Vanda Pharmaceuticals Inc.
Form 424B5
October 29, 2014
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Filed Pursuant to Rule 424(b)(5)
Registration No. 333-191434

PROSPECTUS SUPPLEMENT

(to Prospectus dated October 4, 2013)

5,000,000 Shares

Common Stock

We are offering 5,000,000 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 October 28, 2014, as reported by The NASDAQ Global Market, was $12.03 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 7 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	$ 11.60	$ 58,000,000
Underwriting discount	$ 0.696	$ 3,480,000
Proceeds, before expenses, to Vanda Pharmaceuticals Inc.	$ 10.904	$ 54,520,000

Delivery of the shares of common stock is expected to be made on or about November 3, 2014. We have granted the underwriters an option for a period of 30 days to purchase up to an additional 750,000 shares of our common stock. If the underwriters exercise the option in full, the total underwriting discounts and commissions payable by us will be $4,002,000 and the total proceeds to us, before expenses, will be $66,700,000.

Joint Book-Running Managers

Jefferies **Piper Jaffray**

Co-Managers

JMP Securities **Canaccord Genuity**

Prospectus Supplement dated October 29, 2014.

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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, our, or similar references refer to Vanda Pharmaceuticals Inc. and its subsidiaries on a consolida 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.

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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 our operations in 2003. Our product portfolio includes:

- HETLIOZ® (tasimelteon), a product for the treatment of Non-24-Hour Sleep-Wake Disorder (Non-24), which was approved by the U.S. Food and Drug Administration (FDA) in January 2014 and launched commercially in April 2014; in June 2014, the European Medicines Agency (EMA) accepted for evaluation our Marketing Authorization Application (MAA) for oral HETLIOZ® capsules for the treatment of Non-24;

- Fanapt® (iloperidone), a product for the treatment of schizophrenia, the oral formulation of which is being marketed and sold in the U.S. by Novartis Pharma AG (Novartis), launched in Israel by our distribution partner and expected to be launched in Mexico by our distribution partner in the fourth quarter of 2014; and

- VLY-686 (tradipitant), a small molecule neurokinin-1 receptor (NK-1R) antagonist, which is presently in a Phase 2 study for the treatment of chronic pruritus in atopic dermatitis.

Since we began operations in March 2003, we have devoted substantially all of our resources to the in-licensing and clinical development of our products. Our products target prescription markets with significant unmet medical needs. Our ability to generate revenue and achieve profitability largely depends on our ability, alone or with others, to complete the development of our products, and to obtain the regulatory approvals for and manufacture, market and sell our products, including HETLIOZ® for the treatment of Non-24. 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 activities will necessitate significant uses of working capital throughout 2014 and beyond. We are currently concentrating our efforts on the commercialization of HETLIOZ® in the U.S., which was commenced in April 2014. Additionally, we and our partners continue to pursue market approval of Fanapt® in Europe and other regions, with Mexico and Israel having already approved Fanapt® for the treatment of schizophrenia.

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

products, we have relied upon our deep expertise in the scientific disciplines of pharmacogenetics and pharmacogenomics. These scientific disciplines examine both genetic variations among people that influence response to a particular drug, and the multiple pathways through which drugs affect people.

Our products target prescription markets with significant unmet medical needs. We believe that HETLIOZ® represents an important new treatment option for patients with Non-24. HETLIOZ® is the first U.S. FDA-

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approved product to treat Non-24, a serious chronic circadian rhythm disorder that affects the majority of people who are totally blind. 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.

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THE OFFERING

Common stock we are offering	5,000,000 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 750,000 additional shares of common stock at the public offering price less the underwriting discounts and commissions.
Offering price	$11.60 per share of common stock.
Common stock to be outstanding after this offering	38,901,084 shares (or 39,651,084 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 in connection with the commercialization of HETLIOZ® in the U.S. for the treatment of Non-24, 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. 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

Each share of common stock purchased in this offering will have associated with it one preferred stock purchase right of our Series A Junior Participating Preferred Stock pursuant to the Rights Agreement dated September 25, 2008, as amended.

