

Vanda Pharmaceuticals Inc.  
Form 10-K  
March 13, 2009

**Table of Contents**

**UNITED STATES SECURITIES AND EXCHANGE COMMISSION  
Washington, D.C. 20549**

**Form 10-K**

- o** ANNUAL REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES  
EXCHANGE ACT OF 1934  
For the fiscal year ended December 31, 2008
- o** TRANSITION REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES  
EXCHANGE ACT OF 1934

**Commission File No. 000-51863**

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

**Delaware**  
*(State or other jurisdiction of  
incorporation or organization)*

**03-0491827**  
*(I.R.S. Employer  
Identification No.)*

**9605 Medical Center Drive, Suite 300  
Rockville, Maryland 20850  
(240) 599-4500**  
*(Address and telephone number, including area code, of registrant's principal executive offices)*

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

<b>Title of Each Class</b>	<b>Name of Each Exchange on Which Registered</b>
Common Stock, par value \$0.001	The Nasdaq Stock Market LLC (NASDAQ Global Market)
Rights to Purchase Series A Junior Participating Preferred Stock	The Nasdaq Stock Market LLC (NASDAQ Global Market)

**Securities registered pursuant to Section 12(g) of the Exchange Act: None**

Indicate by check mark if the registrant is a well-known seasoned issuer, as defined in Rule 405 of the Securities Act. Yes  No

Indicate by check mark if the registrant is not required to file reports pursuant to Section 13 or Section 15(d) of the Exchange Act. Yes  No

Indicate by check mark whether the registrant (1) has filed all reports required to be filed by Section 13 or 15(d) of the Securities Exchange Act of 1934 during the preceding 12 months (or for such shorter period that the registrant was required to file such reports), and (2) has been subject to such filing requirements for the past 90 days. Yes  No

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

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

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

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

The aggregate market value of the 17,756,198 shares of Common Stock held by non-affiliates of the registrant was \$58,417,891 as of the last business day of the registrant's most recently completed second quarter based on the closing price of the registrant's Common Stock on such date. Shares of Common Stock held by each executive officer, director and stockholders known by the registrant to own 10% or more of the outstanding stock based on public filings and other information known to the registrant have been excluded since such persons may be deemed affiliates. This determination of affiliate status is not necessarily a conclusive determination for other purposes.

The number of shares of the registrant's Common Stock, par value \$0.001 per share, outstanding as of March 11, 2009 was 26,653,478.

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

#### **DOCUMENTS INCORPORATED BY REFERENCE**

Portions of the registrant's Proxy Statement for its 2009 Annual Meeting of Stockholders to be filed within 120 days after the end of the registrant's fiscal year ended December 31, 2008, are incorporated by reference in Part III of this annual report on Form 10-K.

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**Vanda Pharmaceuticals Inc.  
Form 10-K**

**Table of Contents**

	<b>Page</b>
<b><u>Part I</u></b>	
<u>Cautionary Note Regarding Forward-Looking Statements</u>	2
<u>Item 1. Business</u>	3
<u>Item 1A. Risk Factors</u>	19
<u>Item 1B. Unresolved Staff Comments</u>	34
<u>Item 2. Properties</u>	34
<u>Item 3. Legal Proceedings</u>	34
<u>Item 4. Submission of Matters to a Vote of Security Holders</u>	34
<b><u>Part II</u></b>	
<u>Item 5. Market for Registrant's Common Equity, Related Shareholder Matters and Issuer Purchases of Equity Securities</u>	34
<u>Item 6. Selected Consolidated Financial Data</u>	37
<u>Item 7. Management's Discussion and Analysis of Financial Condition and Results of Operations</u>	39
<u>Item 7A. Qualitative and Quantitative Disclosures about Market Risk</u>	52
<u>Item 8. Financial Statements and Supplementary Data</u>	53
<u>Item 9. Changes in and Disagreements with Accountants on Accounting and Financial Disclosure</u>	53
<u>Item 9A. Controls and Procedures</u>	53
<u>Item 9B. Other Information</u>	54
<b><u>Part III</u></b>	
<u>Item 10. Directors, Executive Officers and Corporate Governance</u>	54
<u>Item 11. Executive Compensation</u>	54
<u>Item 12. Security Ownership of Certain Beneficial Owners and Management and Related Stockholder Matters</u>	54
<u>Item 13. Certain Relationships and Related Transactions, and Director Independence</u>	54
<u>Item 14. Principal Accounting Fees and Services</u>	55
<b><u>Part IV</u></b>	
<u>Item 15. Exhibits and Financial Statements Schedules</u>	55
<u>Signatures</u>	56
<u>Exhibit Index</u>	86
<u>Exhibit 10.23</u>	
<u>Exhibit 10.24</u>	
<u>Exhibit 10.25</u>	
<u>Exhibit 10.26</u>	
<u>Exhibit 10.27</u>	
<u>Exhibit 10.28</u>	
<u>Exhibit 10.29</u>	
<u>Exhibit 10.30</u>	
<u>Exhibit 10.31</u>	
<u>Exhibit 10.32</u>	
<u>Exhibit 23.1</u>	
<u>Exhibit 31.1</u>	
<u>Exhibit 31.2</u>	

Exhibit 32.1

Exhibit 32.2

**Table of Contents**

**PART I**

**CAUTIONARY NOTE REGARDING FORWARD-LOOKING STATEMENTS**

Various statements in this report are forward-looking statements under the securities laws. Words such as, but not limited to, believe, expect, anticipate, estimate, intend, plan, targets, likely, will, would, and could, or other similar expressions or words, identify forward-looking statements. Forward-looking statements are based upon current expectations that involve risks, changes in circumstances, assumptions and uncertainties. Vanda Pharmaceuticals Inc. (We, Vanda or the Company) is at an early stage of development and may not ever have any products that generate significant revenue. Important factors that could cause actual results to differ materially from those reflected in our forward-looking statements include, among others:

- delays in the completion of our clinical trials;
- a failure of our product candidates to be demonstrably safe and effective;
- our failure to obtain regulatory approval for our products or to comply with ongoing regulatory requirements;
- a lack of acceptance of our product candidates in the marketplace, or a failure to become or remain profitable;
- our expectations regarding trends with respect to our costs and expenses;
- our inability to obtain the capital necessary to fund our research and development activities;
- our failure to identify or obtain rights to new product candidates;
- our failure to develop or obtain sales, marketing and distribution resources and expertise or to otherwise manage our growth;
- a loss of any of our key scientists or management personnel;
- losses incurred from product liability claims made against us; and
- a loss of rights to develop and commercialize our products under our license and sublicense agreements.

All written and verbal forward-looking statements attributable to us or any person acting on our behalf are expressly qualified in their entirety by the cautionary statements contained or referred to in this section. We caution investors not to rely too heavily on the forward-looking statements we make or that are made on our behalf. We undertake no obligation, and specifically decline any obligation, to update or revise publicly any forward-looking statements, whether as a result of new information, future events or otherwise.

We encourage you to read the discussion and analysis of our financial condition and our consolidated financial statements contained in this annual report on Form 10-K. We also encourage you to read Item 1A of Part 1 of this annual report on Form 10-K, entitled Risk Factors, which contains a more complete discussion of the risks and uncertainties associated with our business. In addition to the risks described above and in Item 1A of this report, other unknown or unpredictable factors also could affect our results. There can be no assurance that the actual results or developments anticipated by us will be realized or, even if substantially realized, that they will have the expected

consequences to, or effects on, us. Therefore no assurance can be given that the outcomes stated in such forward-looking statements and estimates will be achieved.

**Table of Contents**

**ITEM 1. BUSINESS**

**Overview**

We are a biopharmaceutical company focused on the development and commercialization of clinical-stage drug candidates for central nervous system disorders, with exclusive worldwide commercial rights to two product candidates in clinical development. We believe that each of our product candidates will address a large market with significant unmet medical needs by offering advantages over currently available therapies. Our product portfolio includes:

Iloperidone, a compound for the treatment of schizophrenia. On November 27, 2007, the United States Food and Drug Administration (FDA) accepted a New Drug Application (NDA) for iloperidone for the treatment of schizophrenia. In July 2008, we announced that the FDA had determined that our NDA was not approvable and indicated, among other things, that we would have to conduct additional studies and submit that data before the FDA would approve iloperidone for commercial sale for the treatment of schizophrenia. In September 2008, we met with the FDA to discuss the FDA's determination. The FDA asked us to provide a complete response to the not-approvable letter, which we submitted on November 6, 2008. The FDA accepted our complete response for review and has set a new target action date of May 6, 2009. There are no guarantees that the FDA will provide its response by May 6, 2009, nor can there be any assurances that any such response will be favorable. Pending the FDA's reply to our complete response, we have suspended all non-essential iloperidone-related activities.

Tasimelteon, a compound for the treatment of sleep and mood disorders, including Circadian Rhythm Sleep Disorders (CRSD). In November 2006, Vanda announced positive top-line results from the Phase III trial of tasimelteon in transient insomnia. In June 2008, the Company announced positive top-line results from the Phase III trial of tasimelteon in chronic primary insomnia. We will have to conduct additional trials prior to our filing of an NDA for tasimelteon. Tasimelteon is also ready for Phase II trials for the treatment of depression. Pending a response from the FDA with respect to our NDA for iloperidone, Vanda is concentrating its efforts on the design and evaluation of clinical development options for tasimelteon.

We hold exclusive, worldwide rights to the above compounds and, assuming successful outcomes of our clinical trials and approval by the FDA, we expect to commercialize iloperidone with our own sales force and/or commercial partners in the United States and to seek partners for commercialization of the compound outside of the United States. Given the range of potential indications for tasimelteon, we intend to pursue one or more partnerships for the development and commercialization of tasimelteon worldwide.

On November 3, 2008, we received written notice from Novartis that the license agreement related to VSF-173, a compound for the treatment of excessive sleepiness that we had been developing, had terminated in accordance with its terms as a result of our failure to satisfy a specific development milestone within the time period specified in the license agreement. As a result, we no longer hold any rights with respect to VSF-173 and Novartis has a non-exclusive worldwide license to all information and intellectual property generated by or on behalf of Vanda related to its development of VSF-173. We are currently evaluating any options that we may have with respect to VSF-173, which may include the possibility of entering into a new license agreement or other arrangement with Novartis to allow us to resume our development of VSF-173; however, there can be no assurance that we will be able to enter into such an agreement or arrangement on acceptable terms, or at all.

Our founder and Chief Executive Officer, Mihael H. Polymeropoulos, M.D., started our operations early in 2003 after establishing and leading the Pharmacogenetics Department at Novartis AG (Novartis). In acquiring and developing our compounds we have relied upon our deep expertise in the scientific disciplines of pharmacogenetics and



pharmacogenomics. These scientific disciplines examine both genetic variations among people that influence response to a particular drug, and the multiple pathways through which drugs affect people. We believe that the combination of our expertise in these disciplines and our drug development expertise may provide us with preferential access to compounds discovered by other pharmaceutical

## **Table of Contents**

companies, and will allow us to identify new uses for these compounds. These capabilities should also enable us to shorten the time it takes to commercialize a drug when compared to traditional approaches.

Our two product candidates target large prescription markets with significant unmet medical needs. Sales of antipsychotic drugs were approximately \$20 billion in 2007, according to *Health Market Prognosis* by IMS, a leading pharmaceutical market research company. These sales were achieved despite the safety concerns, moderate efficacy and poor patient compliance that are associated with these drugs. We believe that iloperidone may address some of the shortcomings of currently available drugs, based on its observed safety profile and the extended release injectable formulation for iloperidone that we plan to develop further. According to IMS, in 2006, sales of insomnia drugs generated more than \$4 billion in worldwide sales and worldwide sales of anti-depressants exceeded \$19 billion. However, approved drugs in both the sleep and mood disorders markets have sub-optimal safety and efficacy profiles. We believe tasimelteon may represent a breakthrough in each of these markets, based on the compound's demonstrated efficacy and safety to date and its novel mechanism of action.

### **Our strategy**

Our goal is to create a leading biopharmaceutical company focused on developing and commercializing products that address critical unmet medical needs through the application of our drug development expertise and our pharmacogenetics and pharmacogenomics expertise. The key elements of our strategy to accomplish this goal are to:

*Pursue the clinical development and regulatory approval of our current product candidates.* On November 27, 2007, the FDA accepted the NDA for iloperidone for the treatment of schizophrenia. In July 2008, we announced that the FDA had determined that our NDA was not approvable. On November 6, 2008, we submitted a complete response to the not-approvable letter. The FDA has accepted the complete response for review and has set a new target action date of May 6, 2009. Pending the FDA's reply to our complete response, we have suspended all non-essential iloperidone-related activities. We have successfully completed a Phase III trial of tasimelteon in transient insomnia and announced positive top-line results in November 2006. In addition, we have successfully completed a Phase III trial of tasimelteon in chronic primary insomnia and announced positive top-line results in June 2008. We will need to conduct additional Phase III trials of tasimelteon in chronic sleep disorders prior to filing an NDA for this compound. Tasimelteon is also ready for Phase II trials for the treatment of depression.

*Develop a focused commercialization capability in the United States.* Because we believe that the number of physicians that would generate the majority of prescriptions in the United States for schizophrenia is relatively small, we believe that we can cost-effectively develop our own sales force to market and sell iloperidone in the United States.

*Enter into partnerships to extend our commercial reach.* We intend to seek commercial partners for iloperidone outside the United States and, even if we are able to develop our own sales force to market and sell iloperidone in the United States, we may decide to commercialize iloperidone in the United States with a partner, rather than on our own. In addition, given the range of potential indications for tasimelteon, we intend to pursue one or more partnerships for the development and commercialization of tasimelteon worldwide.

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

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

**Table of Contents****Development programs**

We have the following product candidates in clinical development:

<b>Product candidate</b>	<b>Target indications</b>	<b>Clinical status</b>
Iloperidone (Oral)	Schizophrenia	Pending FDA decision; PDUFA date May 6, 2009
Iloperidone (Injectible)	Schizophrenia	Ready for Phase II trial
Tasimelteon	Sleep Disorders, including CRSD	Phase III trial for transient insomnia completed in 2006 Phase III trial for chronic primary insomnia completed in 2008
	Depression	Ready for Phase II trial

**Iloperidone**

We are developing iloperidone, a compound for the treatment of schizophrenia. The FDA accepted our NDA for iloperidone for the treatment of schizophrenia on November 27, 2007. The application included data from 35 clinical trials and more than 3,000 patients treated with iloperidone and also contains pharmacogenetic data aimed to further improve the benefit/risk profile of iloperidone in the treatment of patients with schizophrenia. In July 2008, we announced that the FDA had determined that our NDA for iloperidone was not approvable and indicated, among other things, that we would have to conduct additional studies and submit that data before the FDA would approve iloperidone for commercial sale for the treatment of schizophrenia. In September 2008, we met with the FDA to discuss the FDA's determination. The FDA asked us to provide a complete response to the not-approvable letter, which we submitted on November 6, 2008. The FDA accepted our complete response for review and has set a new target action date of May 6, 2009. There are no guarantees that the FDA will provide its response by May 6, 2009, nor can there be any assurances that any such response will be favorable. Pending the FDA's reply to our complete response, we have suspended all non-essential iloperidone-related activities.

***Therapeutic opportunity***

Schizophrenia is a chronic, debilitating mental disorder characterized by hallucinations, delusions, racing thoughts and other psychotic symptoms (collectively referred to as positive symptoms), as well as moodiness, anhedonia (inability to feel pleasure), loss of interest, eating disturbances and withdrawal (collectively referred to as negative symptoms), and additionally attention and memory deficits (collectively referred to as cognitive symptoms). Schizophrenia develops in late adolescence or early adulthood in approximately 1% of the world's population. Most schizophrenia patients today are treated with drugs known as atypical antipsychotics, which were first approved in the U.S. in the late 1980s. These antipsychotics have been named atypical for their ability to treat a broader range of negative symptoms than the first-generation typical antipsychotics, which were introduced in the 1950s and are now generic. Atypical antipsychotics are generally regarded as having improved side effect profiles and efficacy relative to typical antipsychotics and currently comprise approximately 90% of schizophrenia prescriptions. The global market for atypical antipsychotics was in excess of \$20 billion in 2007, according to IMS. Currently approved atypical antipsychotics include olanzapine (Zyprexa®) by Eli Lilly and Company, risperidone (Risperdal®) and paliperidone

(Invega®), each by Ortho-McNeil-Janssen Pharmaceuticals, Inc., quetiapine (Seroquel®) by AstraZeneca, aripiprazole (Abilify®) by Bristol-Myers Squibb (BMS), ziprasidone (Geodon®) by Pfizer, and generic clozapine.

***Limitations of current treatments***

The treatment of schizophrenia remains challenging because currently approved antipsychotics, even atypical antipsychotics, often induce serious side effects and offer only modest and occasional efficacy. Side effects include weight gain, diabetes, extrapyramidal symptoms (involuntary bodily movements),

**Table of Contents**

hyperprolactinemia (an elevated secretion of the hormone prolactin which can lead to sexual dysfunction and breast development and milk secretion in women and men), increased somnolence (sleepiness) and cognition difficulties. The side-effect profile and modest efficacy of currently available antipsychotics result in poor patient compliance with prescribed drug regimens. Consequently, there remains a high degree of dissatisfaction with atypical antipsychotics among physicians and patients. Research by LEK Consulting LLC (LEK Consulting), a leading consulting firm, supports this, showing that physicians employ a trial-and-error approach of prescribing a series of different atypical antipsychotics as they attempt to balance side effects and symptom management in each patient. In addition, the Clinical Antipsychotic Trials of Interventional Effectiveness (CATIE) study, conducted by the National Institute of Mental Health and reported in *The New England Journal of Medicine*, found that 74% of patients taking antipsychotics discontinued treatment within 18 months. The average time to discontinuation for these patients in the CATIE study was approximately 6 months.

***Potential advantages of iloperidone***

Iloperidone may offer several advantages over existing therapies. However, the definitive profile of the efficacy and safety of iloperidone will be determined by the final label approved by the FDA. Iloperidone is currently under review by the FDA for the treatment of schizophrenia, with a PDUFA target action date of May 6, 2009. Therefore, the following should not be considered a discussion of the definitive clinical profile of iloperidone.

