are denominated and payable, which may be a foreign currency or units of two or more foreign currencies or a composite currency or currencies, and the terms and conditions relating thereto;

whether the amount of payments of principal of (and premium, if any) or interest, if any, on such debt securities may be determined with reference to an index, formula or other method (which index, formula or method may, but need not be, based on a currency, currencies, currency unit or units or composite currencies) and the manner in which such amounts shall be determined;

any additions to, modifications of or deletions from the terms of such debt securities with respect to the events of default or covenants set forth in the indenture;

any provisions for collateral security for repayment of such debt securities;

whether such debt securities will be issued in certificated and/or book-entry form;

whether such debt securities will be in registered or bearer form and, if in registered form, the denominations thereof if other than \$1,000 and any integral multiple thereof and, if in bearer form, the denominations thereof and terms and conditions relating thereto;

whether issued in the form of one or more global securities and whether all or a portion of the principal amount of the debt securities is represented thereby;

if other than the entire principal amount of the debt securities when issued, the portion of the principal amount payable upon acceleration of maturity, and the terms and conditions of any acceleration;

if applicable, covenants affording holders of debt protection with respect to our operations, financial condition or transactions involving us;

the applicability, if any, of defeasance and covenant defeasance provisions of the applicable indenture;

the terms, if any, upon which such debt securities may be convertible into our common stock or preferred stock and the terms and conditions upon which such conversion will be effected, including, without limitation, the initial conversion price or rate and the conversion period;

Table of Contents

if applicable, any limitations on the ownership or transferability of the common stock or preferred stock into which such debt securities are convertible;

whether and under what circumstances we will pay additional amounts as contemplated in the indenture on such debt securities in respect of any tax, assessment or governmental charge and, if so, whether we will have the option to redeem such debt securities in lieu of making such payment; and

any other material terms of such debt securities.

The debt securities may provide for less than the entire principal amount thereof to be payable upon declaration of acceleration of the maturity thereof. Special federal income tax, accounting and other considerations applicable to these original issue discount securities will be described in the applicable prospectus supplement. The applicable prospectus supplement will set forth material U.S. federal income tax considerations for holders of any debt securities and the securities exchange or quotation system on which any debt securities are listed or quoted, if any.

The applicable indenture may contain provisions that would limit our ability to incur indebtedness or that would afford holders of debt securities protection in the event of a highly leveraged or similar transaction involving us or in the event of a change of control.

Senior Debt Securities

Payment of the principal of premium, if any, and interest on senior debt securities will rank on parity with all of our other senior unsecured and unsubordinated debt.

Subordinated Debt Securities

Payment of the principal of, premium, if any, and interest on subordinated debt securities will be subordinated and junior in right of payment to the prior payment in full of all of our senior debt. We will set forth in the applicable prospectus supplement relating to any subordinated debt securities the subordination terms of such securities as well as the aggregate amount of outstanding indebtedness, as of the most recent practicable date, that by its terms would be senior to the subordinated debt securities. We will also set forth in such prospectus supplement limitations, if any, on issuance of additional senior debt.

Merger, Consolidation or Sale

The applicable indenture will provide that we may consolidate with, or sell, lease or convey all or substantially all of our assets to, or merge with or into, any other corporation, provided that:

either we shall be the continuing corporation, or the successor corporation (if other than the Company) formed by or resulting from any such consolidation or merger or which shall have received the transfer of such assets shall expressly assume payment of the principal of (and premium, if any), and interest on, all of the applicable debt securities and the due and punctual performance and observance of all of the covenants and conditions contained in the applicable indenture;

immediately after giving effect to such transaction and treating any indebtedness which becomes our obligation or an obligation of one of our subsidiaries as a result thereof as having been incurred by us or such subsidiary at the time of such transaction, no event of default under the applicable indenture, and no event which, after notice or the lapse of time, or both, would become such an event of default, shall have occurred and be continuing; and

an officer's certificate and legal opinion covering such conditions shall be delivered to the applicable trustee.