The number of shares of common stock that will be outstanding immediately after this offering as shown above is based on 33,901,084 shares of common stock outstanding as of September 30, 2014 and excludes:

- 652,810 shares of common stock issuable upon the exercise of outstanding options as of September 30, 2014 under our Second Amended and Restated Management Equity Plan (the 2004 Plan), with a weighted average exercise price of $1.74 per share;

5,192,221 shares of common stock issuable upon the exercise of outstanding options as of September 30, 2014 under our 2006 Equity Incentive Plan (the 2006 Plan), with a weighted average exercise price of $11.43 per share;

662,346 shares of common stock issuable upon the vesting of outstanding restricted stock units as of September 30, 2014; and

2,381,075 shares of common stock reserved for future issuance as of September 30, 2014 under the 2006 Plan.

Unless otherwise indicated, all information in this prospectus assumes:

that the underwriters do not exercise their option to purchase up to 750,000 additional shares of our common stock; and

no options, restricted stock units, warrants, or shares of common stock were issued after September 30, 2014, and no outstanding options or warrants were exercised after September 30, 2014 and no outstanding restricted stock units vested after such date.

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SUMMARY CONSOLIDATED FINANCIAL DATA

The following tables present our Summary Consolidated Statements of Operations data for the years ended December 31, 2011 through 2013 as well as for the nine months ended September 30, 2013 and 2014 and consolidated balance sheet data as of September 30, 2014. 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, 2013 and our Quarterly Report on Form 10-Q for the quarter ended September 30, 2014. Our historical results are not necessarily indicative of the results that may be expected in the future.

Consolidated Statement of Operations Data: ***(in thousands, except for share and per share amounts)***	**Year Ended December 31,**			**Nine Months Ended September 30,**	
	2011 [1]	**2012** [1]	**2013** [1]	**2013** [1]	**2014**
		(Audited)		**(Unaudited)**	
Revenues:					
Product revenue, net	$	$	$	$	$ 6,888
Royalty revenue	4,481	5,938	7,090	5,059	4,919
Licensing agreement	26,789	26,789	26,789	20,037	22,981
Total revenues	31,270	32,727	33,879	25,096	34,788
Operating expenses:					
Cost of goods sold		129			901
Research and development	28,858	45,764	28,502	22,233	14,479
Selling, general and administrative	11,294	14,517	25,082	15,154	67,321
Intangible asset amortization	1,495	1,495	1,495	1,118	1,718
Total operating expenses	41,647	61,905	55,079	38,505	84,419
Loss from operations	(10,377)	(29,178)	(21,200)	(13,409)	(49,631)
Other income	461	561	145	101	98
Loss before tax benefit	(9,916)	(28,617)	(21,055)	(13,308)	(49,533)
Tax benefit	(444)				
Net loss	$ (9,472)	$ (28,617)	$ (21,055)	$ (13,308)	$ (49,533)
Basic and diluted net loss per share	$ (0.34)	$ (1.01)	$ (0.69)	$ (0.45)	$ (1.46)
	28,106,831	28,228,409	30,351,353	29,363,162	33,814,154

Weighted average shares outstanding, basic and diluted					

(1) In the first quarter of 2014, the Company elected to change its method of accounting for stock-based compensation from the accelerated attribution method to the straight-line method. The consolidated financial data above for the years ended 2011, 2012 and 2013 and the nine months ended September 30, 2013 have been adjusted to reflect this change. Refer to the Company s quarterly report on Form 10-Q for the quarter ending March 31, 2014 for further information.

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The following table presents selected consolidated balance sheet data as of September 30, 2014 on an actual basis and on an as adjusted basis to reflect the sale of 5,000,000 shares of our common stock in this offering at the public offering price of $11.60 per share, after deducting underwriting discounts and commissions and estimated offering expenses payable by us.