*Efficacy and safety.* In a complete program of Phase II and Phase III trials comprising more than 3,000 patients, iloperidone showed efficacy equivalent to other atypical antipsychotics, as well as a reduced risk of the side effects most associated with atypical antipsychotics, including low weight gain, no induction of diabetes, low extrapyramidal symptoms, including no akathisia (inability to sit still), no hyperprolactinemia, low incidence of sleepiness and low negative effects on cognition relative to placebo. Like other atypical antipsychotics, iloperidone is associated with a prolongation of the heart's QTc interval, but in no instance did any patient taking iloperidone in the controlled portion of a clinical trial have an interval exceeding a 500-millisecond threshold that the FDA has identified as being of particular concern. Two patients experienced a prolongation of 500 milliseconds or more during the open-label extension of one trial. We believe that the safety profile of iloperidone may result in improved patient compliance with their treatment regimen.

*Extended-release injectable formulation.* Prior to our voluntary suspension of all nonessential iloperidone-related activities pending the FDA's reply to our complete response to the not-approvable letter, we were developing an extended-release injectable formulation for iloperidone, which is administered once every four weeks and which we believe will be a compelling complement to our oral formulation for both physicians and patients. Novartis conducted a two-month Phase I/IIa safety trial of this formulation in schizophrenia patients, in which it demonstrated the benefit of consistent release over a four-week time period with no greater side effects relative to oral dosing. If the FDA approves the oral formulation of iloperidone, we intend to resume the development of the injectable formulation and we believe we will need to conduct additional trials with this formulation to be able to file for FDA approval. The commercial potential for our extended-release injectable formulation has been demonstrated by the success of the injectable formulation for risperidone, Risperdal® Consta®, which achieved worldwide sales of approximately \$1.1 billion in 2007, according to Alkermes Company press releases. We believe that our four-week formulation for iloperidone will be an attractive alternative to Risperdal® Consta®, which is required to be injected once every two weeks. Additionally, and unlike Risperdal® Consta®, we do not believe that the injectable formulation for iloperidone will require oral titration, which would result in simplified dosing.

Additionally, we plan to continue to apply our pharmacogenetics and pharmacogenomics expertise to develop tools that may allow physicians to avoid the trial-and-error approach to prescribing antipsychotic medications for their patients.



## **Table of Contents**

*Pharmacogenetic evaluation of iloperidone's efficacy.* Based on the results of our most recent Phase III trial, as well as analyses of prior clinical data for iloperidone, we have determined that certain patients may be more likely to respond to iloperidone and to enjoy better treatment results relative to the general schizophrenia patient population. These patients have a common mutation of a gene, linked to central nervous system function, that is estimated to occur in approximately 70% of schizophrenia patients. We developed a genetic test which we used in our recently completed Phase III trial and confirmed this correlation. According to market research conducted by LEK Consulting, physicians treating schizophrenia patients would enthusiastically welcome a genetic test that would enable them to identify likely responders to iloperidone, given the unpredictable efficacy and serious side effects currently associated with atypical antipsychotics, and be more likely to prescribe iloperidone as a result.

*Pharmacogenetic evaluation of iloperidone's safety.* Based on the results of our most recent Phase III trial, and other pharmacogenetic analysis, we have discovered that patients with an uncommon mutation of a well understood gene affecting drug metabolism experience higher levels of iloperidone in their blood and may experience longer QTc intervals while taking iloperidone. We estimate that this genetic attribute is found in approximately 25-30% of schizophrenia patients, comprised of poor metabolizers (approximately 5-10% of schizophrenia patients) and intermediate metabolizers (approximately 20% of schizophrenia patients). We believe that certain physicians may choose to test patients for this mutation if they have a concern about QTc interval prolongation with respect to a particular patient.

## ***Intellectual property***

Iloperidone and its metabolites, formulations, genetic markers and uses are covered by a total of twenty-two patent and patent application families worldwide. The primary new chemical entity patent covering iloperidone expires normally in 2011 in the United States and 2010 in most of the major markets in Europe. In the United States, the United States Drug Price Competition and Patent Term Restoration act of 1984, more commonly known as the Hatch-Waxman Act provides for an extension of new chemical entity patents for a period of up to five years following the expiration of the patent covering that compound to compensate for time spent in development. We believe that iloperidone will qualify for the full five-year patent term extension. In Europe, similar legislative enactments provide for five-year extensions of new chemical entity patents through the granting of Supplementary Protection Certificates, and we believe that iloperidone will qualify for this extension as well. Consequently, assuming that we are granted all available extensions by the FDA and European regulatory authorities and that we receive regulatory approval, we expect that our rights to commercialize iloperidone will be exclusive until 2016 in the United States and until 2015 in Europe. Additionally, the patent application covering the depot formulation for iloperidone, if it is granted, will expire normally in 2022. Several other patent applications covering metabolites, uses, formulations and genetic markers relating to iloperidone extend beyond 2020. Pursuant to a European Union directive, we may also acquire market exclusivity (sometimes referred to as, data exclusivity) in most European Union countries for iloperidone for a period of 10 years from the date of its regulatory approval in Europe (with the possibility for a further one-year extension), even though the European patents covering iloperidone will likely expire prior to the end of such 10-year period. No generic versions of iloperidone would be permitted to be marketed or sold during this 10-year period in most European countries.

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

## **Tasimelteon**



Tasimelteon is an oral compound in development for sleep and mood disorders, including Circadian Rhythm Sleep Disorders (CRSD). The compound binds selectively to the brain's melatonin receptors, which are thought to govern the body's natural sleep/wake cycle. Compounds that bind selectively to these receptors are thought to be able to help treat sleep disorders, and additionally are believed to offer potential benefits in mood disorders. We announced positive top-line results from our Phase III trial of tasimelteon in transient

## **Table of Contents**

insomnia in November 2006. In June 2008, the Company announced positive top-line results from the Phase III trial of tasimelteon in chronic primary insomnia. Tasimelteon is also ready for Phase II trials for the treatment of depression.

### ***Therapeutic opportunity***

Industry sources estimate that of the 73 million U.S. adults who suffer from some form of insomnia, only approximately 11 million currently receive treatment. Sleep disorders are segmented into three major categories: primary insomnia, secondary insomnia and circadian rhythm sleep disorders. Insomnia is a symptom complex that comprises difficulty falling asleep or staying asleep, or non-refreshing sleep, in combination with daytime dysfunction or distress. The symptom complex can be an independent disorder (primary insomnia) or be a result of another condition such as depression or anxiety (secondary insomnia). Circadian rhythm sleep disorders result from a misalignment of the sleep/wake cycle and an individual's daily activities or lifestyle. The circadian rhythm is the rhythmic output of the human biological clock and is governed primarily by the hormone melatonin. Both the timing of behavioral events (activity, sleep, and social interactions) and the environmental light/dark cycle result in a sleep/wake cycle that follows the circadian rhythm. Examples of circadian rhythm sleep disorders include transient disorders such as jet lag and chronic disorders such as shift work sleep disorder. Market research we have conducted with LEK Consulting indicates that circadian rhythm sleep disorders represent a significant portion of the market for sleep disorders. In 2006, the sleep disorder drug market generated approximately \$4.5 billion in worldwide sales, according to IMS.

There are a number of drugs approved and prescribed for patients with sleep disorders. The most commonly prescribed drugs are hypnotics, such as generic zolpidem, zolpidem tartrate (Ambien CR<sup>®</sup>, sanofi-aventis), eszopiclone (Lunesta<sup>®</sup>, Sepracor, Inc.) and zaleplon (Sonata<sup>®</sup>, King Pharmaceuticals, Inc.). Hypnotics work by acting upon a set of brain receptors known as GABA receptors, which are separate and distinct from the melatonin receptors to which tasimelteon binds. Several drugs in development, including indiplon (Neurocrine Biosciences), also utilize a mechanism of action involving binding to GABA receptors. Members of the benzodiazapine class of sedatives are also approved for insomnia, but their usage has declined due to an inferior safety profile compared to hypnotics. Anecdotal evidence also suggests that sedative antidepressants, such as trazodone and doxepin, are prescribed off-label for insomnia. The FDA approved drugs for treatment of insomnia also include ramelteon (Rozerem<sup>™</sup>, Takeda Pharmaceuticals Company Limited), a compound with a mechanism of action similar to tasimelteon. There are no FDA-approved treatments for insomnia specifically related to Circadian Rhythm Sleep Disorders.

### ***Limitations of current treatments***

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

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

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

We believe that none of the drugs used and approved for sleep, other than Rozerem™, work through the body's natural sleep/wake cycle, which is governed by melatonin. We believe that, for patients whose sleep disruption is due to a misalignment of this sleep/wake cycle and these patients need to sleep (as is the case in circadian rhythm sleep disorders), a drug that naturally modulates the sleep/wake cycle

**Table of Contents**

would be an attractive new alternative because it would address the underlying cause of the sleeplessness, rather than merely addressing its symptoms.

***Potential advantages of tasimelteon***

We believe that tasimelteon may offer efficacy similar to the most efficacious of the approved sleep drugs, and that it may provide significant benefits to patients beyond those offered by the approved drugs. We believe that tasimelteon is unlikely to be scheduled as a controlled substance by the DEA because Rozerem<sup>tm</sup>, which has a similar mechanism of action to tasimelteon, was shown not to have potential for abuse and was not classified as a Schedule IV controlled substance by the DEA. However, despite the fact that the drugs have a similar mechanism of action, our Phase III results have demonstrated that tasimelteon may offer superior sleep maintenance to Rozerem<sup>tm</sup>. Tasimelteon also appears to be safe and well-tolerated, with no significant side effects or effects on next-day performance. For patients with circadian rhythm disorders, tasimelteon may be able to align the patient's sleep/wake cycle with his or her lifestyle, something we believe no approved sleep therapy has demonstrated. For example, in our Phase II trial of tasimelteon in transient insomnia with 37 healthy participants, tasimelteon induced a statistically significant ( $p < 0.025$ ) shift in circadian rhythm of up to five hours on the first night.

***Overview of Phase III clinical trials***

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

Tasimelteon achieved significant results in multiple endpoints, demonstrating a benefit in both sleep onset, or time to fall asleep, and sleep maintenance, or ability to stay asleep. Based on these trial results, we believe that tasimelteon will compare favorably to efficacy achieved by currently approved insomnia drugs, not only for circadian rhythm sleep disorders but also for other types of insomnia. The Phase III trial also demonstrated that tasimelteon was safe and well-tolerated, with no significant side effects versus placebo and no impairment of next-day performance or mood.

In June 2008, we reported positive top-line results in a randomized, double-blind, placebo-controlled Phase III trial in chronic primary insomnia that enrolled 324 patients. The trial examined tasimelteon at 20 and 50 milligrams versus placebo over a period of 35 days. The trial measured time to fall asleep and sleep maintenance, as well as next-day performance. We will need to conduct additional Phase III trials of tasimelteon for the treatment of chronic sleep disorders to receive FDA approval of tasimelteon for the treatment of insomnia.

***Potential indication for depression***

We believe that tasimelteon may also be effective in treating depression. Agomelatine, another drug that acts on the brain's melatonin receptors, has demonstrated efficacy and safety in the treatment of depression that compared favorably to an approved antidepressant, Paxil<sup>®</sup> (paroxetine, GSK), in a Phase III trial. While the precise mechanism for the effect of drugs like tasimelteon, agomelatine and Rozerem<sup>tm</sup>, which act on the brain's melatonin receptors, is currently unknown, it is possible that, by improving sleep, these drugs could improve mood, since depressed patients are likely to have sleep disorders. It is also possible that mood disorders such as depression have an association with circadian rhythm misalignments.

Of the approximately 29 million adults in the United States who suffer from some form of depression, over 11 million are currently treated with a prescription antidepressant medication. Sales of antidepressants exceeded \$19 billion

globally in 2007, according to IMS.

We believe that tasimelteon will be differentiated from approved antidepressants in several ways. In the Phase III trial of agomelatine described above, agomelatine showed significantly improved mood in two weeks, versus four weeks for Paxil®. Consequently, tasimelteon may, with its similar properties to agomelatine,

## **Table of Contents**

offer a more rapid onset of action than approved antidepressants. We believe that tasimelteon should also have an improved side effect profile when compared to approved products because we believe that it should not have the sexual side effects, weight gain, and sleep disruption associated with these products.

Tasimelteon is ready for Phase II trials in depression. It has demonstrated an antidepressant effect in animal models and has completed several Phase I trials, including one with four weeks of exposure, showing none of the serious side effects associated with the approved antidepressants.

### ***Intellectual property***

Tasimelteon and its formulations and uses are covered by a total of eleven patent and patent application families worldwide. The primary new chemical entity patent covering tasimelteon expires normally in 2017 in the United States and in most European markets. We believe that, like iloperidone, tasimelteon will meet the various criteria of the Hatch-Waxman Act and will receive five additional years of patent protection in the United States, which would extend its patent protection in the United States until 2022. In Europe, similar legislative enactments provide for five-year extensions of European new chemical entity patents through the granting of Supplementary Protection Certificates, and we believe that tasimelteon will qualify for such an extension, which would extend European patent protection for tasimelteon until 2022. Several other patent applications covering uses of tasimelteon will, if granted, provide exclusive rights for these uses until 2026. Our rights to the new chemical entity patent covering tasimelteon and related intellectual property have been acquired through a license with BMS. Please see License agreements below for a discussion of this license.

### **License agreements**

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

### ***Iloperidone***

We acquired exclusive worldwide rights to patents for iloperidone through a sublicense agreement with Novartis. A predecessor company of sanofi-aventis, Hoechst Marion Roussel, Inc. (HMRI), discovered iloperidone and completed early clinical work on the compound. In 1996, following a review of its product portfolio, HMRI licensed its rights to the iloperidone patents to Titan Pharmaceuticals, Inc. (Titan) on an exclusive basis. In 1997, soon after it had acquired its rights, Titan sublicensed its rights to iloperidone on an exclusive basis to Novartis. In June 2004, we acquired exclusive worldwide rights to these patents to develop and commercialize iloperidone through a sublicense agreement with Novartis. In partial consideration for this sublicense, we paid Novartis an initial license fee of \$500,000 and are obligated to make future milestone payments to Novartis of less than \$100 million in the aggregate (the majority of which are tied to sales milestones), as well as royalty payments to Novartis at a rate which, as a percentage of net sales, is in the mid-twenties. In November 2007, we met a milestone under this license agreement relating to the acceptance of our filing of the NDA for iloperidone for the treatment of schizophrenia and made a license payment of \$5 million to Novartis.

Our rights with respect to the patents to develop and commercialize iloperidone may terminate, in whole or in part, if we fail to meet certain development or commercialization milestones relating to the time it takes for us to launch iloperidone commercially following regulatory approval, and the time it takes for us to receive regulatory approval following our submission of an NDA or equivalent foreign filing. Additionally, our rights may terminate in whole or in part if we do not meet certain other obligations under our sublicense agreement to make royalty and milestone payments, if we fail to comply with requirements in our sublicense agreement regarding our financial condition, or if we do not abide by certain restrictions in our sublicense agreement regarding other development activities.

*Tasimelteon*

In February 2004, we entered into a license agreement with BMS under which we received an exclusive worldwide license under certain patents and patent applications, and other licenses to intellectual property, to

## **Table of Contents**

develop and commercialize tasimelteon. In partial consideration for the license, we paid BMS an initial license fee of \$500,000. We are also obligated to make future milestone payments to BMS of less than \$40 million in the aggregate (the majority of which are tied to sales milestones) as well as royalty payments based on the net sales of tasimelteon at a rate which, as a percentage of net sales, is in the low teens. We made a milestone payment to BMS of \$1,000,000 under this license agreement in 2006 relating to the initiation of our first Phase III clinical trial for tasimelteon. We are also obligated under this agreement to pay BMS a percentage of any sublicense fees, upfront payments and milestone and other payments (excluding royalties) that we receive from a third party in connection with any sublicensing arrangement, at a rate which is in the mid-twenties. We have agreed with BMS in our license agreement for tasimelteon to use our commercially reasonable efforts to develop and commercialize tasimelteon and to meet certain milestones in initiating and completing certain clinical work.

BMS holds certain rights with respect to tasimelteon in the license agreement. If we have not agreed to one or more partnering arrangements to develop and commercialize tasimelteon in certain significant markets with one or more third parties after the completion of the Phase III program, BMS has the option to exclusively develop and commercialize tasimelteon on its own on pre-determined financial terms, including milestone and royalty payments.

Either party may terminate the tasimelteon license agreement under certain circumstances, including a material breach of the agreement by the other. In the event that BMS has not exercised its option to reacquire the rights to tasimelteon and we terminate our license, or if BMS terminates our license due to our breach, all rights licensed and developed by us under this agreement will revert or otherwise be licensed back to BMS on an exclusive basis.

## **Government regulation**

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

### ***United States government regulation***

#### ***FDA approval process***

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

The steps required before a drug may be marketed in the United States include:

pre-clinical laboratory tests, animal studies and formulation studies under Current Good Laboratory Practices (cGLP)



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submission to the FDA of an investigational new drug application, or IND, which must become effective before human clinical trials may begin

execution of adequate and well-controlled clinical trials to establish the safety and efficacy of the product for each indication for which approval is sought

submission to the FDA of an NDA

## **Table of Contents**

satisfactory completion of an FDA inspection of the manufacturing facility or facilities at which the product is produced to assess compliance with Current Good Manufacturing Practices (cGMP)

FDA review and approval of the NDA

Pre-clinical studies generally are conducted in laboratory animals to evaluate the potential safety and activity of a product. Violation of the FDA's cGLP regulations can, in some cases, lead to invalidation of the studies, requiring these studies to be replicated. In the United States, drug developers submit the results of pre-clinical trials, together with manufacturing information and analytical and stability data, to the FDA as part of the IND, which must become effective before clinical trials can begin in the United States. An IND becomes effective 30 days after receipt by the FDA unless before that time the FDA raises concerns or questions about issues such as the proposed clinical trials outlined in the IND. In that case, the IND sponsor and the FDA must resolve any outstanding FDA concerns or questions before clinical trials can proceed. If these concerns or questions are unresolved, the FDA may not allow the clinical trials to commence.

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

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

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

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

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

Phase III: refers to expanded controlled and uncontrolled clinical trials. These trials are performed after preliminary evidence suggesting effectiveness of a drug has been obtained. Phase III trials are intended to

gather additional information about the effectiveness and safety that is needed to evaluate the overall benefit-risk relationship of the drug and to provide an adequate basis for physician labeling. Phase III trials usually include several hundred to several thousand subjects.