Table of Contents

Covenants

The applicable indenture will contain covenants requiring us to take certain actions and prohibiting us from taking certain actions. The covenants with respect to any series of debt securities will be described in the prospectus supplement relating thereto.

Events of Default, Notice and Waiver

Each indenture will describe specific events of default with respect to any series of debt securities issued thereunder. Such events of default are likely to include (with grace and cure periods):

default in the payment of any installment of interest on any debt security of such series;

default in the payment of principal of (or premium, if any, on) any debt security of such series at its maturity or upon any redemption, by declaration or otherwise;

default in making any required sinking fund payment for any debt security of such series;

default in the performance or breach of any other covenant or warranty of the Company contained in the applicable indenture (other than a covenant added to the indenture solely for the benefit of a series of debt securities issued thereunder other than such series), continued for a specified period of days after written notice as provided in the applicable indenture;

default in the payment of specified amounts of indebtedness of the Company or any mortgage, indenture or other instrument under which such indebtedness is issued or by which such indebtedness is secured, such default having occurred after the expiration of any applicable grace period and having resulted in the acceleration of the maturity of such indebtedness, but only if such indebtedness is not discharged or such acceleration is not rescinded or annulled;

certain events of bankruptcy, insolvency or reorganization, or court appointment of a receiver, liquidator or trustee of the Company or any of our significant subsidiaries or their property; and

any other event of default provided in the applicable resolution of our board of directors or the supplemental indenture under which we issue series of debt securities.

An event of default for a particular series of debt securities does not necessarily constitute an event of default for any other series of debt securities issued under the indenture. Unless otherwise indicated in the applicable prospectus supplement, if an event of default under any indenture with respect to debt securities of any series at the time outstanding occurs and is continuing, then the applicable trustee or the holders of not less than a majority of the principal amount of the outstanding debt securities of that series may declare the principal amount (or, if the debt securities of that series are original issue discount securities or indexed securities, such portion of the principal amounts may be specified in the terms thereof) of all the debt securities of that series to be due and payable immediately by written notice thereof to us (and to the applicable trustee if given by the holders). However, at any time after such a declaration of acceleration with respect to debt securities of such series (or of all debt securities then outstanding under any indenture, as the case may be) has been made, but before a judgment or decree for payment of the money due has been obtained by the applicable trustee, the holders of not less than a majority in principal amount of outstanding debt securities of such series (or of all debt securities then outstanding under the applicable indenture, as the case may be) may rescind and annul such declaration and its consequences if:

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we shall have deposited with the applicable trustee all required payments of the principal of (and premium, if any) and interest on the debt securities of such series (or of all debt securities then outstanding under the applicable indenture, as the case may be), plus certain fees, expenses, disbursements and advances of the applicable trustee; and

all events of default, other than the non-payment of accelerated principal (or specified portion thereof), with respect to debt securities of such series (or of all debt securities then outstanding under the applicable indenture, as the case may be) have been cured or waived as provided in such indenture.

Table of Contents

If an event of default relating to events of bankruptcy, insolvency or reorganization of the Company occurs and is continuing, then the principal amount of all of the debt securities outstanding, and any accrued interest, will automatically become due and payable immediately, without any declaration or other act by the trustee or any holder.

Each indenture also will provide that the holders of not less than a majority in principal amount of the outstanding debt securities of any series (or of all debt securities then outstanding under the applicable indenture, as the case may be) may waive any past default with respect to such series and its consequences, except a default:

in the payment of the principal of (or premium, if any) or interest on any debt security of such series; or

in respect of a covenant or provision contained in the applicable indenture that cannot be modified or amended without the consent of the holder of each outstanding debt security affected thereby.

Each trustee will be required to give notice to the holders of debt securities within 90 days of a default under the applicable indenture unless such default shall have been cured or waived; provided, however, that such trustee may withhold notice to the holders of any series of debt securities of any default with respect to such series (except a default in the payment of the principal of (or premium, if any) or interest on any debt security of such series or in the payment of any sinking fund installment in respect of any debt security of such series) if specified responsible officers of such trustee consider such withholding to be in the interest of such holders.