Consolidated Balance Sheet Data: *(in thousands, except for share and per share amounts)*	**September 30, 2014 Actual (Unaudited)**	**September 30, 2014 As Adjusted (Unaudited)**
ASSETS		
Current assets:		
Cash and cash equivalents	$ 15,308	$ 69,288
Marketable securities	40,781	40,781
Accounts receivable, net	3,696	3,696
Inventory	1,268	1,268
Prepaid expenses and other current assets	3,785	3,785
Restricted cash		
Total current assets	64,838	118,818
Property and equipment, net	2,233	2,233
Intangible asset, net	11,319	11,319
Restricted cash, non-current	785	785
Total assets	$ 79,175	$ 133,155
LIABILITIES AND STOCKHOLDERS EQUITY		
Current liabilities:		
Accounts payable	$ 547	$ 547
Accrued liabilities	6,825	6,825
Deferred rent	241	241
Deferred revenue	31,232	31,232
Total current liabilities	38,845	38,845
Deferred rent, non-current	2,919	2,919
Deferred revenue, non-current	36,235	36,235
Other liabilities	113	113
Total liabilities	78,112	78,112
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 33,901,084 shares issued and outstanding, actual; 38,901,084 shares issued and outstanding, as adjusted	34	39
Additional paid-in capital	358,728	412,703

Accumulated other comprehensive income	4	4
Accumulated deficit	(357,703)	(357,703)
Total stockholders equity	1,063	55,043
Total liabilities and stockholders equity	$ 79,175	$ 133,155

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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

HETLIOZ® may not be commercially successful.

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

- cost of treatment;
- pricing and availability of alternative products;
- the cost and success of our Non-24-Hour Sleep-Wake Disorder (Non-24) awareness campaign;
- our ability to obtain third-party coverage or reimbursement for HETLIOZ®;
- perceived efficacy relative to other available therapies;
- shifts in the medical community to new treatment paradigms or standards of care;
- relative convenience and ease of administration; and
- prevalence and severity of adverse side effects associated with treatment.

Because we only recently initiated the U.S. commercialization of HETLIOZ®, we have limited information with regard to the market acceptance of HETLIOZ® in the U.S. or elsewhere. As a result, we may have to revise our estimates regarding the market acceptance of HETLIOZ® or our strategy to commercialize the product.

In addition, we have incurred and expect to continue to incur significant expenses and to utilize a substantial portion of our cash resources as we continue the commercialization of HETLIOZ® in the U.S., continue our Non-24

awareness campaign and continue to grow our operational capabilities. This represents a significant investment in the commercial success of HETLIOZ®, which is uncertain.

We are heavily dependent on the commercial success of HETLIOZ®, which only recently received marketing authorization and was commercially launched in the U.S., and on the regulatory approval of HETLIOZ® for the treatment of Non-24 in other countries, which may never occur.

Our future success is currently dependent upon the commercial success of HETLIOZ® for the treatment of Non-24 in the U.S. In January 2014, the U.S. Food and Drug Administration (FDA) approved our New Drug Application (NDA) for HETLIOZ® for the treatment of Non-24 and in April 2014, we commenced the U.S. commercial launch of HETLIOZ®. Our future success is also dependent upon successfully obtaining regulatory approval from foreign regulatory bodies to market HETLIOZ® for the treatment of Non-24 in other jurisdictions, and if approved, successfully commercializing HETLIOZ® in such jurisdictions. In June 2014, the European Medicines Agency (EMA) accepted for evaluation our Marketing Authorization Application (MAA) for oral HETLIOZ® capsules for the treatment of Non-24.

If we do not successfully commercialize HETLIOZ® in other countries in which HETLIOZ® may be approved for sale, our ability to generate product sales revenue may be jeopardized and, consequently, our business may be

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seriously harmed. We may not receive regulatory approval in other jurisdictions for HETLIOZ®; and if we do receive regulatory approval in such other jurisdictions for HETLIOZ®, we may not be able to commercialize HETLIOZ® successfully, all of which would have a material adverse effect on our business, results of operations and prospects.

In addition, we have incurred and expect to continue to incur significant expenses as we seek the approval of HETLIOZ® in other jurisdictions. This represents a significant investment in the regulatory success of HETLIOZ®, which is uncertain.