Phase I, II and III testing may not be completed successfully within any specified time period, if at all. The FDA closely monitors the progress of each of the three phases of clinical trials that are conducted in the United States and may, at its discretion, reevaluate, alter, suspend or terminate the testing based upon the data accumulated to that point and the FDA's assessment of the risk/benefit ratio to the patient. A clinical program

**Table of Contents**

is designed after assessing the causes of the disease, the mechanism of action of the active pharmaceutical ingredient of the product candidate and all clinical and pre-clinical data of previous trials performed. Typically, the trial design protocols and efficacy endpoints are established in consultation with the FDA. Upon request through a special protocol assessment, the FDA can also provide specific guidance on the acceptability of protocol design for clinical trials. The FDA or we may suspend or terminate clinical trials at any time for various reasons, including a finding that the subjects or patients are being exposed to an unacceptable health risk. The FDA can also request additional clinical trials be conducted as a condition to product approval. During all clinical trials, physicians monitor the patients to determine effectiveness and to observe and report any reactions or other safety risks that may result from use of the drug candidate.

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

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

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

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

In addition to studies requested by the FDA after approval, we may have to conduct other trials and studies to explore use of the approved compound for treatment of new indications, which require FDA approval. The purpose of these

trials and studies is to broaden the application and use of the drug and its acceptance in the medical community.

## **Table of Contents**

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

On September 27, 2007, the Food and Drug Administration Amendments Act, or the FDAAA, was enacted into law, amending both the FDC Act and the Public Health Service Act. The FDAAA makes a number of substantive and incremental changes to the review and approval processes in ways that could make it more difficult or costly to obtain approval for new pharmaceutical products, or to produce, market and distribute existing pharmaceutical products. Most significantly, the law changes the FDA's handling of postmarket drug product safety issues by giving the FDA authority to require post approval studies or clinical trials, to request that safety information be provided in labeling, or to require an NDA applicant to submit and execute a Risk Evaluation and Mitigation Strategy, or REMS.

The FDAAA also reauthorized the authority of the FDA to collect user fees to fund the FDA's review activities and made certain changes to the user fee provisions to permit the use of user fee revenue to fund FDA's drug safety activities and the review of Direct-to-Consumer advertisements.

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

### *The Hatch-Waxman Act*

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

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

If the ANDA applicant has provided a Paragraph IV certification to the FDA, the applicant must also send notice of the Paragraph IV certification to the NDA and patent holders once the ANDA has been accepted for filing by the FDA. The NDA and patent holders may then initiate a patent infringement lawsuit in response to the notice of the

Paragraph IV certification. The filing of a patent infringement lawsuit within 45 days of the receipt of a Paragraph IV certification automatically prevents the FDA from approving the

## **Table of Contents**

ANDA until the earlier of 30 months, expiration of the patent, settlement of the lawsuit or a decision in the infringement case that is favorable to the ANDA applicant.

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

### ***Foreign regulation***

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

Under European Union regulatory systems, we may submit marketing authorization applications either under a centralized or decentralized procedure. The centralized procedure, which is available for products produced by biotechnology or which are highly innovative, provides for the grant of a single marketing authorization that is valid for all European Union member states. This authorization is a marketing authorization approval. The decentralized procedure provides for mutual recognition of national approval decisions. Under this procedure, the holder of a national marketing authorization may submit an application to the remaining member states. Within 90 days of receiving the applications and assessment report, each member state must decide whether to recognize approval. This procedure is referred to as the mutual recognition procedure.

In addition, regulatory approval of prices is required in most countries other than the United States. We face the risk that the resulting prices would be insufficient to generate an acceptable return to us or our collaborators.

### **Third-party reimbursement and pricing controls**

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

In many foreign markets, including the countries in the European Union and Japan, pricing of pharmaceutical products is subject to governmental control. In the United States, there have been, and we expect that there will



continue to be, a number of federal and state proposals to implement similar governmental pricing control. While we cannot predict whether such legislative or regulatory proposals will be

## **Table of Contents**

adopted, the adoption of such proposals could have a material adverse effect on our business, financial condition and profitability.

### **Marketing and sales**

We have suspended all pre-launch commercial activities relating to iloperidone pending the outcome of the FDA's review of our complete response. We are uncertain at this time when or if we expect to start marketing iloperidone commercially. The time it takes to receive cash inflows from the sale of iloperidone is highly dependent on facts and circumstances that we may not be able to control and are subject to a number of risks. We currently have limited sales, marketing or distribution capabilities and do not plan to continue to develop these capabilities internally, or enter into partnering arrangements to the extent that we believe large sales and marketing forces will be necessary at this time. However, because we believe that the number of physicians that would generate the majority of prescriptions for iloperidone in the United States is relatively small, we believe that we can cost-effectively develop our own sales force to market and sell iloperidone in the United States. We intend to seek commercial partners for iloperidone outside the United States and, even if we are able to develop our own sales force to market and sell iloperidone in the United States, we may decide to commercialize iloperidone in the United States with a partner, rather than on our own. In addition, given the range of potential indications for tasimelteon, we intend to pursue one or more partnerships for the development and commercialization of tasimelteon worldwide.

### **Patents and proprietary rights; Hatch-Waxman protection**

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

Our two current compounds in clinical development are covered by new chemical entity and other patents. These patents cover the active portions of our compounds and provide patent protection for all formulations containing these active portions. The new chemical entity patent for iloperidone is owned by sanofi-aventis, and other patents and patent applications relating to iloperidone are owned by Novartis. BMS owns the new chemical entity patent for tasimelteon. For both compounds we have obtained exclusive worldwide rights to develop and commercialize the compounds covered by these patents through license and sublicense arrangements. For more on these license and sublicense arrangements, please see [License agreements](#) above. In addition, we have generated intellectual property, and filed patent applications covering this intellectual property, for each of the compounds.

The new chemical entity patent covering iloperidone expires normally in 2011 in the United States and in 2010 in most European markets. The new chemical entity patent covering tasimelteon expires in 2017 in the United States and most European markets. Additionally, for each of our late-stage compounds, an additional period of exclusivity in the United States of up to five years following the expiration of the patent covering that compound may be obtained pursuant to the Hatch-Waxman Act. Assuming we gain such a five-year extension and that we continue to have our intellectual property rights under our sublicense and license agreements, we would have exclusive new chemical entity patent rights in the U.S. for iloperidone until 2016 and for tasimelteon until 2022. In Europe, similar legislative enactments may allow us to obtain five-year extensions of the European new chemical entity patents covering our product candidates through the granting of Supplementary Protection Certificates, which would allow us to have exclusive European new chemical entity patent rights for iloperidone until 2015 and for tasimelteon until 2022. Additionally, a directive in the European Union allows companies who receive European regulatory approval for a new compound to have a 10-year period of market exclusivity in most European countries for that compound (with the possibility of a further one-year extension), beginning on the date of such European regulatory approval, regardless of when the European new chemical entity patent covering such compound expires. No generic version of an approved drug may be marketed or sold in most European countries during this 10-year period. This directive may

be of particular importance with respect to iloperidone, since the European new chemical entity patent for iloperidone will likely expire prior to the end of this 10-year period of market exclusivity.

## **Table of Contents**

Aside from the new chemical entity patents covering our current late-stage compounds, as of December 31, 2008 we had twenty-two pending provisional patent applications in the United States, five U.S. national stage applications under U.S.C. 371 and five pending Patent Cooperation Treaty applications. The claims in these various patents and patent applications are directed to compositions of matter, including claims covering other product candidates, pharmaceutical compositions, genetic markers, and methods of use.

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

## **Manufacturing**

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

If any of our product candidates are approved for commercial use, we plan to rely on third-party contract manufacturers to produce sufficient quantities for large-scale commercialization. If we do enter into commercial manufacturing arrangements with third parties, these third-party manufacturers will be subject to extensive governmental regulation. Specifically, regulatory authorities in the markets which we intend to serve will require that drugs be manufactured, packaged and labeled in conformity with cGMP or equivalent foreign standards. We intend to engage only those contract manufacturers who have the capability to manufacture drug products in compliance with cGMP and other applicable standards in bulk quantities for commercial use.

## **Competition**

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

We believe the primary competitors for each of our product candidates are as follows:

For iloperidone in the treatment of schizophrenia, the atypical antipsychotics Risperdal<sup>®</sup> (risperidone), including the depot formulation Risperdal<sup>®</sup> Consta<sup>®</sup>, and Invega<sup>®</sup> (paliperidone), each by Ortho-McNeil-Janssen Pharmaceuticals, Inc., Zyprexa<sup>®</sup> (olanzapine) by Eli Lilly and Company, Seroquel<sup>®</sup> (quetiapine) by AstraZeneca PLC, Abilify<sup>®</sup> (aripiprazole) by BMS/Otsuka Pharmaceutical Co., Ltd., Geodon<sup>®</sup> (ziprasidone) by Pfizer Inc., and generic clozapine, as well as the typical antipsychotics haloperidol, chlorpromazine, thioridazine, and sulpiride (all of which are generic). In addition to the approved products,

compounds in Phase III trials (or for which an NDA has been recently filed) for the treatment of schizophrenia include bifeprunox (Solvay S.A./Lundbeck A/S), and asenapine (Schering-Plough Corporation) and pimavanserin (Acadia Pharmaceuticals).

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

## **Table of Contents**

compounds such as zolpidem, trazodone and doxepin, and over-the-counter remedies such as Benadryl® and Tylenol PM®. In addition to the approved products, compounds in Phase III trials for insomnia (or for which an NDA has been recently filed) include indiplon (Neurocrine Biosciences, Inc.) and low-dose doxepin (Silenor™) by Somaxon Pharmaceuticals, Inc.

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

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

## **Employees**

On December 16, 2008, we committed to a plan of termination that resulted in a work force reduction of 17 employees, including two officers, in order to reduce operating costs. We commenced notification of employees affected by the workforce reduction on December 17, 2008. As of December 31, 2008, we employed 24 full-time employees. This represents approximately a 55% decrease from the 53 employees we had on August 1, 2008.

Of the 24 full-time employees we had as of December 31, 2008, 15 were primarily engaged in research and development activities. None of our employees are represented by a labor union. We have not experienced any work stoppages and consider our employee relations to be good.

## **Corporate information**

We were incorporated in Delaware in 2002. Our principal executive offices are located at 9605 Medical Center Drive, Suite 300, Rockville, Maryland, 20850 and our telephone number is (240) 599-4500. Our website address is [www.vandapharma.com](http://www.vandapharma.com).

## **Available Information**

Vanda Pharmaceuticals Inc. files annual, quarterly, and current reports, proxy statements, and other documents with the Securities and Exchange Commission (SEC) under the Securities Exchange Act of 1934 (the Exchange Act). The public may read and copy any materials that we file with the SEC at the SEC's Public Reference Room at 100 F Street, NE, Washington, DC 20549. The public may obtain information on the operation of the Public Reference Room by calling the SEC at 1-800-SEC-0330. Also, the SEC maintains an Internet website that contains reports, proxy and information statements, and other information regarding issuers, including us, that file electronically with the SEC. The public can obtain any documents that we file with the SEC at [www.sec.gov](http://www.sec.gov).

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

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

**Table of Contents**

**ITEM 1A. RISK FACTORS**

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

**Risks related to our business and industry**

***If we fail to obtain approval for and commercialize our most advanced product candidate, iloperidone, we may have to curtail our product development programs and our business would be materially harmed.***

We have invested a significant portion of our time, financial resources and collaboration efforts in the development of our most advanced product candidate, iloperidone, a compound for the treatment of schizophrenia. Our near-term ability to generate revenues and our future success, in large part, depends on the development and commercialization of iloperidone.

In November 2007, we announced that the FDA had accepted our New Drug Application (NDA) for iloperidone in schizophrenia. On July 25, 2008, we received a letter from the FDA stating that our NDA for iloperidone in schizophrenia was not approvable. The FDA indicated that it would require an additional clinical trial comparing iloperidone to placebo and including an active comparator such as olanzapine (Zyprexa<sup>®</sup>, Eli Lilly and Company) or risperidone (Risperdal<sup>®</sup>, Ortho-McNeil-Janssen Pharmaceuticals, Inc.) in patients with schizophrenia to further demonstrate the compound's efficacy. The FDA also stated that it would require us to obtain additional safety data for patients at a dose range of 20 to 24 mg/day of iloperidone. On September 10, 2008, we met with the FDA to discuss the FDA's position. The FDA asked us to provide a complete response to the not-approvable letter, which we submitted on November 6, 2008. The FDA accepted the complete response for review and has set a new target action date of May 6, 2009. If we are unable to satisfactorily demonstrate efficacy compared to placebo as well as an active comparator, if the FDA disagrees with our characterization approach or does not agree that we have demonstrated adequate efficacy for iloperidone, if we fail to resolve questions raised in the FDA's correspondence regarding the iloperidone NDA or if we otherwise fail to meet FDA requirements for the NDA or obtain FDA approval for, and successfully commercialize, iloperidone, we may never realize revenue from this product and we may have to curtail our other product development programs. As a result, our business would be materially harmed.

***Our success is dependent on the success of our two product candidates in clinical development: iloperidone and tasimelteon. If either of these product candidates is determined to be unsafe or ineffective in humans, whether in clinical trials or commercially, our business will be materially harmed.***

Despite the positive results of our completed trials, we are uncertain whether either of our current product candidates in clinical development will ultimately prove to be effective and safe in humans. Frequently, product candidates that have shown promising results in clinical trials have suffered significant setbacks in later clinical trials or even after they are approved for commercial sale. Future uses of any of our product candidates, whether in clinical trials or commercially, may reveal that the product candidate is ineffective, unacceptably toxic, has other undesirable side effects or is otherwise not fit for further use. If we are unable to discover and develop products that are safe and effective, our business will be materially harmed.



**Table of Contents**

***Any failure or delay in completing clinical trials for our product candidates could severely harm our business.***

Pre-clinical studies and clinical trials required to demonstrate the safety and efficacy of our product candidates are time-consuming and expensive and together take several years to complete. The completion of clinical trials for our product candidates may be delayed by many factors, including:

our inability to manufacture or obtain from third parties materials sufficient for use in pre-clinical studies and clinical trials

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 product candidates during clinical trials

unforeseen safety issues or side effects

governmental or regulatory delays and changes in regulatory requirements and guidelines

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

***We face heavy government regulation, and FDA regulatory approval of our products is uncertain.***

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

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

a drug candidate 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 do

the FDA may not approve our manufacturing process

the FDA may change their approval policies or adopt new regulations

the FDA may not meet, or may extend, the PDUFA date with respect to a particular NDA

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

Moreover, if and when our products do obtain marketing approval, the marketing, distribution and manufacture of such products would remain subject to extensive ongoing regulatory requirements. Failure to comply with applicable regulatory requirements could result in:

warning letters

finances

civil penalties

**Table of Contents**

injunctions

recall or seizure of products

total or partial suspension of production

refusal of the government to grant future approvals

withdrawal of approvals

criminal prosecution

Any delay or failure by us to obtain regulatory approvals for our product candidates could diminish competitive advantages that we may attain and would adversely affect the marketing of our products. We have not received regulatory approval to market any of our product candidates in any jurisdiction.

In November 2007, we announced that the FDA had accepted the NDA for iloperidone in schizophrenia. In July 2008, we announced that the FDA had determined that our NDA was not approvable and indicated, among other things, that we would have to conduct additional studies and submit that data before the FDA would approve iloperidone for commercial sale for the treatment of schizophrenia. Performance and completion of additional clinical studies will require years of testing and, even if positive results are achieved, may not result in the FDA's approval of iloperidone. In September 2008, we met with the FDA to discuss the FDA's determination. The FDA asked us to provide a complete response to the not-approvable letter, which we submitted on November 6, 2008. The FDA has accepted the complete response for review and has set a new target action date of May 6, 2009. We have no assurances that the response we receive from the FDA will be favorable. An unfavorable response may have a materially harmful effect on our business.

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

We 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 our discovery, research and development work. In addition, we cannot predict the extent of government regulations or the impact of new governmental regulations that might significantly harm the discovery, development, production and marketing of our products. We may be required to incur significant costs to comply with current or future laws or regulations, and we may be adversely affected by the cost of such compliance.

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

We intend to market our products outside the United States with one or more commercial partners. In order to market our products in foreign jurisdictions, we 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. We have no experience with obtaining any such foreign approvals. Additionally, the foreign regulatory

approval process may include all of the risks associated with obtaining FDA approval. For all of these reasons, we may not obtain foreign regulatory approvals on a timely basis, if at all. Approval by the FDA does not ensure approval by regulatory authorities in other countries or jurisdictions, and approval by one foreign regulatory authority does not ensure approval by regulatory authorities in other foreign countries or jurisdictions or by the FDA. We may 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.

**Table of Contents**

***Our product candidates may cause undesirable side effects or have other properties that could delay or prevent their regulatory approval or limit their marketability.***

Undesirable side effects caused by our product candidates could interrupt, delay or halt clinical trials and could result in the denial of regulatory approval by the FDA or other regulatory authorities for any or all targeted indications, and in turn prevent us from commercializing our product candidates and generating revenues from their sale. For example, like many other drugs in its class, iloperidone is associated with a prolongation of the heart's QTc interval, which is a measurement of specific electrical activity in the heart as captured on an electrocardiogram, corrected for heart rate. A QTc interval that is significantly prolonged may result in an abnormal heart rhythm with adverse consequences including fainting, dizziness, loss of consciousness and death. No patient in the controlled portion of any of iloperidone's clinical trials was observed to have an interval that exceeded a 500-millisecond threshold of particular concern to the FDA. Two patients experienced a prolongation of 500 milliseconds or more during the open-label extension of one trial. We will continue to assess the side effect profile of iloperidone and our other product candidates in our ongoing clinical development program.

In addition, if any of our product candidates receive marketing approval and we or others later identify undesirable side effects caused by the product, we could face one or more of the following:

regulatory authorities may require the addition of labeling statements, such as a "black box" warning or a contraindication

regulatory authorities may withdraw their approval of the product

we may be required to change the way the product is administered, conduct additional clinical trials or change the labeling of the product

our reputation may suffer

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

***Our product candidates may never achieve market acceptance even if we obtain regulatory approvals.***

Even if we receive regulatory approvals for the sale of our product candidates, 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 of our product candidates 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 the product candidate, and the effectiveness of our marketing and distribution capabilities. If our product candidates fail to gain market acceptance, we may be unable to earn sufficient revenue to continue our business. If our product candidates 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.