Each indenture will provide that no holders of debt securities of any series may institute any proceedings, judicial or otherwise, with respect to such indenture or for any remedy thereunder, except in the case of failure of the applicable trustee, for 60 days, to act after it has received a written request to institute proceedings in respect of an event of default from the holders of not less than 25% in principal amount of the outstanding debt securities of such series, as well as an offer of indemnity reasonably satisfactory to it. This provision will not prevent, however, any holder of debt securities from instituting suit for the enforcement of payment of the principal of (and premium, if any) and interest on such debt securities at the respective due dates thereof.

Each indenture provides that in case an event of default shall occur and be known to any trustee and not be cured, the trustee must use the same degree of care as a prudent person would use in the conduct of his or her own affairs in the exercise of the trustee's power. Subject to provisions in each indenture relating to its duties in case of default, no trustee will be under any obligation to exercise any of its rights or powers under an indenture at the request or direction of any holders of any series of debt securities then outstanding under such indenture, unless such holders shall have offered to the trustee thereunder reasonable security or indemnity. The holders of not less than a majority in principal amount of the outstanding debt securities of any series (or of all debt securities then outstanding under an indenture, as the case may be) shall have the right to direct the time, method and place of conducting any proceeding for any remedy available to the applicable trustee, or of exercising any trust or power conferred upon such trustee. However, a trustee may refuse to follow any direction which is in conflict with any law or the applicable indenture, which may involve such trustee in personal liability or which may be unduly prejudicial to the holders of debt securities of such series not joining therein.

Within 120 days after the close of each fiscal year, we will be required to deliver to each trustee a certificate, signed by one of several specified officers, stating whether or not such officer has knowledge of any default under the applicable indenture and, if so, specifying each such default and the nature and status thereof.

Modification of the Indenture

Each indenture provides that we and the trustee may enter into supplemental indentures without the consent of the holders of debt securities to:

secure any debt securities;

evidence the assumption by a successor corporation of our obligations;

add covenants for the protection of the holders of debt securities;

Table of Contents

cure any ambiguity or correct any inconsistency in the indenture;

establish the forms or terms of debt securities of any series; and

evidence and provide for the acceptance of appointment by a successor trustee.

It is anticipated that modifications and amendments of an indenture may be made by us and the trustee, with the consent of the holders of not less than a majority in principal amount of each series of the outstanding debt securities issued under the indenture that are affected by the modification or amendment, provided that no such modification or amendment may, without the consent of each holder of such debt securities affected thereby:

change the stated maturity date of the principal of (or premium, if any) or any installment of interest, if any, on any such debt security;

reduce the principal amount of (or premium, if any) or the interest, if any, on any such debt security or the principal amount due upon acceleration of an original issue discount security;

change the time or place or currency of payment of principal of (or premium, if any) or interest, if any, on any such debt security;

impair the right to institute suit for the enforcement of any such payment on or with respect to any such debt security;

reduce any amount payable on redemption;

modify any of the subordination provisions or the definition of senior indebtedness applicable to any subordinated debt securities in a manner adverse to the holders of those securities;

reduce the above-stated percentage of holders of debt securities necessary to modify or amend the indenture; or

modify the foregoing requirements or reduce the percentage of outstanding debt securities necessary to waive compliance with certain provisions of the indenture or for waiver of certain defaults.

A record date may be set for any act of the holders with respect to consenting to any amendment. The holders of not less than a majority in principal amount of outstanding debt securities of each series affected thereby will have the right to waive our compliance with certain covenants in such indenture. Each indenture will contain provisions for convening meetings of the holders of debt securities of a series to take permitted action.

A prospectus supplement may set forth modifications or additions to these provisions with respect to a particular series of debt securities.

Conversion or Exchange Rights

A prospectus supplement will describe the terms, if any, on which a series of debt securities may be convertible into or exchangeable for our common stock, preferred stock or other securities. These terms will also include provisions as to whether conversion or exchange is mandatory, at the option of the holder or at our option. Such provisions will also include the conversion or exchange price (or manner or calculation thereof), the conversion or exchange period, the events requiring an adjustment of the conversion or exchange price, and provisions affecting conversion

or exchange in the event of the redemption of such series of debt securities.