As a company, we have minimal 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 difficult.

At present, we as a company have minimal marketing experience, other than providing assistance to Novartis relating to the U.S. commercialization of Fanapt® (iloperidone). Therefore, in order for us to successfully commercialize HETLIOZ®, Fanapt® (outside the U.S. and Canada) or our other products, we must either acquire or continue to internally develop sales, marketing and distribution capabilities, or enter into collaborations with partners to perform these services for us. We may, in some instances, rely significantly on sales, marketing and distribution arrangements with our collaborative partners and other third parties. For example, we rely completely on Novartis to market, sell and distribute Fanapt® in the U.S. and, if regulatory approval is obtained, Canada.

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

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

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

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

product revenues.

Even after obtaining regulatory approvals for the sale of our products, the commercial success of these products will depend, among other things, on their acceptance by physicians, patients, third-party payors and other members of the medical community as a therapeutic and cost-effective alternative to competing products and treatments. The degree of market acceptance of any product will depend on a number of factors, including the demonstration of its safety and efficacy, its cost-effectiveness, its potential advantages over other therapies, the reimbursement policies of government and third-party payors with respect to such product, our ability to attract and maintain corporate partners, including pharmaceutical companies, to assist in commercializing our products,

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receipt of regulatory clearance of marketing claims for the uses that we or our partners are developing and the effectiveness of our and our partners marketing and distribution capabilities. If our approved products fail to gain market acceptance, we may be unable to earn sufficient revenue to continue our business. If our approved products do not become widely accepted by physicians, patients, third-party payors and other members of the medical community, it is unlikely that we will ever become profitable on a sustained basis or achieve significant revenues.

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

As of September 30, 2014, we had 60 full-time employees and, as a result, we rely, and expect to continue to rely, on outsourcing arrangements for a significant portion of our activities, including sales, distribution, medical affairs, clinical research, data collection and analysis, manufacturing, financial reporting and accounting and human resources, as well as for certain functions as a public company. We may have limited control over these third parties and we cannot guarantee that they will perform their obligations in an effective and timely manner.

Disruptions to our HETLIOZ® supply chain could materially affect our ability to commercialize HETLIOZ®, thereby reducing our future earnings and prospects.

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

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

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

warning letters;

fines;

civil penalties;

injunctions;

recall or seizure of products;

total or partial suspension of production;

refusal of the government to grant future approvals;

withdrawal of approvals; and

criminal prosecution.

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

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

Our and our partners activities, including the sale and marketing of our products, are subject to extensive government regulation and oversight, including regulation under the federal Food, Drug and Cosmetic Act and other federal and state statutes. We are also subject to the provisions of the Federal Anti-Kickback Statute and several similar state laws, which prohibit payments intended to induce physicians or others either to purchase or arrange for or recommend the purchase of healthcare products or services. While the federal law applies only to products or services for which payment may be made by a federal healthcare program, state laws may apply regardless of whether federal funds may be involved. These laws constrain the sales, marketing and other promotional activities of manufacturers 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.

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

We intend to market our products in foreign jurisdictions. In order to market our products in foreign jurisdictions, we or our partners may be required to obtain separate regulatory approvals and to comply with numerous and varying regulatory requirements. The approval procedure varies among countries and jurisdictions and can involve additional trials, and the time required to obtain approval may differ from that required to obtain FDA approval. Additionally, the foreign regulatory approval process may include all of the risks associated with obtaining FDA approval. For all of these reasons, we or our partners may not obtain foreign regulatory approvals on a timely basis, if at all. Approval by the FDA does not ensure approval by regulatory authorities in other countries or jurisdictions, and approval by one foreign regulatory authority does not ensure approval by regulatory authorities in other foreign countries or jurisdictions or by the FDA. We or our partners may not be able to file for regulatory approvals and may not receive necessary approvals to commercialize our products in any market. The failure to obtain these approvals could harm our business materially.

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 with third parties on terms that may not be attractive to us.