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

Our activities will necessitate significant uses of working capital for the foreseeable future. Our capital requirements will depend on many factors, including the success of our research and development efforts, the satisfaction of certain regulatory requirements, payments received under contractual agreements with other parties, if any, and the status of competitive products. However, given the recent decision by the FDA with respect to the NDA for iloperidone, and that any additional study or studies required by the FDA in order to obtain approval of iloperidone would require significant capital in excess of our currently available resources,

## **Table of Contents**

we are now operating under a reduced spending plan and believe that, if we continue to operate under our reduced spending plan, our existing cash, cash equivalents and marketable securities will be sufficient to fund operations at least through 2010. In budgeting for our activities, we have relied on a number of assumptions, including assumptions that we will not conduct any additional clinical trials for either of the oral or injectable formulations of iloperidone, that we will not engage in any further commercial activities related to iloperidone, that we will not engage in further in-licensing activities, that we will not receive any proceeds from potential partnerships, that we will not conduct additional trials for tasimelteon, that we will be able to retain our key personnel, that we will continue to seek FDA approval of iloperidone, that we will continue to evaluate clinical and pre-clinical compounds for potential development, and that we will not incur any significant contingent liabilities.

We may need to raise additional funds if one or more of our assumptions proves to be incorrect or if we choose to resume our commercialization efforts with respect to iloperidone, expand our product development efforts, conduct additional clinical trials for one or more of our product candidates or seek to acquire additional product candidates, and we may decide to raise additional funds even before they are needed if the conditions for raising capital are favorable. In our capital-raising efforts, we may seek to sell additional equity or debt securities or obtain a bank credit facility. The sale of additional equity or debt securities, if convertible, could result in dilution to our stockholders. The incurrence of indebtedness would result in increased fixed obligations and could also result in covenants that would restrict our operations. However, we may not be able to raise additional funds on acceptable terms, or at all. Given the current global economic climate, we may have more difficulty raising funds than we would during a period of economic stability. If we are unable to secure sufficient capital to fund our research and development activities, we may not be able to continue operations, or we may have to enter into 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 collaborations, if consummated prior to proof-of-efficacy or safety of a given product candidate, could impair our ability to realize value from that product candidate.

***We have incurred operating losses in each year since our inception and expect to continue to incur substantial and increasing losses for the foreseeable future.***

We have a limited operating history. We have not generated any revenue from product sales to date and we cannot estimate with precision the extent of our future losses. We do not currently have any products that have been approved for commercial sale and we may never generate revenue from selling products or achieve profitability. We expect to continue to incur substantial and increasing losses for the foreseeable future, particularly if we receive FDA approval of our iloperidone NDA and resume commercial planning and activities or we otherwise increase our research, clinical development and administrative activities. As a result, we are uncertain when or if we will achieve profitability and, if so, whether we will be able to sustain it. We have been engaged in identifying and developing compounds and product candidates since March 2003. As of December 31, 2008, we have accumulated net losses of approximately \$225.0 million. Our ability to achieve revenue and profitability is dependent on our ability to complete the development of our product candidates, obtain necessary regulatory approvals, and have our products manufactured and marketed. We cannot assure you that we will be profitable even if we successfully commercialize our products. Failure to become and remain profitable may adversely affect the market price of our common stock and our ability to raise capital and continue operations.

***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.***

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. 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 and commercialization of our product candidates. The parties with which we



## **Table of Contents**

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. Their failure to meet their obligations could adversely affect clinical development of our product candidates. Moreover, these parties may also have relationships with other commercial entities, some of which may compete with us. If they assist our competitors, it could harm our competitive position.

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

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

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 product candidates. We do not have long-term agreements with any of these third parties, and if they are unable or unwilling to perform for any reason, we may not be able to locate alternative acceptable manufacturers or formulators or enter into favorable agreements with them. Any inability to acquire sufficient quantities of our product candidates in a timely manner from these third parties could delay clinical trials and prevent us from developing our product candidates in a cost-effective manner or on a timely basis. In addition, manufacturers of our product candidates are subject to cGMP and similar foreign standards and we do not have control over compliance with these regulations by our manufacturers. If one of our contract manufacturers fails to maintain compliance, the production of our product candidates could be interrupted, resulting in delays and additional costs. In addition, if the facilities of such manufacturers do not pass a pre-approval plant inspection, the FDA will not grant approval 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 United States, there may be difficulties in importing our compounds or their components into the United States as a result of, among other things, FDA import inspections, incomplete or inaccurate import documentation or defective packaging

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

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

We rely on our manufacturers to purchase from third-party suppliers the materials necessary to produce our product candidates for our clinical trials. Suppliers may not sell these materials to our manufacturers at the times we need them or on commercially reasonable terms. We do not have any control over the process or timing of the acquisition of these materials by our manufacturers. Moreover, we currently do not have any agreements for the commercial production of these materials. If our manufacturers are unable to obtain these materials for our clinical trials, product testing and potential regulatory approval of our product candidates could be delayed, significantly affecting our ability

to develop our product candidates. If we or our manufacturers are unable to purchase these materials after regulatory approval has been obtained for our product candidates, the commercial launch of our product candidates would be delayed or there would be a

## **Table of Contents**

shortage in supply, which would materially affect our ability to generate revenues from the sale of our product candidates.

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

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

developing products

undertaking pre-clinical testing and clinical trials

obtaining FDA and other regulatory approvals of products

manufacturing and marketing products

These companies may invest heavily and quickly to discover and develop novel products that could make our product candidates obsolete. Accordingly, our competitors may succeed in obtaining patent protection, receiving FDA approval or commercializing superior products or other competing products before we do.

We believe the primary competitors for each of our product candidates are as follows:

For iloperidone in the treatment of schizophrenia, the atypical antipsychotics risperidone, including the depot formulation Risperdal® Consta®, and Invega® (paliperidone), each by Ortho-McNeil-Janssen Pharmaceuticals, Inc., Zyprexa® (olanzapine) by Eli Lilly and Company, Seroquel® (quetiapine) by AstraZeneca PLC, Abilify® (aripiprazole) by Bristol-Myers Squibb Company/Otsuka Pharmaceutical Co., Ltd., Geodon® (ziprasidone) by Pfizer Inc., and generic clozapine, as well as the typical antipsychotics haloperidol, chlorpromazine, thioridazine, and sulpiride (all of which are generic). In addition to the approved products, compounds in Phase III trials (or for which an NDA has been recently filed) for the treatment of schizophrenia include bifeprunox (Solvay S.A./Lundbeck A/S), and asenapine (Schering-Plough Corporation) and pimavanserin (Acadia Pharmaceuticals).

For tasimelteon in the treatment of insomnia, Rozerem™ (ramelteon) by Takeda Pharmaceuticals Company Limited, hypnotics such as Ambien® CR (zolpidem) by sanofi-aventis, Lunesta® (eszopiclone) by Sepracor Inc. and Sonata® (zaleplon) by King Pharmaceuticals, Inc., generic compounds such as zolpidem, trazodone and doxepin, and over-the-counter remedies such as Benadryl® and Tylenol PM®. In addition to the approved products, compounds in Phase III trials for insomnia (or for which an NDA has been recently filed) include indiplon (Neurocrine Biosciences, Inc.) low-dose doxepin (Silenor™) by Somaxon Pharmaceuticals, Inc. and Intermezza® (zolpidem tartarate sublingual lozenge) by Transcept Pharmaceuticals, Inc.

For tasimelteon in the treatment of depression, generic antidepressants such as paroxetine, sertraline, fluoxetine and bupropion, Lexapro® (escitalopram) by Lundbeck A/S /Forest Pharmaceuticals Inc., and Effexor® (venlafaxine) by Wyeth as well as other compounds such as Cymbalta® (duloxetine) by Eli Lilly and Valdoxan (agomelatine) by Novartis and Les Laboratoires Servier.

Additionally, our ability to compete may be affected because insurers and other third-party payors in some cases seek to encourage the use of cheaper, generic products, which could make our products less attractive.

***We have no experience selling, marketing or distributing products and no internal capability to do so.***

At present, we have limited marketing and sales personnel. In order for us to commercialize any of our product candidates following regulatory approval, if any, we must either acquire or internally develop sales, marketing and distribution capabilities, or enter into collaborations with partners to perform these services for us. We may not be able to establish sales and distribution partnerships on acceptable terms or at all, and if we

**Table of Contents**

do enter into a distribution arrangement, our success will be dependent upon the performance of our partner. In the event that we attempt to acquire or develop our own in-house sales, marketing and distribution capabilities, factors that may inhibit our efforts to commercialize our products 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 product

the lack of complementary products to be offered by our sales personnel, which may put us at a competitive disadvantage against companies with broader product lines

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

***We will need to increase the size of our organization upon regulatory approval of any of our product candidates, if any, and we may experience difficulties in managing this growth.***

As of December 31, 2008, we had 24 full-time employees. While we have currently suspended our commercial activities and are operating under a reduced spending plan, if we resume our commercial activities, we will need to expand our managerial, operational, financial and other resources in order for us to manage and fund our operations, continue our development activities and commercialize our product candidates. Our current personnel, systems and facilities are not adequate to support this future growth. To manage our growth, we must:

manage our clinical trials effectively

manage our internal development efforts effectively

improve our operational, financial, accounting and management controls, reporting systems and procedures

build marketing and sales organizations in order to commercialize iloperidone

attract and retain sufficient numbers of talented employees

We may be unable to successfully implement these tasks on a larger scale and, accordingly, may not achieve our development and commercialization goals.

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

A component of our business strategy is acquiring rights to develop and commercialize compounds discovered or developed by other pharmaceutical and biotechnology companies for which we may find effective uses and markets through our unique pharmacogenetics and pharmacogenomics expertise. Competition for the acquisition of these compounds is intense. If we are not able to identify opportunities to acquire rights to commercialize additional products, 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 product candidates. Moreover, if other firms develop pharmacogenetics and pharmacogenomics capabilities, we may face increased competition in identifying and acquiring additional product candidates.

***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 product candidates.***

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

## **Table of Contents**

other principal member of our management team or scientific staff, would impair our ability to identify, develop and market new products.

***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 of pharmaceutical products. For example, we face a risk of product liability exposure related to the testing of our product candidates in clinical trials and will face even greater risks upon any commercialization by us of our product candidates. We believe that we may be at a greater risk of product liability claims relative to other pharmaceutical companies because our compounds are intended to treat behavioral disorders, and it is possible that we may be held liable for the behavior and actions of patients who use our compounds. These lawsuits may divert our management from pursuing our business strategy and may be costly to defend. In addition, if we are held liable in any of these lawsuits, we may incur substantial liabilities and 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 \$5,000,000, 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. In addition, product liability insurance is becoming increasingly expensive, and we may not be able to obtain or maintain sufficient insurance coverage at an acceptable cost or otherwise to protect against potential product liability claims, which could prevent or inhibit the commercial production and sale of our products.

***Legislative or regulatory reform of the healthcare system in the U.S. and foreign jurisdictions may affect our 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 ability to set prices for our products which we believe are fair, and our ability to generate revenues and achieve and maintain profitability.

Specifically, in both the United States 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 ability to sell our products profitably. In the United States, the Medicare Prescription Drug Improvement and Modernization Act of 2003 reforms the way Medicare will cover and reimburse for pharmaceutical products. This legislation could decrease the coverage and price that we 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 to go through the process of seeking reimbursement from Medicare and private payors. Our products may not be considered cost effective, and coverage and reimbursement may not be available or sufficient to allow us to sell our 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.

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 candidate 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.





## **Table of Contents**

***Recently enacted legislation may make it more difficult and costly for us to obtain regulatory approval of our product candidates and to produce, to market and to distribute our existing products.***

On September 27, 2007, then-President Bush signed into law the Food and Drug Administration Amendments Act of 2007 or the FDAAA. The FDAAA grants a variety of new powers to the FDA, many of which are aimed at assuring drug safety and monitoring the safety of drug products after approval. The recently enacted amendments would 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 new law are subject to substantial civil monetary penalties. Additional measures have also been enacted to address the perceived shortcomings in the FDA's handling of drug safety issues, and to limit pharmaceutical company sales and promotional practices. While we expect the FDAAA to have a substantial effect on the pharmaceutical industry, the extent of that effect is not yet known. As the FDA issues regulations, guidance and interpretations relating to the new legislation, the impact on the industry as well as our business will become clearer. The new 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 ability to commercialize approved products successfully may be hindered, and our business may be harmed as a result.

***Our quarterly operating results may fluctuate significantly.***

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

our addition or termination of development programs

variations in the level of expenses related to our existing two product candidates or future development programs

our execution of collaborative, licensing or other arrangements, and the timing of payments we may make or receive under these arrangements

any intellectual property infringement lawsuit in which we may become involved

regulatory developments affecting our product candidates or those of our competitors

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

### **Risks related to intellectual property and other legal matters**

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

Iloperidone is based in part on patents and other intellectual property owned by sanofi-aventis and Novartis. Titan Pharmaceuticals, Inc. (Titan) holds an exclusive license from sanofi-aventis to the intellectual property owned by sanofi-aventis, and Titan has sublicensed its rights under such license on an exclusive basis to Novartis. We have acquired exclusive rights to this and other intellectual property through a further sublicense from Novartis. Our rights with respect to the intellectual property to develop and commercialize iloperidone may terminate, in whole or in part, if we fail to meet certain milestones contained in our sublicense agreement with Novartis relating to the time it takes for us to launch iloperidone commercially following regulatory approval, and the time it takes for us to receive regulatory approval following our

## **Table of Contents**

submission of an NDA or equivalent foreign filing. We may also lose our rights to develop and commercialize iloperidone if we fail to pay royalties to Novartis, if we fail to comply with certain requirements in the sublicense agreement regarding our financial condition, or if we fail to comply with certain restrictions regarding our other development activities. Finally, our rights to develop and commercialize iloperidone may be impaired if we do not cure breaches by Novartis and Titan of similar obligations contained in these sublicense and license agreements, although we are not aware of any such breach by Titan or Novartis. In the event of an early termination of our sublicense agreement, all rights licensed and developed by us under this agreement may be extinguished, which would have a material adverse effect on our business.

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

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

In addition to the rights we have licensed from Novartis and BMS relating to our product candidates, we rely upon intellectual property we own relating to our products, including patents, patent applications and trade secrets. As of December 31, 2008 we had twenty-two pending provisional patent applications in the United States, five U.S. national stage applications under U.S.C. 371 and five pending Patent Cooperation Treaty applications, which permit the pursuit of patents outside of the U.S., relating to our product candidates in clinical development. 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 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 United States. As a result, we may encounter significant problems in protecting and defending our intellectual property both in the United States 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 product candidates, our business will be materially harmed.***

The United States Drug Price Competition and Patent Term Restoration Act of 1984, more commonly known as the Hatch-Waxman Act, provides for an extension of patent protection for drug compounds for a period of up to five years to compensate for time spent in development. Assuming we gain a five-year extension for each of our current product

candidates in clinical development, and that we continue to have rights under our sublicense and license agreements with respect to these product candidates, we would have

**Table of Contents**

exclusive rights to iloperidone's United States new chemical entity patent (the primary patent covering the compound as a new composition of matter) until 2016 and to tasimelteon's United States new chemical entity patent until 2022. In Europe, similar legislative enactments allow patent protection in the European Union to be extended for up to five years through the grant of a Supplementary Protection Certificate. Assuming we gain such a five-year extension for each of our current product candidates in clinical development, and that we continue to have rights under our sublicense and license agreements with respect to these product candidates, we would have exclusive rights to iloperidone's European new chemical entity patents until 2015 and to tasimelteon's European new chemical entity patents until 2022. Additionally, a directive in the European Union provides that companies who receive regulatory approval for a new compound will have a 10-year period of market exclusivity for that compound (with the possibility of a further one-year extension) in most countries in Europe, beginning on the date of such European regulatory approval, regardless of when the European new chemical entity patent covering such compound expires. A generic version of the approved drug may not be marketed or sold in Europe during such market exclusivity period. This directive may be of particular importance with respect to iloperidone, since the European new chemical entity patent for iloperidone will likely expire prior to the end of this 10-year period of market exclusivity. However, there is no assurance that we will receive the extensions of our patents or other exclusive rights available under the Hatch-Waxman Act or similar foreign legislation. If we fail to receive such extensions and exclusive rights, our ability to prevent competitors from manufacturing, marketing and selling generic versions of our products will be materially harmed.

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

Our commercial success depends in part on our not infringing the patents and proprietary rights of third parties. Third parties may assert that we are employing their proprietary technology without authorization. In addition, third parties may obtain patents in the future and claim that use of our technologies infringes upon these patents. Furthermore, parties making claims against us may obtain injunctive or other equitable relief, which could effectively block our ability to develop and commercialize one or more of our product candidates. Defense of these claims, regardless of their merit, would divert substantial financial and employee resources from our business. In the event of a successful claim of infringement against us, we may have to pay substantial damages, obtain one or more licenses from third parties or pay royalties. In addition, even in the absence of litigation, we may need to obtain additional licenses from third parties to advance our research or allow commercialization of our product candidates. We may fail to obtain any of these licenses at a reasonable cost or on reasonable terms, if at all. In that event, we would be unable to develop and commercialize further one or more of our product candidates.

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

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

Our research and development activities involve the controlled use of potentially hazardous substances, including toxic chemical and biological materials. We could be held liable for any contamination, injury or other damages resulting from these hazardous substances. In addition, our operations produce hazardous waste products. While third parties are responsible for disposal of our hazardous waste, we could be liable under environmental laws for any required cleanup of sites at which our waste is disposed. Federal, state, foreign and local laws and regulations govern the use, manufacture, storage, handling and disposal of these hazardous materials. If we fail to comply with these laws and regulations at any time, or if they change, we may be subject to criminal sanctions and substantial civil liabilities,

which may adversely affect our business.

Even if we continue to comply with all applicable laws and regulations regarding hazardous materials, we cannot eliminate the risk of accidental contamination or discharge and our resultant liability for any injuries or

## **Table of Contents**

other damages caused by these accidents. Although we maintain pollution liability insurance, our coverage limit under this insurance is \$2,000,000, and while we believe this amount and type of insurance is sufficient to cover risks typically associated with our handling of materials, the insurance may not cover all environmental liabilities, and these limits may not be high enough to cover potential liabilities for these damages fully. The amount of uninsured liabilities may exceed our financial resources and materially harm our business.