Registered Global Securities

We may issue the debt securities of a series in whole or in part in the form of one or more fully registered global securities that we will deposit with a depository or with a nominee for a depository identified in the applicable prospectus supplement and registered in the name of such depository or nominee. In such case, we will

Table of Contents

issue one or more registered global securities denominated in an amount equal to the aggregate principal amount of all of the debt securities of the series to be issued and represented by such registered global security or securities.

Unless and until it is exchanged in whole or in part for debt securities in definitive registered form, a registered global security may not be transferred except as a whole:

by the depositary for such registered global security to its nominee;

by a nominee of the depositary to the depositary or another nominee of the depositary; or

by the depositary or its nominee to a successor of the depositary or a nominee of the successor.

The prospectus supplement relating to a series of debt securities will describe the specific terms of the depositary arrangement with respect to any portion of such series represented by a registered global security. We anticipate that the following provisions will apply to all depositary arrangements for debt securities:

ownership of beneficial interests in a registered global security will be limited to persons that have accounts with the depositary for the registered global security, those persons being referred to as participants, or persons that may hold interests through participants;

upon the issuance of a registered global security, the depositary for the registered global security will credit, on its book-entry registration and transfer system, the participants' accounts with the respective principal amounts of the debt securities represented by the registered global security beneficially owned by the participants;

any dealers, underwriters, or agents participating in the distribution of the debt securities will designate the accounts to be credited; and

ownership of any beneficial interest in the registered global security will be shown on, and the transfer of any ownership interest will be effected only through, records maintained by the depositary for the registered global security (with respect to interests of participants) and on the records of participants (with respect to interests of persons holding through participants).

The laws of some states may require that certain purchasers of securities take physical delivery of the securities in definitive form. These laws may limit the ability of those persons to own, transfer or pledge beneficial interests in registered global securities.

So long as the depositary for a registered global security, or its nominee, is the registered owner of the registered global security, the depositary or the nominee, as the case may be, will be considered the sole owner or holder of the debt securities represented by the registered global security for all purposes under the indenture. Except as set forth below, owners of beneficial interests in a registered global security:

will not be entitled to have the debt securities represented by a registered global security registered in their names;

will not receive or be entitled to receive physical delivery of the debt securities in the definitive form; and

will not be considered the owners or holders of the debt securities under the indenture.

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Accordingly, each person owning a beneficial interest in a registered global security must rely on the procedures of the depositary for the registered global security and, if the person is not a participant, on the procedures of a participant through which the person owns its interest, to exercise any rights of a holder under the indenture.

We understand that under existing industry practices, if we request any action of holders or if an owner of a beneficial interest in a registered global security desires to give or take any action that a holder is entitled to give

Table of Contents

or take under the indenture, the depositary for the registered global security would authorize the participants holding the relevant beneficial interests to give or take the action, and those participants would authorize beneficial owners owning through those participants to give or take the action or would otherwise act upon the instructions of beneficial owners holding through them.

We will make payments of principal and premium, if any, and interest, if any, on debt securities represented by a registered global security registered in the name of a depositary or its nominee to the depositary or its nominee, as the case may be, as the registered owners of the registered global security. None of the Company, the trustee or any other agent of the Company or the trustee will be responsible or liable for any aspect of the records relating to, or payments made on account of, beneficial ownership interests in the registered global security or for maintaining, supervising or reviewing any records relating to the beneficial ownership interests.

We expect that the depositary for any debt securities represented by a registered global security, upon receipt of any payments of principal and premium, if any, and interest, if any, in respect of the registered global security, will immediately credit participants' accounts with payments in amounts proportionate to their respective beneficial interests in the registered global security as shown on the records of the depositary. We also expect that standing customer instructions and customary practices will govern payments by participants to owners of beneficial interests in the registered global security held through the participants, as is now the case with the securities held for the accounts of customers in bearer form or registered in street name. We also expect that any of these payments will be the responsibility of the participants.