Our activities will necessitate significant uses of working capital throughout 2014 and beyond. It is uncertain whether our existing funds will be sufficient to meet our operating needs. As of September 30, 2014, our total

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cash and cash equivalents and marketable securities were $56.1 million. Our long term capital requirements are expected to depend on many factors, including, among others:

- our ability to commercialize HETLIOZ® globally;
- 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 amount of royalty and milestone payments received from our commercial partners;
- our ability to commercialize Fanapt® outside the U.S. and Canada;
- the number of potential formulations and products 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.

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.

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 products and our ability to identify and develop additional products 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;

undertaking pre-clinical testing and clinical trials;

obtaining FDA and other regulatory approvals of products; and

manufacturing, marketing and selling products.

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

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

For HETLIOZ® 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 (including Ambien CR®), Lunesta® (eszopiclone) by Sunovion Pharmaceuticals Inc., Sonata® (zaleplon) by Pfizer Inc., Silenor® (doxepin) by Pernix Therapeutics, generic products such as zolpidem, trazodone and doxepin, and over-the-counter remedies such as Benadryl® and Tylenol PM®. The class of melatonin agonists includes Rozerem® (ramelteon) by Takeda Pharmaceuticals Company Limited, Valdoxan® (agemelatine) by Servier, Circadin® (long-acting melatonin) by Neurim Pharmaceuticals and the food supplement melatonin.

For Fanapt® in the treatment of schizophrenia, the atypical antipsychotics competitors are Risperdal® (risperidone), including the depot formulation Risperdal® Consta® and Invega® (paliperidone), including the depot formulation Invega® Sustenna®, each by Ortho-McNeil-Janssen Pharmaceuticals, Inc., Zyprexa® (olanzapine), including the depot formulation Zyprexa® Relprevv , each by Eli Lilly and Company, Seroquel® (quetiapine) by AstraZeneca PLC, Abilify® (aripiprazole) by BMS/Otsuka Pharmaceutical Co., Ltd., Abilify® Maintena® (the depot formulation of Abilify®) by Lundbeck/Otsuka Pharmaceutical Co., Ltd., Geodon® (ziprasidone) by Pfizer Inc., Saphris® (asenapine) by Actavis plc, Latuda® (lurasidone) by Sunovion Pharmaceuticals Inc., and generic clozapine, as well as the typical antipsychotics haloperidol, chlorpromazine, thioridazine, and sulpiride (all of which are generic).

Additionally, we may face competition from newly developed generic products. Under the U.S. Drug Price Competition and Patent Term Restoration Act of 1984, more commonly known as the Hatch-Waxman Act, newly approved drugs and indications may benefit from a statutory period of non-patent marketing exclusivity. The Hatch-Waxman Act seeks to stimulate competition by providing incentives to generic pharmaceutical manufacturers to introduce non-infringing forms of patented pharmaceutical products and to challenge patents on branded pharmaceutical products. If we are unsuccessful at challenging an Abbreviated New Drug Application (ANDA), filed pursuant to the Hatch-Waxman Act, cheaper generic versions of our products, which may be favored by insurers and third-party payors, may be launched commercially, which would harm our business.

Novartis began selling, marketing and distributing our first approved product, Fanapt®, in the U.S. in the first quarter of 2010 and our ability to generate meaningful product revenue from Fanapt® will depend on the success

of this product in the marketplace.

Our ability to generate product revenue from Fanapt® will depend on the success of Fanapt® and the sales of this product by Novartis in the U.S. The ability of Fanapt® to generate meaningful product revenue will depend on many factors, including the following:

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

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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 payors;

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

the size of the market for Fanapt®;

successfully expanding and sustaining manufacturing capacity to meet demand;

cost and availability of raw materials;

safety concerns in the marketplace for schizophrenia therapies;

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

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

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

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® 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 ability to generate meaningful product revenue from Fanapt® depends 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., we expect that some or all of these commercial and development milestones will not be achieved by Novartis. In May 2014, we commenced arbitration proceedings with Novartis relating to the license of Fanapt®.

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, 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, we will receive limited revenues from them. Over time, Novartis has reduced the size of the Fanapt® sales organization and this could have a negative impact on the success of the product in the United States. We do not expect Novartis to commercialize Fanapt® in Canada. 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 an adverse effect on our financial condition and results of operations.