### **Risks related to our common stock**

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

The stock market has from time to time experienced significant price and volume fluctuations, and the market prices of the securities of life sciences companies without product revenues, such as ours, have historically been highly volatile. Between December 31, 2007 and December 31, 2008, the high and low sale prices of our common stock as reported on the NASDAQ Global Market varied between \$7.13 and \$0.45. The following factors, in addition to the other risk factors described in this section, may also have a significant impact on the market price of our common stock:

publicity regarding actual or potential testing or trial results relating to products under development by us or our competitors

the outcome of regulatory review relating to products under development by us or our competitors

regulatory developments in the United States and foreign countries

developments concerning any collaboration or other strategic transaction we may undertake

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

actual or anticipated variations in our quarterly operating results

changes in estimates of our financial results or recommendations by securities analysts

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

publicity regarding actual or potential transactions involving the Company

economic and other external factors beyond our control

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

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

A small number of institutional investors and private equity funds hold a significant number of shares of our common stock. Sales by these stockholders of a substantial number of shares, or the expectation of such sales, could cause a significant reduction in the market price of our common stock. Additionally, a small number of early investors in our company have rights, subject to certain conditions, to require us to file registration statements to permit the resale of

their shares in the public market or to include their shares in registration statements that we may file for ourselves or other stockholders.

In addition to our outstanding common stock, as of December 31, 2008, there were a total of 4,453,629 shares of common stock that we have registered and that we are obligated to issue upon the exercise of currently outstanding options granted under our Second Amended and Restated Management Equity Plan and 2006 Equity Incentive Plan. Upon the exercise of these options in accordance with their respective terms, these shares may be resold freely, subject to restrictions imposed on our affiliates under Rule 144. If significant sales of these shares occur in short periods of time, these sales could reduce the market price of our common stock. Any reduction in the trading price of our common stock could impede our ability to raise capital on attractive terms.



**Table of Contents**

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

Our common stock is currently listed for quotation on the NASDAQ Global Market. We are required to meet specified financial requirements in order to maintain our listing on the NASDAQ Global Market. One such requirement is that we maintain a minimum closing bid price of at least \$1.00 per share for our common stock. Our common stock has recently closed at prices below the minimum bid requirement. If the closing bid price of a share of the Company's common stock were to fall below \$1.00 for a period of thirty (30) consecutive business days, the Company would receive a deficiency notice from NASDAQ advising us that we have 180 calendar days to regain compliance by maintaining a minimum closing bid price of at least \$1.00 for a minimum of ten consecutive business days. Under certain circumstances, NASDAQ could require that the minimum closing bid price exceed \$1.00 for more than ten consecutive days before determining that a company complies with its continued listing standards. On October 16, 2008, NASDAQ announced that, effective as of such date and through Friday, January 16, 2009, it has suspended the enforcement of the rules requiring a minimum \$1.00 closing bid price. NASDAQ has extended its suspension of the rules requiring a minimum \$1.00 closing bid price. These rules will be reinstated on Monday, April 20, 2009. If in the future, we fail to satisfy the NASDAQ Global Market's continued listing requirements, our common stock could be delisted from the NASDAQ Global Market, in which case we may transfer to the NASDAQ Capital Market, which generally has lower financial requirements for initial listing or, if we fail to meet its listing requirements, the over-the-counter bulletin board. There are many factors that may adversely affect our minimum bid price, including those described in Item 1A Risk Factors of Part I of this annual report on Form 10-K, which contains a more complete discussion of those factors and other risks. Many of these factors are outside of our control. As a result, we may not be able to sustain compliance with the minimum bid price rule in the long term. Any potential delisting of our common stock from the NASDAQ Global Market would make it more difficult for our stockholders to sell our stock in the public market and would likely result in decreased liquidity and increased volatility for our common stock.

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

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

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

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

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

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

**Table of Contents**

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

require that directors only be removed from office for cause

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

limit who may call special meetings of stockholders

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

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

Moreover, on September 25, 2008, our board of directors adopted a rights agreement, the provisions of which could result in significant dilution of the proportionate ownership of a potential acquirer and, accordingly, could discourage, delay or prevent a change in our management or control over us.

***We may lose some or all of the value of some of our marketable securities.***

We engage one or more third parties to manage some of our cash consistent with an investment policy that allows a range of investments and maturities. The investments are intended to preserve principal while providing liquidity adequate to meet projected cash requirements. Risks of principal loss are intended to be minimized through diversified short and medium term investments of high quality, but the investments are not, in every case, guaranteed or fully insured. In light of recent changes in the credit market, some high quality short-term investment securities, similar to the types of securities that we invest in, have suffered illiquidity or events of default. From time to time, we may suffer losses on our marketable securities, which could have a material adverse impact on our operations.

***Unstable market conditions may have serious adverse consequences on our business.***

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

There is a risk that one or more of our current service providers, manufacturers and other partners may encounter difficulties during challenging economic times, which would directly affect our ability to attain our operating goals on schedule and on budget.

***One of our stockholders has notified us that it intends to nominate a competing slate of directors for election at this year's annual meeting of stockholders and to propose resolutions to our stockholders relating to our bylaws and the ongoing operations of our company.***

On February 13, 2009, we received two letters from one of our stockholders, Tang Capital Partners, LP (TCP), stating its intent to, among other things, nominate two directors to stand for election at our 2009 annual meeting of stockholders and submit proposals at the annual meeting to amend our bylaws and request that our board of directors take action to liquidate the Company. TCP seeks to replace two directors, our current Chief Executive Officer and the Chairman of our board.

**Table of Contents**

TCP has also notified us that it intends to propose a series of amendments to our bylaws which, if approved by the affirmative vote of at least 80% of the voting power of all of the outstanding shares of capital stock of the Company entitled to vote generally in the election of directors, would require unanimous approval of the members of the board of directors for a number of critical operating matters, including raising capital, executing material contracts, and hiring certain key employees. If the proposed bylaw amendments are approved, it will be very difficult for us to implement our current strategy and further the development of our compounds because, notwithstanding a consensus on the board, any one director, whether nominated by the board, TCP or any other stockholder, will have a veto on these and other critical operating matters.

In addition, TCP has requested that our board of directors take action to liquidate the Company and distribute the remaining cash to our stockholders. If we fail to take such action, TCP or other stockholders may attempt to compel a liquidation of the Company through litigation or some other means. Such litigation could result in substantial costs and divert management's attention and resources, which could harm our business, operating results and financial conditions.

**ITEM 1B. UNRESOLVED STAFF COMMENTS**

Not applicable.

**ITEM 2. PROPERTIES**

Our current headquarters are located in Rockville, Maryland, consisting of approximately 27,000 square feet of office and laboratory space. Our lease for this facility expires in 2016.

Management believes that the leased facilities are suitable and adequate to meet the Company's anticipated needs.

**ITEM 3. LEGAL PROCEEDINGS**

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

**ITEM 4. SUBMISSION OF MATTERS TO A VOTE OF SECURITY HOLDERS**

None.

**PART II**

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

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

<b>Year Ended December 31, 2007</b>	<b>High</b>	<b>Low</b>
First quarter 2007	\$ 32.00	\$ 21.69
Second quarter 2007	\$ 24.31	\$ 18.75

Third quarter 2007	\$ 21.50	\$ 13.23
Fourth quarter 2007	\$ 19.40	\$ 6.49

**Table of Contents**

<b>Year Ended December 31, 2008</b>	<b>High</b>	<b>Low</b>
First quarter 2008	\$ 7.13	\$ 2.70
Second quarter 2008	\$ 6.59	\$ 2.98
Third quarter 2008	\$ 4.03	\$ 0.76
Fourth quarter 2008	\$ 1.02	\$ 0.45

As of March 11, 2009, there were 27 holders of record of our common stock.

**Dividends**

The Company has not paid dividends to its shareholders (other than a dividend of preferred share purchase rights which was declared on September 25, 2008) since its inception and does not plan to pay dividends in the foreseeable future. The Company currently intends to retain earnings, if any, to finance the growth of the Company.

**Table of Contents**

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

The following graph shows the cumulative total return, assuming the investment of \$100 on April 12, 2006 (the date of the initial public offering) on an investment in each of the Company's common stock, the NASDAQ Composite Index and the Amex Biotechnology Index (in either case, assuming reinvestment of dividends). The comparisons in the table are required by the SEC and are not intended to forecast or be indicative of possible future performance of the Company's common stock. We have not paid dividends to our stockholders since the inception and do not plan to pay dividends in the foreseeable future. The following graph and related information is being furnished solely to accompany this Form 10-K pursuant to Item 201(e) of Regulation S-K and shall not be deemed soliciting materials or to be filed with the SEC (other than as provided in Item 201), nor shall such information be incorporated by reference into any of our filings under the Securities Act of 1933 or the Securities Exchange Act of 1934, whether made before or after the date hereof, and irrespective of any general incorporation language in any such filing.



**Table of Contents****ITEM 6. SELECTED CONSOLIDATED FINANCIAL DATA**

The consolidated statements of operations data for the years ended December 31, 2008, 2007 and 2006 and the consolidated balance sheet data as of December 31, 2008 and 2007 are each derived from our audited consolidated financial statements included in this annual report on Form 10-K. The consolidated statements of operations data for the years ended December 31, 2005, 2004 and for the period from March 13, 2003 (inception) to December 31, 2003 and the consolidated balance sheet data as of December 31, 2006, 2005, 2004 and 2003 are each derived from our audited consolidated financial statements not included herein. Our historical results for any prior period are not necessarily indicative of results to be expected in any future period.

The following data should be read together with our consolidated financial statements and accompanying notes and the section entitled Management's discussion and analysis of financial condition and results of operations included in this annual report on Form 10-K.

	Year Ended December 31,					Period from March 13, 2003 (Inception) to December 31, 2003		
	2008	2007	2006	2005	2004			
<b>Statements of operations data</b>								
Revenue	\$	\$	\$	\$	\$	33,980	\$	47,565
Operating expenses:								
Research and development	23,935,541	47,234,867	52,070,776	16,890,615	7,442,983			2,010,532
General and administrative	28,909,580	32,803,508	13,637,664	7,396,038	2,119,394			1,052,659
Total operating expenses	52,845,121	80,038,375	65,708,440	24,286,653	9,562,377			3,063,191
Loss from operations	(52,845,121)	(80,038,375)	(65,708,440)	(24,286,653)	(9,528,397)			(3,015,626)
Total other income, net	1,780,880	5,978,564	2,197,821	410,001	59,060			44,805
Loss before tax provision	(51,064,241)	(74,059,811)	(63,510,619)	(23,876,652)	(9,469,337)			(2,970,821)
Tax provision		9,879	549	7,649	4,949			
Net loss	(51,064,241)	(74,069,690)	(63,511,168)	(23,884,301)	(9,474,286)			(2,970,821)
Beneficial conversion feature-deemed dividend to preferred stockholders(1)				(33,486,623)				

Net loss attributable to common stockholders	\$ (51,064,241)	\$ (74,069,690)	\$ (63,511,168)	\$ (57,370,924)	\$ (9,474,286)	\$ (2,970,821)
Basic and diluted net loss per share applicable to common stockholders	\$ (1.92)	\$ (2.81)	\$ (3.97)	\$ (3,374.33)	\$ (3,137.18)	\$ (983.72)
Shares used in calculation of basic and diluted net loss per shares attributable to common stockholders	26,650,126	26,360,177	16,001,815	17,002	3,020	3,020

(1) In September and December of 2005, we completed the sale of an additional 27,235,783 shares of Series B preferred stock for net proceeds of approximately \$33.5 million. After evaluating the fair value of the common stock obtainable upon conversion by the stockholders, we determined that the issuance of the Series B preferred stock sold in 2005 resulted in a beneficial conversion feature which was fully accreted in 2005 and is recorded as a deemed dividend to preferred stockholders of approximately \$33.5 million for the year ended December 31, 2005.

**Table of Contents**

	2008	2007	As of December 31,		2004	2003
			2006	2005		
<b>Balance sheet data</b>						
Cash and cash equivalents	\$ 39,079,304	\$ 41,929,533	\$ 30,928,895	\$ 21,012,815	\$ 16,259,770	\$ 7,165,722
Marketable securities	7,378,798	51,223,291	941,981	10,141,189		
Working capital	44,334,703	74,177,567	24,714,285	28,308,434	14,827,621	6,204,248
Total assets	49,933,843	96,860,780	36,260,276	35,752,770	17,752,241	8,385,913
Total liabilities	3,913,569	13,131,849	9,503,404	5,087,963	1,808,654	1,378,880
Convertible preferred stock				61,795,187	28,308,564	9,963,541
Deficit accumulated during the development stage	(224,974,507)	(173,910,266)	(99,840,576)	(36,329,408)	(12,445,107)	(2,970,821)
Total stockholders equity	46,020,274	83,728,931	26,756,872	30,664,807	15,943,587	7,007,033

38

**Table of Contents**

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

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

**Overview**

We are a biopharmaceutical company focused on the development and commercialization of clinical-stage product candidates for central nervous system disorders, with exclusive worldwide commercial rights to two product candidates in clinical development. Our lead product candidate, iloperidone, is a compound for the treatment of schizophrenia. On November 27, 2007, the United States Food and Drug Administration (FDA) accepted our New Drug Application (NDA) for iloperidone in schizophrenia. In July 2008, we announced that the FDA had determined that our NDA was not approvable and indicated, among other things, that we would have to conduct additional studies and submit that data before the FDA would approve iloperidone for commercial sale for the treatment of schizophrenia. In September 2008, we met with the FDA to discuss the FDA's determination. The FDA asked us to provide a complete response to the not-approvable letter, which we submitted on November 6, 2008. The FDA accepted the complete response for review and has set a new target action date of May 6, 2009. There are no guarantees that the FDA will provide its response by May 6, 2009, nor can there be any assurances that any such response will be favorable. Pending the FDA's reply to our complete response, we have suspended all non-essential iloperidone-related activities. Our second product candidate, tasimelteon is a compound for the treatment of sleep and mood disorders. In November 2006, we announced positive top-line results from our Phase III trial of tasimelteon in transient insomnia. In June 2008, the Company announced positive top-line results from the Phase III trial of tasimelteon in chronic primary insomnia. Tasimelteon is also ready for Phase II trials for the treatment of depression.

We will have to conduct additional Phase III trials for tasimelteon in chronic sleep disorders prior to our filing of an NDA for tasimelteon. Assuming successful outcomes of our clinical trials and approval by the FDA, we expect to commercialize iloperidone with our own sales force and/or commercial partners in the United States, and to seek partners for commercialization of the compound outside of the United States. Given the range of potential indications for tasimelteon, we intend to pursue one or more partnerships for the development and commercialization of tasimelteon worldwide.

We are a development stage enterprise and have accumulated net losses of approximately \$225.0 million since the inception of our operations through December 31, 2008. We have no product revenues to date and have no approved products for sale. Since we began our operations in March 2003, we have devoted substantially all of our resources to the in-licensing and clinical development of our product candidates. Our future operating results will depend largely on our ability to successfully develop and commercialize our lead product candidate, iloperidone, and on the progress of other product candidates currently in our research and development pipeline. The results of our operations will vary significantly from year-to-year and quarter-to-quarter and depend on a number of factors, including risks related to our business, risks related to our industry, and other risks which are detailed in Item 1A of Part I of this report, entitled Risk Factors.

We completed our initial public offering in April 2006. The offering totaled 5,964,188 shares of common stock at a public offering price of \$10.00, resulting in net proceeds to the Company of approximately \$53.3 million, after deducting underwriters' discounts and commissions as well as offering expenses. Upon completion of the initial public offering, all shares of the Company's Series A preferred stock and Series B preferred stock were converted into an aggregate of 15,794,632 shares of common stock.

**Table of Contents**

In January 2007 we completed our follow-on offering, consisting of 4,370,000 shares of common stock at a public offering price of \$27.29 per share, resulting in net proceeds to the Company of approximately \$111.3 million after deducting underwriting discounts and commissions and offering expenses.

Our activities will necessitate significant uses of working capital for the foreseeable future. Our capital requirements will depend on many factors, including the success of our research and development efforts, the satisfaction of certain regulatory requirements, payments received under contractual agreements with other parties, if any, and the status of competitive products. However, given the receipt of the not-approvable letter from the FDA with respect to the NDA for iloperidone, and that any additional studies required by the FDA prior to its approval of iloperidone would require significant capital in excess of our currently available resources, we are now operating under a reduced spending plan. On December 16, 2008, we committed to a plan of termination that resulted in a work force reduction of 17 employees, including two officers, in order to reduce operating costs. As of December 31, 2008, the Company employed 24 full-time employees. This represents approximately a 55% decrease from the 53 employees the Company had on August 1, 2008. We believe that, if we continue to operate under our reduced spending plan, our existing cash, cash equivalents and marketable securities will be sufficient to fund operations at least through the second quarter 2010. In budgeting for our activities, we have relied on a number of assumptions, including assumptions that we will not conduct any additional clinical trials for either of the oral or injectable formulations of iloperidone, that we will not engage in any further commercial activities related to iloperidone, that we will not engage in further in-licensing activities, that we will not receive any proceeds from potential partnerships, that we will not conduct additional trials for tasimelteon, that we will be able to retain our key personnel, that we will continue to seek FDA approval of iloperidone, that we will continue to evaluate clinical and pre-clinical compounds for potential development, and that we will not incur any significant contingent liabilities.

We may need to raise additional funds if one or more of our assumptions proves to be incorrect or if we choose to resume our commercialization efforts with respect to iloperidone, expand our product development efforts, conduct additional clinical trials for one or more of our product candidates or seek to acquire additional product candidates, and we may decide to raise additional funds even before they are needed if the conditions for raising capital are favorable. In our capital-raising efforts, we may seek to sell additional equity or debt securities or obtain a bank credit facility. The sale of additional equity or debt securities, if convertible, could result in dilution to our stockholders. The incurrence of indebtedness would result in increased fixed obligations and could also result in covenants that would restrict our operations. However, we may not be able to raise additional funds on acceptable terms, or at all. Given the current global economic climate, we may have more difficulty raising funds than we would during a period of economic stability. If we are unable to secure sufficient capital to fund our research and development activities, we may not be able to continue operations, or we may have to enter into 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 collaborations, if consummated prior to proof-of-efficacy or safety of a given product candidate, could impair our ability to realize value from that product candidate.