If the depositary for any debt securities represented by a registered global security is at any time unwilling or unable to continue as depositary or ceases to be a clearing agency registered under the Exchange Act, we will appoint an eligible successor depositary. If we fail to appoint an eligible successor depositary within 90 days, we will issue the debt securities in definitive form in exchange for the registered global security. In addition, we may at any time and in our sole discretion decide not to have any of the debt securities of a series represented by one or more registered global securities. In such event, we will issue debt securities of that series in a definitive form in exchange for all of the registered global securities representing the debt securities. The trustee will register any debt securities issued in definitive form in exchange for a registered global security in such name or names as the depositary, based upon instructions from its participants, shall instruct the trustee.

We may also issue bearer debt securities of a series in the form of one or more global securities, referred to as bearer global securities. We will deposit these bearer global securities with a common depositary for Euroclear System and Clearstream Bank Luxembourg, Societe Anonyme, or with a nominee for the depositary identified in the prospectus supplement relating to that series. The prospectus supplement relating to a series of debt securities represented by a bearer global security will describe the specific terms and procedures, including the specific terms of the depositary arrangement and any specific procedures for the issuance of debt securities in definitive form in exchange for a bearer global security, with respect to the position of the series represented by a bearer global security.

Discharge, Defeasance and Covenant Defeasance

We can discharge or defease our obligations under the indenture as set forth below. Unless otherwise set forth in the applicable prospectus supplement, the subordination provisions applicable to any subordinated debt securities will be expressly subject to the discharge and defeasance provisions of the indenture.

We may discharge some of our obligations to holders of any series of debt securities that have not already been delivered to the trustee for cancellation and that have either become due and payable or are by their terms to become due and payable within one year (or are scheduled for redemption within one year). We may effect a discharge by irrevocably depositing with the trustee cash or U.S. government obligations, as trust funds, in an amount certified to be sufficient to pay when due, whether at maturity, upon redemption or otherwise, the principal of, premium, if any, and interest on the debt securities and any mandatory sinking fund payments.

Table of Contents

Unless otherwise provided in the applicable prospectus supplement, we may also discharge any and all of our obligations to holders of any series of debt securities at any time (defeasance). We also may be released from the obligations imposed by any covenants of any outstanding series of debt securities and provisions of the indenture, and we may omit to comply with those covenants without creating an event of default (covenant defeasance). We may effect defeasance and covenant defeasance only if, among other things:

we irrevocably deposit with the trustee cash or U.S. government obligations, as trust funds, in an amount certified to be sufficient to pay at maturity (or upon redemption) the principal, premium, if any, and interest on all outstanding debt securities of the series; and

we deliver to the trustee an opinion of counsel from a nationally recognized law firm to the effect that the holders of the series of debt securities will not recognize income, gain or loss for U.S. federal income tax purposes as a result of the defeasance or covenant defeasance and that defeasance or covenant defeasance will not otherwise alter the holders' U.S. federal income tax treatment of principal, premium, if any, and interest payments on the series of debt securities, which opinion, in the case of legal defeasance, must be based on a ruling of the Internal Revenue Service issued, or a change in U.S. federal income tax law.

Although we may discharge or defease our obligations under the indenture as described in the two preceding paragraphs, we may not avoid, among other things, our duty to register the transfer or exchange of any series of debt securities, to replace any temporary, mutilated, destroyed, lost or stolen series of debt securities or to maintain an office or agency in respect of any series of debt securities.

Redemption of Securities

Debt securities may also be subject to optional or mandatory redemption on terms and conditions described in the applicable prospectus supplement.

From and after notice has been given as provided in the applicable indenture, if funds for the redemption of any debt securities called for redemption shall have been made available on such redemption date, such debt securities will cease to bear interest on the date fixed for such redemption specified in such notice, and the only right of the holders of the debt securities will be to receive payment of the redemption price.

Notices

Holders of our debt securities will receive notices by mail at their addresses as they appear in the security register.