FDA regulatory approval of our products is uncertain.

The research, testing, manufacturing and marketing of products such as those that we have developed or that we or 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 products, we or our partners must

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demonstrate to the satisfaction of the applicable regulatory agency that, among other things, the product is safe and effective for its intended use. In addition, we or our partners must show that the manufacturing facilities used to produce such products are in compliance with current Good Manufacturing Practices regulations (cGMP).

The process of obtaining FDA and other required regulatory approvals and clearances can take many years and will require us and our partners, as applicable, 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 product, the disease or condition that the product is in development for, and the requirements applicable to that particular product. The FDA can delay, limit or deny approval of a product for many reasons, including that:

- a product may not be shown to be safe or effective;
- the FDA 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 product 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 products.

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

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

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

If our products 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 HETLIOZ® in January 2014 and the NDA for Fanapt® in May 2009, and the positive results of our completed trials for HETLIOZ® and Fanapt®, 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

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approved for commercial sale. Future uses of our products, 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 products are determined to be unsafe or ineffective in humans, our business will be materially harmed.

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

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

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

Clinical development efforts performed by us 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 products and the size of the prospective patient population. The commencement and rate of completion of clinical trials for our products 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 products 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 products, we or they may not receive the regulatory approvals needed to market that product. Therefore, any failure or delay in commencing or completing these clinical trials would harm our business materially.

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

Undesirable side effects caused by our products could interrupt, delay or halt clinical trials and could result in the denial of regulatory approval by the FDA or other regulatory authorities for any or all targeted indications, and in turn prevent us or our partners from commercializing or continuing the commercialization of such products and generating revenues from their sale. We and our partners, as applicable, will continue to assess the side effect profile of our products in ongoing clinical development programs. However, we cannot predict whether the

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commercial use of our approved products (or our products in development, if and when they are approved for commercial use) will produce undesirable or unintended side effects that have not been evident in the use of, or in clinical trials conducted for, such products to date. 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 product, we, our partners or others later identify undesirable side effects caused by such product, 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 product;
- we or our partners may be required to change the way the product is administered, conduct additional clinical trials or change the labeling of the product; and
- our, our partners or the products reputation may suffer.

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

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 products since March 2003, which has required, and will continue to require, significant research and development expenditures. The continued commercial launch for HETLIOZ® will require substantial additional expenditures.

As of September 30, 2014, we had an accumulated deficit of $357.7 million, and we cannot estimate with precision the extent of our future losses. In April 2014, we commercially launched HETLIOZ® in the U.S. for the treatment of Non-24. The continuing commercialization of HETLIOZ® and our continuing Non-24 awareness campaign will require substantial additional expenditures. In addition, we may not succeed in commercializing HETLIOZ® or any other products. Our ability to generate meaningful product revenue prior to successfully commercializing HETLIOZ® 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. We do not expect Novartis to commercialize Fanapt® in Canada. 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. and we may not succeed in commercializing Fanapt® outside of the U.S. and Canada. We may not be profitable even if our products are successfully commercialized. We may be unable to fully develop, obtain regulatory approval for, commercialize, manufacture, market, sell and derive revenue from our products in the timeframes we project, if at all, and our inability to do so would materially and adversely impact the market price of our common stock and our ability to raise capital and continue operations.

There can be no assurance that we will achieve sustained profitability. 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 products, particularly HETLIOZ® for the treatment of Non-24, both in the U.S. and in foreign countries;

our ability to successfully commercialize HETLIOZ® in the U.S. and other jurisdictions in which HETLIOZ® may receive regulatory approval, if any;

our ability to successfully raise awareness regarding Non-24 in the medical and patient communities;

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Novartis ability to successfully market and sell Fanapt® in the U.S.;

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;

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

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

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

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

the costs of our marketing or awareness campaigns;

the progress of our research and development programs for our products, including clinical trials;

the time and expense that will be required to pursue FDA and/or foreign regulatory approvals for our products 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 additional products we pursue;

how competing technological and market developments affect our products;

- the cost of possible acquisitions of technologies, products, 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 (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 or credits could have a material adverse effect on our results of operations and cash flows.