*Iloperidone.* Iloperidone is our product candidate under development to treat schizophrenia. We submitted an NDA for iloperidone for the treatment of schizophrenia to the FDA on September 27, 2007 and on November 27, 2007, the FDA accepted our NDA. The application included data from 35 clinical trials and more than 3,000 patients treated with iloperidone and also contained pharmacogenetic data aimed to further improve the benefit/risk profile of iloperidone in the treatment of patients with schizophrenia. In July 2008, we announced that the FDA had determined that our NDA was not approvable and indicated, among other things, that we would have to conduct additional studies and submit that data before the FDA would approve iloperidone for commercial sale for the treatment of schizophrenia. Performance and completion of these additional studies will require years of testing and, even if positive results are achieved, may not result in the FDA's approval of iloperidone. In September 2008, we met with the FDA to discuss the FDA's determination. The FDA asked us to provide a complete response to the not-approvable letter, which we submitted on November 6, 2008. The FDA accepted the complete response for review and has set a

new target action date of May 6, 2009. There are no guarantees that the FDA will provide its response by May 6, 2009, nor can there

**Table of Contents**

be any assurances that any such response will be favorable. Pending the FDA's reply to our complete response, we have suspended all non-essential iloperidone-related activities.

From inception to December 31, 2008 we incurred approximately \$74.5 million in research and development costs directly attributable to our development of iloperidone, including a \$5.0 million milestone license fee paid to Novartis in 2007 upon the acceptance of our NDA.

We are also developing a 4-week injectable formulation for iloperidone, for which we already have early Phase II data from a study previously conducted by Novartis. We have completed essential manufacturing activities and intend to conduct additional clinical trials if and when, we receive following FDA approval of the oral dose formulation for iloperidone. If the FDA approves the oral formulation of iloperidone, we intend to resume the development of the injectable formulation and we believe we will need to conduct additional trials with this formulation to be able to file for FDA approval.

*Tasimelteon.* Tasimelteon is our product candidate under development to treat sleep and mood disorders. Tasimelteon is a melatonin receptor agonist that works by adjusting the human body clock of circadian rhythm. Tasimelteon has successfully completed a Phase III trial for the treatment of transient insomnia in November 2006. In June 2008, we announced positive top-line results from the Phase III trial of tasimelteon in chronic primary insomnia. The trial was a randomized, double-blind, and placebo-controlled study with 324 patients. The trial measured time to fall asleep and sleep maintenance, as well as next-day performance. We will have to conduct additional trials prior to our filing of an NDA for tasimelteon to treat sleep disorders. Tasimelteon is also ready for Phase II trials for the treatment of depression.

From inception to December 31, 2008, we incurred approximately \$51.3 million in direct research and development costs directly attributable to our development of tasimelteon, including a \$1.0 million milestone license fee paid to BMS in 2006 upon the initiation of our Phase III program.

*VSF-173.* On November 3, 2008, we received written notice from Novartis that our license agreement with respect to VSF-173 had terminated in accordance with its terms as a result of our failure to satisfy a specific development milestone within the time period specified in the license agreement. As a result, we no longer have any rights with respect to VSF-173 and Novartis has a non-exclusive worldwide license to all information and intellectual property generated by us or on our behalf related to our development of VSF-173. We are currently evaluating any options that we may have with respect to VSF-173, which may include the possibility of entering into a new license agreement or other arrangement with Novartis to allow us to resume our development of VSF-173; however, there can be no assurance that we will be able to enter into such an agreement or arrangement on acceptable terms, or at all.

From inception to December 31, 2008, we incurred approximately \$6.7 million in research and development costs directly attributable to our development of VSF-173, including a milestone license fee of \$1.0 million paid to Novartis upon the initiation of our first Phase II clinical trial in March of 2007.

*Revenues.* We generated some revenue during the period from March 13, 2003 (inception) to December 31, 2003 and during the year ended December 31, 2004 under research and development contracts that were derived principally from consulting agreements we entered into during our start-up phase to defray research costs. We completed our obligations during those periods under these agreements and no longer seek such arrangements.

We have not generated any other operating revenue since our inception. Any revenue that we may receive in the near future is expected to consist primarily of license fees, milestone payments and research and development reimbursement payments to be received from potential partners. If our development efforts result in clinical success, regulatory approval and successful commercialization of our products, we could generate revenue from sales of our



products and from receipt of royalties on sales of licensed products.

*Research and development expenses.* Our research and development expenses consist primarily of fees paid to third-party professional service providers in connection with the services they provide for our clinical trials, costs of contract manufacturing services, costs of materials used in clinical trials and research and development, costs for regulatory consultants and filings, depreciation of capital resources used to develop our

**Table of Contents**

products, all related facilities costs, and salaries, benefits and stock-based compensation expenses related to our research and development personnel. We expense research and development costs as incurred, including payments made to date under our license agreements. We believe that significant investment in product development is a competitive necessity and plan to continue these investments in order to realize the potential of our product candidates and pharmacogenetics and pharmacogenomics expertise. From inception through December 31, 2008, we incurred research and development expenses in the aggregate of approximately \$150.0 million, including stock-based compensation expenses of approximately \$7.5 million. We expect our research and development expenses to increase as we continue to develop our product candidates. We also expect to incur licensing costs in the future that could be substantial, as we continue our efforts to develop our product candidates and to evaluate potential in-license product candidates.

The following table summarizes our product development initiatives for the years ended December 31, 2008 to December 31, 2004 and the period from March 13, 2003 (inception) to December 31, 2003 and for the period from March 13, 2003 (inception) to December 31, 2008. Included in the following table are the research and development expenses recognized in connection with our product candidates in clinical development. Included in Other product candidates are the costs directly related to research initiatives for all other product candidates.

	<b>Year Ended December 31, 2008</b>	<b>Year Ended December 31, 2007</b>	<b>Year Ended December 31, 2006</b>	<b>Year Ended December 31, 2005</b>	<b>Year Ended December 31, 2004</b>	<b>March 13, 2003 (inception) to December 31, 2003(2)</b>	<b>Period from March 13, 2003 (Inception) to December 31, 2008</b>
Direct project costs(1)							
iloperidone	\$ 8,485,000	\$ 20,668,000	\$ 36,455,000	\$ 7,798,000	\$ 1,123,000	\$	\$ 74,529,000
tasimelteon	11,344,000	18,947,000	11,665,000	6,133,000	3,221,000		51,310,000
VSF-173	737,000	3,404,000	1,058,000	943,000	568,000		6,710,000
Other product candidates	1,443,000	2,095,000	1,098,000	899,000	1,037,000		6,572,000
Total direct product costs	22,009,000	45,114,000	50,276,000	15,773,000	5,949,000		139,121,000
Indirect project costs(1)							
Facility(3)	683,000	495,000	578,000	247,000	259,000		2,262,000
Depreciation	330,000	423,000	474,000	375,000	345,000	69,000	2,016,000
Other indirect overhead costs	913,000	1,203,000	743,000	496,000	890,000	1,941,000	6,186,000

Total indirect expenses	1,926,000	2,121,000	1,795,000	1,118,000	1,494,000	2,010,000	10,464,000
Total research and development expenses	\$ 23,935,000	\$ 47,235,000	\$ 52,071,000	\$ 16,891,000	\$ 7,443,000	\$ 2,010,000	\$ 149,585,000

- (1) Many of our research and development costs are not attributable to any individual project because we share resources across several development projects. We record direct costs, including personnel costs and related benefits and stock-based compensation, on a project-by-project basis. We record indirect costs that support a number of our research and development activities in the aggregate.
- (2) In 2003, there were no active development programs in process for our product candidates listed in the table.
- (3) In 2003, all facility-related costs were allocated to general and administrative expenses.

*General and administrative expenses.* General and administrative expenses consist primarily of salaries and other related costs for personnel, including stock-based compensation, serving executive, finance, accounting, information technology, marketing and human resource functions. Other costs include facility costs not otherwise included in research and development expenses and fees for legal, accounting and other professional services. We expect our general and administrative expenses to decrease in 2009 as we operate under a reduced spending plan pending a response from the FDA to our complete response to the not-approvable letter related to iloperidone. From inception through December 31, 2008, we incurred general and

## **Table of Contents**

administrative expenses in the aggregate of approximately \$85.9 million, including stock-based compensation expenses of approximately \$36.6 million.

*Interest and other income, net.* Interest income consists of interest earned on our cash and cash equivalents, marketable securities and restricted cash. Interest expense consists of interest incurred on equipment debt.

### **Critical accounting policies**

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

Our significant accounting policies are described in the notes to our audited consolidated financial statements for the year ended December 31, 2008 included in this annual report on Form 10-K. However, we believe that the following accounting policies are important to understanding and evaluating our reported financial results, and we have accordingly included them in this discussion.

*Accrued expenses.* As part of the process of preparing financial statements we are required to estimate accrued expenses. The estimation of accrued expenses involves identifying services that have been performed on our behalf, and then estimating the level of service performed and the associated cost incurred for such services as of each balance sheet date in the financial statements. Accrued expenses include professional service fees, such as lawyers and accountants, contract service fees, such as those under contracts with clinical monitors, data management organizations and investigators in conjunction with clinical trials, fees to contract manufacturers in conjunction with the production of clinical materials, and fees for marketing and other commercialization activities. Pursuant to our assessment of the services that have been performed on clinical trials and other contracts, we recognize these expenses as the services are provided. Our assessments include, but are not limited to: (1) an evaluation by the project manager of the work that has been completed during the period, (2) measurement of progress prepared internally and/or provided by the third-party service provider, (3) analyses of data that justify the progress, and (4) management's judgment. In the event that we do not identify certain costs that have begun to be incurred or we under- or over-estimate the level of services performed or the costs of such services, our reported expenses for such period would be too low or too high.

*Stock-based compensation.* We adopted Statement of Financial Accounting Standards No. 123(R), *Share Based Payment*, (SFAS 123(R)) on January 1, 2006 using the modified prospective transition method of implementation and adopted the accelerated attribution method. Prior to January 1, 2006 we followed APB Opinion No. 25, *Accounting for Stock Issued to Employees* (APB 25), and related interpretations, in accounting for our stock-based compensation plans, rather than the alternative fair value accounting method provided for under SFAS No. 123, *Accounting for Stock-Based Compensation*.

We currently use the Black-Scholes-Merton option pricing model to determine the fair value of stock options. The determination of the fair value of stock options on the date of grant using an option pricing model is affected by our stock price as well as assumptions regarding a number of complex and subjective variables. These variables include the expected stock price volatility over the expected term of the awards, actual and projected employee stock option exercise behaviors, risk-free interest rate and expected dividends. Expected volatility rates are based on historical volatility of the common stock of comparable entities and other factors due to the lack of historic information of the Company's publicly traded common stock. The expected term of options granted is based on the transition approach

provided by Staff Accounting Bulletin ( SAB ) No. 107 as the options meet the plain vanilla criteria required by this method. The risk-free interest rates are based on the U.S. Treasury yield for a period consistent with the expected term of the option in effect at the time of the grant. We have not paid dividends to our stockholders since the inception and do not plan to pay dividends in the foreseeable future. The stock-based compensation expense for a period is also

**Table of Contents**

affected by expected forfeiture rate for the respective option grants. If our estimates of the fair value of these equity instruments or expected forfeitures are too high or too low, it would have the effect of overstating or understating expenses.

Total stock-based compensation expense, related to all of the Company's stock-based awards, recognized under SFAS 123(R) for the years ended December 31, 2008, 2007, 2006 and recognized for the period from March 13, 2003 (inception) to December 31, 2008, was comprised of the following:

	<b>Year Ended December 31,</b>			<b>Period from March 13, 2003 (Inception) to December 31, 2008</b>
	<b>2008</b>	<b>2007</b>	<b>2006</b>	
Research and development	\$ 1,748,000	\$ 4,259,000	\$ 742,000	\$ 7,540,000
General and administrative	11,667,000	15,228,000	5,350,000	36,635,000
Total stock-based compensation expense	\$ 13,415,000	\$ 19,487,000	\$ 6,092,000	\$ 44,175,000

**Recent Accounting Pronouncements**

In December 2007, the FASB issued SFAS No. 141(R), a revision of SFAS No. 141, *Business Combinations*. The revision is intended to simplify existing guidance and converge rulemaking under U.S. generally accepted accounting principles with international accounting standards. This statement applies prospectively to business combinations where the acquisition date is on or after the beginning of the first annual reporting period beginning on or after December 15, 2008. Early adoption is prohibited. The implementation of this standard will not have a material impact on our consolidated financial position and results of operations.

In June 2008, the FASB issued FSP EITF 03-6-1, *Determining Whether Instruments Granted in Share-Based Payment Transactions Are Participating Securities* (FSP EITF 03-6-1). FSP EITF 03-6-1 clarified that all outstanding unvested share-based payment awards that contain rights to nonforfeitable dividends participate in undistributed earnings with common shareholders. Awards of this nature are considered participating securities and the two-class method of computing basic and diluted earnings per share must be applied. FSP EITF 03-6-1 is effective for fiscal years beginning after December 15, 2008. The implementation of this standard will not have a material impact on our consolidated financial position and results of operations.

In November 2008, the FASB ratified EITF Issue No. 08-6, *Equity method Investment Accounting Considerations* (EITF 08-6). EITF 08-6 addresses a number of matters associated with the impact of SFAS No. 141R and SFAS No. 160 on the accounting for equity method investments including initial recognition and measurement and subsequent measurement issues. EITF 08-6 is effective, on a prospective basis, for fiscal years beginning after December 15, 2008 and interim periods within those fiscal years. The implementation of this standard will not have a material impact on our consolidated financial position and results of operations.

**Results of operations**

We have a limited history of operations. We anticipate that our results of operations will fluctuate for the foreseeable future due to several factors, including any possible payments made or received pursuant to licensing or collaboration agreements, progress of our research and development efforts, and the timing and outcome of clinical trials and related possible regulatory approvals. Our limited operating history makes predictions of future operations difficult or impossible. Since our inception, we have incurred significant losses. As of December 31, 2008, we had a deficit accumulated during the development stage of approximately \$225.0 million. We anticipate incurring additional losses for the foreseeable future, and these losses may be incurred at increasing rates.

**Table of Contents*****Year ended December 31, 2008 compared to year ended December 31, 2007***

*Research and development expenses.* Research and development expenses decreased by approximately \$23.3 million, or 49%, to approximately \$23.9 million for the year ended December 31, 2008 compared to approximately \$47.2 million for the year ended December 31, 2007.

The following table discloses the components of research and development expenses reflecting all of our project expenses for the years ended December 31, 2008 and 2007:

<b>Research and Development Expenses</b>	<b>Year Ended December 31,</b>	
	<b>2008</b>	<b>2007</b>
Direct project costs:		
Clinical trials	\$ 7,441,000	\$ 14,595,000
Contract research and development, consulting, materials and other direct costs	8,731,000	16,253,000
Milestone license fees		6,000,000
Salaries, benefits and related costs	4,089,000	4,007,000
Stock-based compensation	1,748,000	4,259,000
Total direct costs	22,009,000	45,114,000
Indirect project costs	1,926,000	2,121,000
Total	\$ 23,935,000	\$ 47,235,000

Direct costs decreased by approximately \$23.1 million primarily as a result of the absence of any milestone license payments in 2008, lower expenses relating to our NDA for iloperidone and lower clinical trial and manufacturing expenses and by decreases in stock-based compensation expense. Clinical trials expense decreased by approximately \$7.2 million primarily due to the costs incurred in 2007 in our Phase III trial of iloperidone in schizophrenia and in our tasimelteon clinical pharmacology trials that were completed in 2007. The clinical trial costs incurred in 2008 relate primarily to our Phase III trial of tasimelteon in primary insomnia that we initiated during the third quarter of 2007. Contract research and development, consulting, materials and other direct costs decreased by approximately \$7.5 million primarily as a result of decreased development costs incurred in connection with the lower manufacturing costs for the iloperidone and tasimelteon programs netted with the increase in consulting fees incurred with the engagement of the regulatory consultant to assist us in our efforts to obtain FDA approval of the iloperidone NDA. Prior to FDA approval of our products, manufacturing related costs are included in research and development expense. There were no milestone license fees incurred in 2008. Stock-based compensation expense decreased by approximately \$2.5 million as a result of the lower fair value of options granted during 2008 compared to options granted in prior periods and the reversal of cumulative amortization of deferred stock-based compensation related to the cancellation of unvested options in connection with the workforce reduction in December 2008.

*General and administrative expenses.* General and administrative expenses decreased related to approximately \$3.9 million, or 12%, to approximately \$28.9 million for the year ended December 31, 2008 from approximately \$32.8 million for the year ended December 31, 2007.



**Table of Contents**

The following table analyzes the components of our general and administrative expenses for the years ended December 31, 2008 and 2007:

<b>General and Administrative Expenses</b>	<b>Year Ended December 31,</b>	
	<b>2008</b>	<b>2007</b>
Salaries, benefits and related costs	\$ 4,946,000	\$ 3,263,000
Stock-based compensation	11,667,000	15,228,000
Marketing and related consulting services	5,731,000	8,047,000
Legal and other professional expenses	3,719,000	3,142,000
Other expenses	2,847,000	3,124,000
<b>Total</b>	<b>\$ 28,910,000</b>	<b>\$ 32,804,000</b>

Salaries, benefits and related costs increased by approximately \$1.7 million for the year ended December 31, 2008 due to a severance accrual of \$1.0 million relating to the workforce reduction in December 2008. Stock-based compensation expense decreased by approximately \$3.6 million as a result of the reversal of cumulative amortization of deferred stock-based compensation related to the cancellation of unvested options in connection with the workforce reduction in December 2008 and to the lower fair value of options granted during 2008 compared to options granted in prior periods. Marketing and related consulting services decreased by approximately \$2.3 million due to the decrease in our market research and other pre-commercial launch activities following receipt of the not-approvable letter from the FDA regarding the Company's NDA for iloperidone. Legal and other professional expenses increased by approximately \$577,000 due primarily to a higher level of consulting activity in 2008 in support of business development activities. Other expenses decreased approximately \$277,000 primarily due to lower accounting fees relating to compliance with the Sarbanes-Oxley Act (Sarbanes-Oxley). The 2007 accounting fees for Sarbanes-Oxley were higher due to the first year implementation for the Company to be compliant with Sarbanes-Oxley.