Title

We may treat the person in whose name a debt security is registered on the applicable record date as the owner of the debt security for all purposes, whether or not it is overdue.

Governing Law

Unless otherwise set forth in the applicable prospectus supplement, New York law will govern the indentures and the debt securities, without regard to its conflicts of law principles.

Concerning the Trustee

Each indenture provides that there may be more than one trustee under the indenture, each with respect to one or more series of debt securities. If there are different trustees for different series of debt securities, each trustee will be a trustee of a trust under the indenture separate and apart from the trust administered by any other

Table of Contents

trustee under the indenture. Except as otherwise indicated in this prospectus or any prospectus supplement, any action permitted to be taken by a trustee may be taken by such trustee only with respect to the one or more series of debt securities for which it is the trustee under the indenture. Any trustee under the indenture may resign or be removed with respect to one or more series of debt securities. All payments of principal of, premium, if any, and interest on, and all registration, transfer, exchange, authentication and delivery (including authentication and delivery on original issuance of the debt securities) of, the debt securities of a series will be effected by the trustee with respect to that series at an office designated by the trustee in New York, New York.

Each indenture contains limitations on the right of the trustee, should it become a creditor of the Company, to obtain payment of claims in some cases or to realize on certain property received in respect of any such claim as security or otherwise. The trustee may engage in other transactions. If it acquires any conflicting interest relating to any duties with respect to the debt securities, however, it must eliminate the conflict or resign as trustee.

WARRANTS

We may issue warrants for the purchase of debt securities, preferred stock, common stock, or any combination thereof. We may issue warrants independently or together with any other securities offered by any prospectus supplement and may be attached to or separate from the other offered securities. Each series of warrants will be issued under a separate warrant agreement to be entered into by us with a warrant agent. The warrant agent will act solely as our agent in connection with the warrants and will not assume any obligation or relationship of agency or trust for or with any holders or beneficial owners of warrants. Further terms of the warrants and the applicable warrant agreements will be set forth in the applicable prospectus supplement.

The applicable prospectus supplement relating to any particular issue of warrants will describe the terms of the warrants, including, as applicable, the following:

the title of the warrants;

the aggregate number of the warrants;

the price or prices at which the warrants will be issued;

the designation, terms and number of shares of preferred stock or common stock or principal amount of debt securities purchasable upon exercise of the warrants;

the designation and terms of the offered securities, if any, with which the warrants are issued and the number of the warrants issued with each offered security;

the date, if any, on and after which the warrants and the related debt securities, preferred stock or common stock will be separately transferable;

the price at which each share of preferred stock, common stock or underlying debt securities purchasable upon exercise of the warrants may be purchased or the manner of determining such price;

the date on which the right to exercise the warrants shall commence and the date on which that right shall expire;

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the minimum or maximum amount of the warrants which may be exercised at any one time;

information with respect to book-entry procedures, if any;

a discussion of certain federal income tax considerations; and

any other material terms of the warrants, including terms, procedures and limitations relating to the exchange and exercise of the warrants.

We and the warrant agent may amend or supplement the warrant agreement for a series of warrants without the consent of the holders of the warrants issued thereunder to effect changes that are not inconsistent with the provisions of the warrants and that do not materially and adversely affect the interests of the holders of the warrants.

Table of Contents

USE OF PROCEEDS

We currently intend to use the net proceeds from the sale of our securities for general corporate purposes, which may include commercial launch activities, sales and marketing expenditures, funding of clinical trials, research and development, regulatory activities, acquisitions of companies, products, intellectual property or other technology, investments, capital expenditures, and for any other purposes that we may specify in any prospectus supplement. While we have no current plans for any specific acquisitions at this time, we believe opportunities may exist from time to time to expand our current business through strategic alliances or acquisitions of other companies, products or compounds. We have not yet determined the amount of net proceeds to be used specifically for any of the foregoing purposes. Accordingly, our management will have significant discretion and flexibility in applying the net proceeds from the sale of these securities. Pending any use, as described above, we intend to invest the net proceeds in high-quality, short-term, interest-bearing securities. Our plans to use the estimated net proceeds from the sale of these securities may change, and if they do, we will update this information in a prospectus supplement.