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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 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. 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 (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 could be delayed.

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

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

- not provide us accurate or timely information regarding their inventories, the number of patients who are using HETLIOZ® or complaints about HETLIOZ®;

- reduce their efforts or discontinue to sell or support or otherwise not effectively sell or support HETLIOZ®;

not devote the resources necessary to sell HETLIOZ® in the volumes and within the time frames that we expect;

be unable to satisfy financial obligations to us or others; or

cease operations.

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

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

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

In January 2014, we entered into a manufacturing agreement with Patheon Pharmaceuticals Inc. (Patheon) for the manufacture of commercial supplies of HETLIOZ® 20 mg capsules. This agreement has an initial term of five years. If Patheon is unable to perform its duties under the manufacturing agreement, it could adversely affect sales of our HETLIOZ® products, delay clinical trials and prevent us from developing our HETLIOZ® products in a cost-effective manner or on a timely basis. We do not have exclusive long-term agreements with any other third party manufacturers. If any of our third party manufacturers, including Patheon, 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 in a timely manner from these third parties could adversely affect sales of our products, delay clinical trials and prevent us from developing our products in a cost-effective manner or on a timely basis. In addition, manufacturers of our products are subject to cGMP and similar foreign standards and we do not have control over compliance with these regulations by our manufacturers. If one of our contract manufacturers fails to maintain compliance, the production of our products could be interrupted, resulting in delays and additional costs. In addition, if the facilities of such manufacturers do not pass a pre-approval or post-approval plant inspection, the FDA will not grant approval and may institute restrictions on the marketing or sale of our products.

Our manufacturing strategy presents the following additional risks:

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

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

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

We and our partners rely on manufacturers to purchase from third-party suppliers the materials necessary to produce our products for clinical trials and commercialization. Suppliers may not sell these materials to such manufacturers at

the times we 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 products and commercial scale manufacturing could be delayed, significantly affecting our and our partners ability to further develop and commercialize our products. If we, our manufacturers or our partners, as applicable, are unable to purchase these materials for our products, there would be a shortage in supply or the commercial launch of such products would be delayed, which would materially and adversely affect our or our partners ability to generate revenues from the sale of such products.

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

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

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

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

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

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

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

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

The risk that we may be sued on product liability claims is inherent in the development and sale of pharmaceutical products. For example, we face a risk of product liability exposure related to the testing of our products in clinical trials and will face even greater risks upon commercialization by us or our partners of our products. We believe that we may be at a greater risk of product liability claims relative to other pharmaceutical companies because our products

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 products. These lawsuits may divert our management from pursuing our business strategy and may be costly to defend. In addition, if we are held liable in any of these lawsuits, we may incur substantial liabilities and we or our partners may be forced to limit or

forego further commercialization of one or more of our products. Although we maintain product liability insurance, our aggregate coverage limit under this insurance is $20.0 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 products, this coverage may be inadequate, we may be unable to obtain adequate coverage at an acceptable cost or we may be unable to get adequate coverage at all or our insurer may disclaim coverage as to a future claim. This could prevent the commercialization or limit the commercial potential of our products. Even if we are able to maintain insurance that we believe is adequate, our results of operations and financial condition may be materially adversely affected by a product liability claim. Uncertainties resulting from the initiation and continuation of products liability litigation or other proceedings could have a material adverse effect on our ability to compete in the marketplace. Product liability litigation and other related proceedings may also require significant management time.

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 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 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 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. 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 may not be considered cost effective, and coverage and reimbursement may not be available or sufficient to allow the sale of such products on a competitive and profitable basis. Further federal and state proposals and healthcare reforms are likely which could limit the prices that can be charged for the drugs we develop and may further limit our commercial opportunity. Our results of operations could be materially adversely affected by the Medicare prescription drug coverage legislation, by the possible effect of this legislation on amounts that private insurers will pay and by other healthcare reforms that may be enacted or adopted in the future.