*Other income, net.* Net other income for the year ended December 31, 2008 was approximately \$1.8 million compared to approximately \$6.0 million for the year ended December 31, 2007. Interest income decreased by approximately \$4.1 million due to lower average cash and marketable securities balances for the year and lower short-term interest rates which generated substantially lower interest income than in 2007. Other income for the year ended December 31, 2007 includes approximately \$71,000 in revenue recognized from a grant from the Economic Development Board in Singapore. We do not expect to receive similar grants in the future.

The following table analyzes the components of our other income, net amounts:

	<b>Year Ended December 31,</b>	
	<b>2008</b>	<b>2007</b>
Interest income	\$ 1,781,000	\$ 5,907,000
Other income		71,000
<b>Total, net</b>	<b>\$ 1,781,000</b>	<b>\$ 5,978,000</b>

***Year ended December 31, 2007 compared to year ended December 31, 2006***

*Research and development expenses.* Research and development expenses decreased by approximately \$4.8 million, or 9.3%, to approximately \$47.2 million for the year ended December 31, 2007 compared to approximately \$52.1 million for the year ended December 31, 2006.

**Table of Contents**

The following table discloses the components of research and development expenses reflecting all of our project expenses for the years ended December 31, 2007 and 2006:

<b>Research and Development Expenses</b>	<b>Year Ended December 31,</b>	
	<b>2007</b>	<b>2006</b>
Direct project costs:		
Clinical trials	\$ 14,595,000	\$ 36,249,000
Contract research and development, consulting, materials and other costs	16,253,000	8,958,000
Milestone license fees	6,000,000	1,000,000
Salaries, benefits and related costs	4,007,000	3,327,000
Stock-based compensation	4,259,000	742,000
Total direct costs	45,114,000	50,276,000
Indirect project costs	2,121,000	1,795,000
Total	\$ 47,235,000	\$ 52,071,000

Direct costs decreased by approximately \$5.2 million primarily as a result of lower clinical trial expenses for the Company's iloperidone and tasimelteon Phase III trials that were primarily completed in 2006, offset by increase in clinical manufacturing activities for both iloperidone and tasimelteon and by increases in milestone license fees and stock-based compensation expense. Clinical trials expense decreased by approximately \$21.7 million primarily due to the costs incurred in 2006 in our Phase III trial of iloperidone in schizophrenia and in our Phase III trial of tasimelteon in transient insomnia that were completed primarily in 2006. The clinical trial costs incurred in 2007 relate primarily to our Phase II trial of VSF-173 in excessive sleepiness, to our Phase III trial of tasimelteon in chronic insomnia that we initiated during the fourth quarter of 2007, and to the completion of our Phase III trial of iloperidone in schizophrenia. Contract research and development, consulting, materials and other direct costs increased by approximately \$7.3 million primarily as a result of increased NDA related expenses and development costs incurred in connection with the manufacturing of clinical supply materials for our iloperidone and tasimelteon programs. Prior to FDA approval of our products, manufacturing related costs are included in research and development expense. Milestone license fees increased by \$5.0 million due to the milestone license fee payment to Novartis during 2007 upon the acceptance of our NDA filing for iloperidone during 2007. Salaries, benefits and related costs increased approximately \$680,000 for the year ended December 31, 2007 due to an increase in personnel to support the development and clinical trial activities for iloperidone and tasimelteon. Stock-based compensation expense increased by approximately \$3.5 million as a result of the higher fair value of options granted during 2007 compared to options granted in prior periods.

*General and administrative expenses.* General and administrative expenses increased approximately \$19.2 million, or 141%, to approximately \$32.8 million for the year ended December 31, 2007 from approximately \$13.6 million for the year ended December 31, 2006.

The following table analyzes the components of our general and administrative expenses for the years ended December 31, 2007 and 2006:

**Year Ended**

<b>General and Administrative Expenses</b>	<b>December 31,</b>	
	<b>2007</b>	<b>2006</b>
Salaries, benefits and related costs	\$ 3,263,000	\$ 2,609,000
Stock-based compensation	15,228,000	5,350,000
Marketing and related consulting services	8,047,000	1,187,000
Legal and other professional expenses	3,142,000	1,760,000
Other expenses	3,124,000	2,732,000
Total	\$ 32,804,000	\$ 13,638,000

**Table of Contents**

Salaries, benefits and related costs increased by approximately \$654,000 for the year ended December 31, 2007 due to an increase in personnel as we continued to develop the administrative, market research, business development and other functions required to support the development and clinical trial activities for iloperidone, tasimelteon and our other product candidates. Stock-based compensation expense increased by approximately \$9.9 million as a result of the higher fair value of options granted during 2007 compared to options granted in prior periods. Marketing and related consulting services increased by approximately \$6.9 million due to the increase in our market research and other pre-commercial launch activities. Legal and other professional expenses increased by approximately \$1.4 million due primarily to an increase in legal, accounting and other professional expenses associated with being a public company as well as due to a higher level of consulting activity in 2007 in support of business development activities. Other expenses increased approximately \$392,000 primarily due to increased insurance costs.

*Other income, net.* Net other income in the year ended December 31, 2007 was approximately \$6.0 million compared to net other income of approximately \$2.2 million in the year ended December 31, 2006. Interest income increased by approximately \$3.7 million due to higher average cash and marketable securities balances for the year and higher short-term interest rates which generated substantially higher interest income than in 2006. Other income for the year ended December 31, 2007 includes approximately \$71,000 in revenue recognized from a grant from the Economic Development Board in Singapore. We do not expect to receive similar grants in the future.

Our other income, net for the years ended December 31, 2007 and 2006 are as follows:

	<b>Year Ended December 31,</b>	
	<b>2007</b>	<b>2006</b>
Interest income	\$ 5,907,000	\$ 2,203,000
Interest expense		(5,000)
Other income	71,000	
Total, net	\$ 5,978,000	\$ 2,198,000

**Liquidity and capital resources**

We have funded our operations through December 31, 2008 principally with the net proceeds from private preferred stock offerings totaling approximately \$62.0 million, with net proceeds from our April 2006 initial public offering of approximately \$53.3 and with net proceeds from our January 2007 follow-on offering of approximately \$111.3 million.

At December 31, 2008, our total cash and cash equivalents and marketable securities were approximately \$46.5 million, compared to approximately \$93.2 million at December 31, 2007. Our cash and cash equivalents are deposits in operating accounts and highly liquid investments with an original maturity of 90 days or less at date of purchase and consist of time deposits, investments in money market funds with commercial banks and financial institutions, and commercial paper of high-quality corporate issuers.

**Table of Contents**

As of December 31, 2008 and 2007 our liquidity resources are summarized as follows:

	<b>As of December 31,</b>	
	<b>2008</b>	<b>2007</b>
<b>Balance sheet data</b>		
Cash and cash equivalents	\$ 39,079,000	\$ 41,930,000
U.S. Treasury and government agencies	2,000,000	3,980,000
U.S. corporate debt	5,252,000	33,339,000
U.S. asset-backed securities	127,000	5,925,000
Marketable securities, short-term	7,379,000	43,244,000
U.S. Treasury and government agencies		2,002,000
U.S. corporate debt		1,970,000
U.S. asset-backed securities		4,007,000
Marketable securities, long-term		7,979,000
	\$ 46,458,000	\$ 93,153,000

As of December 31, 2008, we maintained all of our cash, cash equivalents and marketable securities in three financial institutions. Deposits held with these institutions may exceed the amount of insurance provided on such deposits, but we do not anticipate any losses with respect to such deposits.

In September 2006, the FASB issued Statement No. 157, *Fair Value Measurements* (SFAS 157). SFAS 157 defines fair value, establishes a framework for measuring fair value in accordance with GAAP, and expands disclosures about fair value measurements. In February 2008, the FASB agreed to delay the effective date of SFAS 157 for all nonfinancial assets and nonfinancial liabilities, except those that are recognized or disclosed at fair value in the financial statements on a recurring basis, to fiscal years beginning after November 15, 2008. The Company has adopted the provisions of SFAS 157 as of January 1, 2008, for financial instruments. Although the adoption of SFAS 157 did not materially impact its financial condition, results of operations, or cash flow, the Company is now required to provide additional disclosures as part of its financial statements. Under FAS No. 159, entities are permitted to choose to measure many financial instruments and certain other items at fair value. The Company did not elect the fair value measurement option under FAS No. 159, *The Fair Value Option for Financial Assets and Financial Liabilities* including an amendment to FAS 115 (SFAS 159), for any of its financial assets or liabilities.

SFAS 157 establishes a three-tier fair value hierarchy, which prioritizes the inputs used in measuring fair value. These tiers include:

Level 1 defined as observable inputs such as quoted prices in active markets

Level 2 defined as inputs other than quoted prices in active markets that are either directly or indirectly observable

Level 3 defined as unobservable inputs in which little or no market data exists, therefore requiring an entity to develop its own assumptions



**Table of Contents**

As of December 31, 2008, the Company held certain assets that are required to be measured at fair value on a recurring basis. The Company currently does not have non-financial assets and non-financial liabilities that are required to be measured at fair value on a recurring basis.

Description :	Fair Value Measurements at Reporting Date Using			
	December 31, 2008	Quoted Prices in Active Markets for Identical Assets (Level 1)	Significant Other Observable Inputs (Level 2)	Significant Unobservable Inputs (Level 3)
Available-for-sale securities	\$ 7,378,798	\$ 1,999,860	\$ 5,378,938	\$
Total	\$ 7,378,798	\$ 1,999,860	\$ 5,378,938	\$

Our activities will necessitate significant uses of working capital throughout 2009 and beyond. Based on our current operating plans, we believe that our existing cash, cash equivalents and marketable securities will be sufficient to meet our anticipated operating needs through the second quarter of 2010, and after that time we will require additional capital. In budgeting for our activities, we have relied on a number of assumptions, including assumptions that we will not conduct any additional clinical trials for either the oral or injectable formulations of iloperidone, that we will not engage in any further commercial activities related to iloperidone, that we will not engage in further in-licensing activities, that we will not receive any proceeds from potential partnerships, that we will not conduct additional trials for tasimelteon, that we will be able to retain our key personnel, that we will continue to seek FDA approval of iloperidone, that we will continue to evaluate clinical and pre-clinical compounds for potential development, and that we will not incur any significant contingent liabilities.

We may need to raise additional funds if one or more of our assumptions proves to be incorrect or if we choose to resume our commercialization efforts with respect to iloperidone, expand our product development efforts, conduct additional clinical trials for one or more of our product candidates or seek to acquire additional product candidates, and we may decide to raise additional funds even before they are needed if the conditions for raising capital are favorable. 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 research and development activities, we may not be able to continue operations, or we may have to enter into 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 collaborations, if consummated prior to proof-of-efficacy or safety of a given product candidate, could impair our ability to realize value from that product candidate.

**Cash flow**

The following table summarizes our cash flows for the years ended December 31, 2008, 2007 and 2006.

**Year Ended December 31,**



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	<b>2008</b>	<b>2007</b>	<b>2006</b>
Net cash (used in) provided by Operating activities	\$ (45,955,000)	\$ (51,641,000)	\$ (51,620,000)
Investing activities	43,088,000	(48,760,000)	8,221,000
Financing activities		111,403,000	53,315,000
Effect of foreign currency translation	17,000	(1,000)	
Net change in cash and cash equivalents	\$ (2,850,000)	\$ 11,001,000	\$ 9,916,000

**Table of Contents*****Year ended December 31, 2008 compared to year ended December 31, 2007***

Net cash used in operations was approximately \$46.0 million for the year ended December 31, 2008 and \$51.6 million for the year ended December 31, 2007. The net loss for the year ended December 31, 2008 of approximately \$51.1 million was offset primarily by non-cash charges for depreciation and amortization of approximately \$531,000, stock-based compensation of approximately \$13.4 million, and decreases in accrued expenses and accounts payable of approximately \$9.4 million, principally related to clinical trial expenses. Net cash provided by investing activities for the year ended December 31, 2008 was approximately \$43.1 million and consisted primarily of net maturities and sales of marketable securities of approximately \$44.0 million. There was no net cash provided by financing activities for the year ended December 31, 2008.

***Year ended December 31, 2007 compared to year ended December 31, 2006***

Net cash used in operations was approximately \$51.6 million for both of the years ended December 31, 2007 and 2006. The net loss for the year ended December 31, 2007 of approximately \$74.1 million was offset primarily by non-cash charges for depreciation and amortization of approximately \$572,000, stock-based compensation of approximately \$19.6 million, and an increase in accrued expenses and accounts payable of approximately \$3.7 million, principally related to clinical trial expenses and expenses incurred in preparation of the commercial launch of iloperidone, and other net changes in working capital. Net cash used in investing activities for the year ended December 31, 2007 was approximately \$48.8 million and consisted primarily of net purchases of marketable securities of approximately \$48.7 million. Net cash provided by financing activities for the year ended December 31, 2007 was approximately \$111.4 million, consisting primarily of net proceeds from our January 2007 follow-on offering of approximately \$111.3 million.

**Contractual obligations and commitments**

The following table summarizes our long-term contractual cash obligations as of December 31, 2008:

	<b>Cash Payments Due by Period</b>						<b>After</b>
	<b>Total</b>	<b>2009</b>	<b>2010</b>	<b>2011</b>	<b>2012</b>	<b>2013</b>	<b>2013</b>
Severance payments	\$ 1,613,000	\$ 1,597,000	\$ 16,000	\$	\$	\$	\$
Operating leases	5,673,000	685,000	706,000	727,000	749,000	771,000	2,035,000
<b>Total</b>	<b>\$ 7,286,000</b>	<b>\$ 2,282,000</b>	<b>\$ 722,000</b>	<b>\$ 727,000</b>	<b>\$ 749,000</b>	<b>\$ 771,000</b>	<b>\$ 2,035,000</b>

*Severance payments.* On December 16, 2008, we committed to a plan of termination that resulted in a work force reduction of 17 employees, including two officers, in order to reduce operating costs. We commenced notification of employees affected by the workforce reduction on December 17, 2008. As of December 31, 2008, we employed 24 full-time employees. This represents approximately a 55% decrease from the 53 employees we had on August 1, 2008.

*Operating leases.* Our commitments under operating leases shown above consist of payments relating to our real estate leases for our current headquarters located in Rockville, Maryland, expiring in 2016.

*Clinical research organization contracts and other contracts.* We have entered into agreements with clinical research organizations responsible for conducting and monitoring our clinical trials for iloperidone and tasimelteon, and have also entered into agreements with clinical supply manufacturing organizations and other outside contractors who will be responsible for additional services supporting our ongoing clinical development processes. These contractual obligations are not reflected in the table above because we may terminate them on no more than 60 days notice without incurring additional charges (other than charges for work completed but not paid for through the effective date of termination and other costs incurred by our contractors in closing out work in progress as of the effective date of termination).

*Consulting fees.* We have engaged a regulatory consultant to assist us in our efforts to obtain FDA approval of the iloperidone NDA. We have committed to initial consulting expenses in the aggregate amount of \$2.0 million pursuant to this engagement, which was expensed in 2008. In addition, we retained the

## **Table of Contents**

services of the consultant on a monthly basis at a retainer fee of \$250,000 per month effective as of January 1, 2009. In the event that the iloperidone NDA is approved by the FDA, we will be obligated to pay the consultant a success fee of \$6.0 million, which amount will be offset by the aggregate amount of all monthly retainer fees previously paid to the consultant (Success Fee). In addition to these fees, we are obligated to reimburse the consultant for its ordinary and necessary business expenses incurred in connection with its engagement. We may terminate the engagement at any time; however, we will remain obligated to pay any remaining Success Fee if the iloperidone NDA is approved by the FDA following such termination.

*License agreements.* In February 2004 and June 2004, we entered into separate licensing agreements with BMS and Novartis, respectively, for the exclusive rights to develop and commercialize our two compounds in clinical development. We are obligated to make payments under the conditions in the agreements upon the achievement of specified clinical, regulatory and commercial milestones. If the products are successfully commercialized we will be required to pay certain royalties based on net sales for each of the licensed products. Please see the notes to the consolidated financial statements included with this report for a more detailed description of these license agreements.

As a result of the successful commencement of the Phase III clinical study of tasimelteon in March 2006, we met the first milestone specified in our licensing agreement with BMS and subsequently paid a license fee of \$1,000,000. During March 2007, we met our first milestone under the license agreement with Novartis for VSF-173 relating to the initiation of the Phase II clinical trial and subsequently paid a license fee of \$1,000,000. On November 3, 2008, we received written notice from Novartis that the license agreement related to VSF-173 had terminated in accordance with its terms as a result of our failure to satisfy a specific development milestone within the time period specified in the license agreement. As a result, we no longer hold any rights with respect to VSF-173 and Novartis has a non-exclusive worldwide license to all information and intellectual property generated by or on behalf of Vanda related to its development of VSF-173. As a result of the acceptance by FDA of our NDA for iloperidone in October 2007, we met a milestone under our license agreement with Novartis and subsequently paid a \$5,000,000 milestone license fee. No amounts were recorded as liabilities relating to the license agreements included in the consolidated financial statements as of December 31, 2008, since the amounts, timing and likelihood of these payments are unknown and will depend on the successful outcome of future clinical trials, regulatory filings, favorable FDA regulatory approvals, growth in product sales and other factors. For a more detailed description of the risks associated with the outcome of such clinical trials, regulatory filings, FDA approvals and product sales, please see the section Risk Factors, Item 1A of Part I of this annual report on Form 10-K.

## **ITEM 7A. QUALITATIVE AND QUANTITATIVE DISCLOSURES ABOUT MARKET RISK**

### **Foreign exchange**

We currently incur a portion of our operating expenses in currencies other than U.S. Dollars, the reporting currency for our consolidated financial statements, and we have determined that such operating expenses have not been significant to date. As a result, we have not been impacted materially by changes in exchange rates and do not expect to be impacted materially for the foreseeable future. However, if operating expenses incurred outside of the United States increase, our results of operations could be adversely impacted by changes in exchange rates. We do not currently hedge foreign currency fluctuations and do not intend to do so for the foreseeable future.

### **Interest rates**

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

of our investments.