RATIO OF FIXED CHARGES AND PREFERENCE DIVIDENDS TO EARNINGS

Our ratio of combined fixed charges and preference dividends to earnings for each of the five most recently completed fiscal years and any required interim periods will each be specified in a prospectus supplement or in a document that we file with the SEC and incorporate by reference pertaining to the issuance, if any, by us of preference securities in the future.

DIVIDEND POLICY

We have never declared or paid cash dividends on our common stock. We currently intend to retain all available funds and any future earnings for use in the operation of our business and do not anticipate paying any cash dividends in the foreseeable future. Any future determination to declare cash dividends will be made at the discretion of our board of directors, subject to compliance with certain covenants under our credit facilities, which restrict or limit our ability to declare of pay dividends, and will depend on our financial condition, results of operations, capital requirements, general business conditions and other factors that our board of directors may deem relevant.

PLAN OF DISTRIBUTION

We may sell the securities covered by this prospectus in any of three ways (or in any combination):

to or through underwriters or dealers;

directly to a limited number of purchasers or to a single purchaser; or

through agents.

Each time we offer and sell securities, we will provide a prospectus supplement that will set forth the terms of the offering of the securities covered by this prospectus, including:

the name or names of any underwriters, dealers or agents and the amounts of securities underwritten or purchased by each of them;

the purchase price of the securities and the proceeds we will receive from the sale;

any over-allotment options under which underwriters may purchase additional securities;

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any underwriting discounts or commissions or agency fees and other items constituting underwriters' or agents' compensation;

Table of Contents

the initial public offering price of the securities;

any discounts, commissions or concessions allowed or reallocated or paid to dealers; and

any securities exchange or market on which the securities may be listed.

Any public offering price and any discounts or concessions allowed or reallocated or paid to dealers may be changed from time to time.

Underwriters or dealers may offer and sell the securities from time to time in one or more transactions, including negotiated transactions, at a fixed public offering price or at varying prices determined at the time of sale. If underwriters or dealers are used in the sale of any securities, the securities will be acquired by such underwriters or dealers for their own account and may be resold from time to time in one or more transactions described above. We may offer the securities to the public through underwriting syndicates represented by managing underwriters, or directly by underwriters or dealers. Subject to certain conditions, the underwriters or dealers will be obligated to purchase all the securities of the series offered by the prospectus supplement. We will describe the nature of any such relationship in the prospectus supplement, naming the underwriter or dealer.

We may use underwriters with whom we have a material relationship. We may sell the securities through agents from time to time. The prospectus supplement will name any agent involved in the offer or sale of the securities and any commissions we pay to them. Unless the prospectus supplement states otherwise, any agent will be acting on a best efforts basis for the period of its appointment.

We may authorize underwriters, dealers or agents to solicit offers by certain purchasers to purchase securities from us at the public offering price set forth in the prospectus supplement pursuant to delayed delivery contracts providing for payment and delivery on a specified date in the future. The prospectus supplement will set forth the conditions to these contracts and any commissions we pay for solicitation of these contracts.

LEGAL MATTERS

The validity of the securities being offered hereby will be passed upon by Gunderson Dettmer Stough Villeneuve Franklin & Hachigian, LLP, Waltham, Massachusetts.

EXPERTS

The consolidated financial statements and management's assessment of the effectiveness of internal control over financial reporting (which is included in Management's Report on Internal Control over Financial Reporting) incorporated in this prospectus by reference to the Annual Report on Form 10-K for the year ended December 31, 2009 have been so incorporated in reliance on the report of PricewaterhouseCoopers LLP, an independent registered public accounting firm, given on the authority of said firm as experts in auditing and accounting.

Table of Contents

Shares
Common Stock

Prospectus Supplement

Joint Book-Running Managers

Lazard Capital Markets

August , 2013

Piper Jaffray & Co.