The Patient Protection and Affordable Care Act of 2010, as amended by the Health Care and Education Reconciliation Act of 2010, (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.

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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. We will continue to evaluate the PPACA, as amended, the implementation of regulations or guidance related to various provisions of the PPACA by federal agencies, as well as trends and changes that may be encouraged by the legislation and that may potentially impact on our business over time. These developments could, however, have a material adverse effect on our business, financial condition and results of operations.

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

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

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

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

In addition, the Food and Drug Administration Amendments Act of 2007 (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.

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

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

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

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

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

Although we have no experience in acquiring businesses, we may acquire businesses or assets that complement or augment our existing business. If we acquire businesses with promising products or technologies, we may not be able to realize the benefit of acquiring such businesses if we are unable to move one or more products through preclinical and/or clinical development to regulatory approval and commercialization. Integrating any newly acquired businesses or technologies could be expensive and time-consuming, resulting in the diversion of resources from our current business. We may not be able to integrate any acquired business successfully. We cannot assure 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 operating results may fluctuate significantly.

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

product sales;

cost of product sales;

marketing and other expenses;

manufacturing or supply issues;

the timing and amount of royalties or milestone payments;

our addition or termination of development programs;

variations in the level of expenses related to our products or future development programs;

regulatory developments affecting our products or those of our competitors; our execution of collaborative, licensing or other arrangements, and the timing of payments we may make or receive under these arrangements;

any intellectual property infringement or other lawsuit in which we may become involved; and

the timing and recognition of stock-based compensation expense.

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

Risks related to intellectual property and other legal matters

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

HETLIOZ® 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 HETLIOZ® in the license agreement. Either party may terminate the license agreement under certain circumstances, including a material breach of the agreement by the other. In the event we terminate our license, or if BMS terminates our license due to our breach, all rights to HETLIOZ® (including any intellectual property we develop with respect to HETLIOZ®) licensed and developed by us under this agreement will revert or otherwise be licensed back to BMS on an exclusive basis. Any termination or reversion of our rights to develop or commercialize HETLIOZ®, including any reacquisition by BMS of our rights, may have a material adverse effect on our business.

Fanapt® is based in part on patents and other intellectual property owned by Sanofi and Novartis. Titan Pharmaceuticals, Inc. (Titan) holds an exclusive license from Sanofi to the intellectual property owned by Sanofi, 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. 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 (Eli Lilly and Company (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.

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

In addition to the rights we have licensed from BMS, Novartis and Lilly relating to our products, we rely upon intellectual property we own relating to these products, including patents, patent applications and trade secrets. As of September 30, 2014, excluding in-licensed patents and patent applications, we had 33 patent and patent application families, most of which have been filed in key markets including the U.S., relating to HETLIOZ® and Fanapt®. In addition, we had five other patent applications relating to products 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, our business will be harmed.

The Hatch-Waxman Act provides for an extension of patent term for drugs for a period of up to five years to compensate for time spent in development. Assuming we gain a five-year patent term restoration for HETLIOZ®, and that we continue to have rights under our license agreement with respect to this product, we would have exclusive rights to HETLIOZ® s U.S. new chemical entity patent (the primary patent covering the product as a new composition of matter) until 2022 and HETLIOZ® s U.S. method of use patent (the patent covering the method of treatment as described in the HETLIOZ® label approved by the FDA) until 2033.

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 s new chemical entity patent relating to Fanapt® to November 2016. A directive in the European Union provides that companies that receive regulatory approval for a new product will have a 10-year period of market exclusivity for that product (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 product expires. A generic version of the approved drug may not be marketed or sold in Europe during such market exclusivity period. This directive is of material importance with respect to Fanapt®, since the European new chemical entity patent for Fanapt® has expired. Assuming we gain a five-year patent term restoration for VLY-686, and that we continue to have rights under our license agreement with respect to this product, we would have exclusive rights to VLY-686 s U.S. new chemical entity patent until 2029.

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

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Furthermore, parties making claims against us may obtain injunctive o