## **Table of Contents**

### **Effects of inflation**

Our most liquid assets are cash and cash equivalents and marketable securities. Because of their liquidity, these assets are not directly affected by inflation. We also believe that we have intangible assets in the value of our intellectual property. In accordance with generally accepted accounting principles, we have not capitalized the value of this intellectual property on our balance sheet. Due to the nature of this intellectual property, we believe that these intangible assets are not affected by inflation. Because we intend to retain and continue to use our equipment, furniture and fixtures and leasehold improvements, we believe that the incremental inflation related to replacement costs of such items will not materially affect our operations. However, the rate of inflation affects our expenses, such as those for employee compensation and contract services, which could increase our level of expenses and the rate at which we use our resources.

### **Marketable securities**

We deposit our cash with financial institutions that we consider to be of high credit quality and purchase marketable securities which are generally investment grade, liquid, short-term fixed income securities and money-market instruments denominated in U.S. dollars. We are monitoring one corporate note affected by the current credit crisis. The note is expected to mature in May 2009 and we expect minimal losses, if any.

### **Off-balance sheet arrangements**

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

## **ITEM 8. FINANCIAL STATEMENTS AND SUPPLEMENTARY DATA**

The consolidated financial statements and related financial statement schedules required to be filed are indexed on page 57 and are incorporated herein.

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

None.

## **ITEM 9A. CONTROLS AND PROCEDURES**

### **Conclusion Regarding the Effectiveness of Disclosure Controls and Procedures**

Under the supervision and with the participation of the Company's management, including the Chief Executive Officer and Acting Chief Financial Officer, the Company evaluated the effectiveness of the design and operation of the Company's disclosure controls and procedures (as defined in Rules 13a-15(e) and 15d-15(e) under the Exchange Act) as of December 31, 2008. Based upon that evaluation, the Company's Chief Executive Officer and Acting Chief Financial Officer concluded that the Company's disclosure controls and procedures are effective as of December 31, 2008, the end of the period covered by this annual report, to ensure that the information required to be disclosed by the Company in the reports that it files or submits under the Exchange Act is recorded, processed, summarized and reported within the time periods specified in the SEC's rules and forms, and that such information is accumulated and communicated to our management, including our Chief Executive Officer and Acting Chief Financial Officer, as appropriate to allow timely decisions regarding required disclosures.

**Management's Report on Internal Control Over Financial Reporting**

The Company's management is responsible for establishing and maintaining adequate internal control over financial reporting, as such term is defined in Exchange Act Rule 13a-15(f), for the Company. Under the supervision and with the participation of management, including the Company's Chief Executive Officer and Acting Chief Financial Officer, an evaluation of the effectiveness of the Company's internal control over financial reporting was conducted based on the framework in *Internal Control - Integrated Framework* issued

**Table of Contents**

by the Committee of Sponsoring Organizations of the Treadway Commission ( COSO ). Based on that evaluation, the Company s management concluded that the Company s internal control over financial reporting was effective as of December 31, 2008.

There has been no change in our internal control over financial reporting (as defined in Rules 13a-15(f) and 15d-15(f) of the Exchange Act) during the fourth quarter of 2008 that has materially affected, or is reasonably likely to materially affect, our internal control over financial reporting, other than the termination of the employment of our former Chief Financial Officer in connection with our workforce reduction, which we commenced in December 2008. We instituted certain changes to our key controls to mitigate segregation of duties issues related to a reduced accounting and finance department. However, the changes did not materially affect our internal control over financial reporting as of December 31, 2008.

The effectiveness of the Company s internal control over financial reporting as of December 31, 2008 has been audited by PricewaterhouseCoopers LLP, an independent registered public accounting firm, as stated in their report which appears on page 58 of this Form 10-K.

**ITEM 9B. OTHER INFORMATION**

None.

**PART III**

**ITEM 10. DIRECTORS, EXECUTIVE OFFICERS AND CORPORATE GOVERNANCE**

Information required under this item will be contained in the Company s Proxy Statement for the Annual Meeting of Stockholders to be filed with the SEC within 120 days after the end of the fiscal year ended December 31, 2008, under the captions Election of Directors, Executive Officers, Corporate Governance , and Section 16(a) Beneficial Ownership Reporting Compliance and is incorporated herein by reference pursuant to General Instruction G(3) to Form 10-K.

**ITEM 11. EXECUTIVE COMPENSATION**

Information required under this item will be contained in the Company s Proxy Statement for the Annual Meeting of Stockholders to be filed with the SEC within 120 days after the end of the fiscal year ended December 31, 2008, under the captions Corporate Governance and Executive Compensation, and is incorporated herein by reference pursuant to General Instruction G(3) to Form 10-K, except that information required by Item 407(e)(5) of Regulation S-K will be deemed furnished in this Form 10-K and will not be deemed incorporated by reference into any filing under the Securities Act of 1933 or the Securities Exchange Act of 1934, except to the extent that we specifically incorporate it by reference into such filing.

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

In addition to the information set forth under the caption Securities Authorized for Issuance Under Equity Compensation Plans in Part II of this annual report on Form 10-K, information required under this item will be contained in the Company s Proxy Statement for the Annual Meeting of Stockholders to be filed with the SEC within 120 days after the end of the fiscal year ended December 31, 2008, under the caption Security Ownership by Certain Beneficial Owners and Management and is incorporated herein by reference pursuant to General Instruction G(3) to Form 10-K.



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

Information required under this item will be contained in the Company's Proxy Statement for the Annual Meeting of Stockholders to be filed with the SEC within 120 days after the end of the fiscal year ended

**Table of Contents**

December 31, 2008, under the caption "Corporate Governance" and is incorporated herein by reference pursuant to General Instruction G(3) to Form 10-K.

**ITEM 14. PRINCIPAL ACCOUNTING FEES AND SERVICES**

Information required under this item will be contained in the Company's Proxy Statement for the Annual Meeting of Stockholders to be filed with the SEC within 120 days after the end of the fiscal year ended December 31, 2008, under the caption "Ratification of Selection of Independent Registered Public Accounting Firm" and is incorporated herein by reference pursuant to General Instruction G(3) to Form 10-K.

**PART IV**

**ITEM 15. EXHIBITS AND FINANCIAL STATEMENTS SCHEDULES**

The consolidated financial statements filed as part of this annual report on Form 10-K are listed and indexed at page 57. Certain schedules are omitted because they are not applicable, or not required, or because the required information is included in the consolidated financial statements or notes thereto.

The Exhibits listed in the Exhibit Index immediately preceding the Exhibits are filed as part of this annual report on Form 10-K.

**Table of Contents****Signatures**

Pursuant to the requirements of Section 13 and 15(d) of the Securities Exchange Act of 1934, the registrant has duly caused this annual report on Form 10-K to be signed on its behalf by the undersigned, thereunto duly authorized, in Rockville, Maryland, on March 13, 2009.

VANDA PHARMACEUTICALS INC.

By: /s/ MIHAEL H. POLYMEROPOULOS, M.D.  
 Mihael H. Polymeropoulos, M.D.  
*Chief Executive Officer*

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

Name	Title	Date
/s/ MIHAEL H. POLYMEROPOULOS, M.D. Mihael H. Polymeropoulos, M.D.	President and Chief Executive Officer and Director (principal executive officer)	March 13, 2009
/s/ STEPHANIE R. IRISH Stephanie R. Irish	Acting Chief Financial Officer and Treasurer (principal financial and accounting officer)	March 13, 2009
/s/ ARGERIS N. KARABELAS, Ph.D. Argeris N. Karabelas, Ph.D.	Chairman of the Board and Director	March 13, 2009
/s/ RICHARD W. DUGAN Richard W. Dugan	Director	March 13, 2009
/s/ BRIAN K. HALAK, Ph.D. Brian K. Halak, Ph.D.	Director	March 13, 2009
/s/ HOWARD PIEN Howard Pien	Director	March 13, 2009
/s/ DAVID RAMSAY David Ramsay	Director	March 13, 2009

/s/ H. THOMAS WATKINS

Director

March 13, 2009

H. Thomas Watkins

**Vanda Pharmaceuticals Inc.**

**Index to consolidated financial statements**

	<b>Page(s)</b>
<u>Report of Independent Registered Public Accounting Firm</u>	58
Consolidated financial statements	
<u>Balance sheets at December 31, 2008 and 2007</u>	59
<u>Statements of operations for the years ended December 31, 2008, 2007 and 2006 and the period from March 13, 2003 (inception) to December 31, 2008</u>	60
<u>Statements of changes in stockholders' equity for the period from March 13, 2003 (inception) to December 31, 2004 and for the years ended December 31, 2005, 2006, 2007 and 2008</u>	61
<u>Statements of cash flows for the years ended December 31, 2008, 2007 and 2006 and the period from March 13, 2003 (inception) to December 31, 2008</u>	65
<u>Notes to the consolidated financial statements</u>	66

**Table of Contents**

**Report of Independent Registered Public Accounting Firm**

To the Board of Directors and Stockholders  
of Vanda Pharmaceuticals Inc. (A development stage enterprise)

In our opinion, the accompanying consolidated balance sheets and the related consolidated statements of operations, of changes in stockholders' equity, and of cash flows present fairly, in all material respects, the financial position of Vanda Pharmaceuticals Inc. and Subsidiary (collectively, the Company) (a development stage enterprise) at December 31, 2008 and 2007, and the results of their operations and their cash flows for each of the three years in the period ended December 31, 2008 and for the period from March 13, 2003 (date of inception) to December 31, 2008, in conformity with accounting principles generally accepted in the United States of America. Also in our opinion, the Company maintained, in all material respects, effective internal control over financial reporting as of December 31, 2008, based on criteria established in *Internal Control - Integrated Framework* issued by the Committee of Sponsoring Organizations of the Treadway Commission (COSO). The Company's management is responsible for these financial statements, for maintaining effective internal control over financial reporting and for its assessment of the effectiveness of internal control over financial reporting, included in Management's Report on Internal Control Over Financial Reporting appearing under Item 9A. Our responsibility is to express opinions on these financial statements and on the Company's internal control over financial reporting based on our audits (which were integrated audits in 2008 and 2007). We conducted our audits in accordance with the standards of the Public Company Accounting Oversight Board (United States). Those standards require that we plan and perform the audits to obtain reasonable assurance about whether the financial statements are free of material misstatement and whether effective internal control over financial reporting was maintained in all material respects. Our audits of the financial statements included examining, on a test basis, evidence supporting the amounts and disclosures in the financial statements, assessing the accounting principles used and significant estimates made by management, and evaluating the overall financial statement presentation. Our audit of internal control over financial reporting included obtaining an understanding of internal control over financial reporting, assessing the risk that a material weakness exists, and testing and evaluating the design and operating effectiveness of internal control based on the assessed risk. Our audits also included performing such other procedures as we considered necessary in the circumstances. We believe that our audits provide a reasonable basis for our opinions.

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

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

Baltimore, Maryland

March 13, 2009

**Table of Contents**

**Vanda Pharmaceuticals Inc.**  
**(A development stage enterprise)**

**Consolidated Balance Sheets**

	<b>December 31,</b>	
	<b>2008</b>	<b>2007</b>
<b>Assets</b>		
Current assets		
Cash and cash equivalents	\$ 39,079,304	\$ 41,929,533
Marketable securities	7,378,798	43,243,960
Prepaid expenses and other current assets	1,287,400	1,781,881
<b>Total current assets</b>	<b>47,745,502</b>	<b>86,955,374</b>
Marketable securities, long-term		7,979,331
Property and equipment, net	1,758,111	1,345,845
Deposits		150,000
Restricted cash	430,230	430,230
<b>Total assets</b>	<b>\$ 49,933,843</b>	<b>\$ 96,860,780</b>
<b>Liabilities and stockholders equity</b>		
Current liabilities		
Accounts payable	\$ 512,382	\$ 2,988,069
Accrued liabilities	2,898,417	9,789,738
<b>Total current liabilities</b>	<b>3,410,799</b>	<b>12,777,807</b>
Deferred rent	502,770	354,042
<b>Total liabilities</b>	<b>3,913,569</b>	<b>13,131,849</b>
Commitments		
Stockholders equity		
Preferred stock, \$0.001 par value; 20,000,000 shares authorized and none issued and outstanding at December 31, 2008 and 2007		
Common stock, \$0.001 par value; 150,000,000 shares authorized, 26,653,478 and 26,652,728 shares issued and outstanding at December 31, 2008 and 2007, respectively	26,653	26,653
Additional paid-in capital	270,988,157	257,600,368
Accumulated other comprehensive income (loss)	(20,029)	12,176
Deficit accumulated during the development stage	(224,974,507)	(173,910,266)
<b>Total stockholders equity</b>	<b>46,020,274</b>	<b>83,728,931</b>
<b>Total liabilities and stockholders equity</b>	<b>\$ 49,933,843</b>	<b>\$ 96,860,780</b>



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

**Table of Contents**

**Vanda Pharmaceuticals Inc.**  
**(A development stage enterprise)**

**Consolidated Statements of Operations**

	<b>Year Ended December 31,</b>			<b>Period from</b>
	<b>2008</b>	<b>2007</b>	<b>2006</b>	<b>March 13, 2003</b>
				<b>(inception) to</b>
				<b>December 31,</b>
				<b>2008</b>
Revenues from services	\$	\$	\$	\$ 81,545
Operating expenses:				
Research and development	23,935,541	47,234,867	52,070,776	149,585,314
General and administrative	28,909,580	32,803,508	13,637,664	85,918,843
Total operating expenses	52,845,121	80,038,375	65,708,440	235,504,157
Loss from operations	(52,845,121)	(80,038,375)	(65,708,440)	(235,422,612)
Other income (expense):				
Interest income	1,780,880	5,907,219	2,202,654	10,479,669
Interest expense			(4,833)	(80,485)
Other income, net		71,345		71,947
Total other income, net	1,780,880	5,978,564	2,197,821	10,471,131
Loss before tax provision	(51,064,241)	(74,059,811)	(63,510,619)	(224,951,481)
Tax provision		9,879	549	23,026
Net loss	(51,064,241)	(74,069,690)	(63,511,168)	(224,974,507)
Beneficial conversion feature deemed dividend to preferred stockholders				(33,486,623)
Net loss attributable to common stockholders	\$ (51,064,241)	\$ (74,069,690)	\$ (63,511,168)	\$ (258,461,130)
Basic and diluted net loss per share attributable to common stockholders	\$ (1.92)	\$ (2.81)	\$ (3.97)	
Shares used in calculation of basic and diluted net loss per share attributable to common stockholders	26,650,126	26,360,177	16,001,815	

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

**Table of Contents**

**Vanda Pharmaceuticals Inc.  
(A development stage enterprise)**

**Statements of Changes in Stockholders' Equity**

Series A Preferred Stock	Series B Preferred Stock	Common Stock	Additional Paid-in Capital	Deferred Stock-Based Compensation	Accumulated Other Comprehensive Loss	Deficit Accumulated During the Development Stage
Par Value	Shares	Par Value	Shares	Par Value	Loss	Stage
\$		\$		\$	\$	\$
000 9,963,541			3,020	3		
	15,040,654	18,345,023				
				281,130	(281,130)	
					23,196	
				14,937		(12,445,107)
					(2,576)	
000 \$ 9,963,541	15,040,654	\$ 18,345,023	3,020	\$ 3	\$ 340,637	\$ (257,934)
					\$ (2,576)	\$ (12,445,107)

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

**Table of Contents**

**Vanda Pharmaceuticals Inc.**  
**(A development stage enterprise)**

**Statements of Changes in Stockholders' Equity**

Series A Preferred Stock	Series B Preferred Stock		Common Stock		Additional Paid-in Capital	Deferred Stock-Based Compensation	Accumulated Other Comprehensive Loss	Deficit Accumulated During the Development Stage
	Shares	Par Value	Shares	Par Value				
\$ 9,963,541	15,040,654	\$ 18,345,023	3,020	\$ 3	\$ 340,637	\$ (257,934)	\$ (2,576)	\$ (12,445,100)
	27,235,783	33,486,623						
			95,925	96	31,658			
					18,788,385	(18,788,385)		
					1,702,625	(1,702,625)		
					3,119,676			
						1,982,501		
					33,486,623			
					(33,486,623)			

(23,884,30

(17,711)

2,678

\$ 9,963,541 42,276,437 \$ 51,831,646 98,945 \$ 99 \$ 23,982,981 \$ (18,766,443) \$ (17,609) \$ (36,329,40

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

**Table of Contents**

**Vanda Pharmaceuticals Inc.**  
**(A development stage enterprise)**

**Statements of Changes in Stockholders' Equity**

	Series B Preferred Stock		Common Stock		Additional Paid-in	Deferred Stock-Based Compensation	Accumulated Other Comprehensive Income (Loss)	Def Accum Durin Develop
Value	Shares	Par Value	Shares	Par Value	Capital			Sta
963,541	42,276,437	\$ 51,831,646	98,945	\$ 99	\$ 23,982,981	\$ (18,766,443)	\$ (17,609)	\$ (36,
					(18,766,443)	18,766,443		
			5,964,188	5,964	53,323,987			
963,541)	(42,276,437)	(51,831,646)	15,794,632	15,795	61,779,392			
			222,233	223	78,301			
			48,536	48	48,543			
					6,092,339			
					39,488			(63,
							17,007	
							(2,667)	
			22,128,534	22,129	126,578,588		(3,269)	(99,
			154,194	154	148,486			

4,370,000      4,370      111,250,480

19,486,844

135,970

(74,

(12,940)

28,385

\$                    26,652,728    \$ 26,653    \$ 257,600,368    \$                    \$ 12,176    \$ (173,

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



**Table of Contents**

**Vanda Pharmaceuticals Inc.  
(A development stage enterprise)**

**Statements of Changes in Stockholders' Equity**

	Series A Preferred Stock Par Shares	Series B Preferred Stock Par Value	Common Stock Shares	Common Stock Par Value	Additional Paid-In Capital	Deferred Stock Compensation	Accumulated Other Comprehensive Loss	Deficit Accumulated During the Development Stage	Accumulated Comprehensive Loss
2007	\$	\$	26,652,728	\$ 26,653	\$ 257,600,368	\$	\$ 12,176	\$ (173,910,266)	\$
			750		13,415,460				
						(27,671)			
Loss:								(51,064,241)	(51,064,241)
							16,220		16,220
							(48,425)		(48,425)
Loss									\$ (51,096,446)
2008	\$	\$	26,653,478	\$ 26,653	\$ 270,988,157	\$	\$ (20,029)	\$ (224,974,507)	

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

**Table of Contents**

**Vanda Pharmaceuticals Inc.**  
**(A development stage enterprise)**

**Consolidated Statements of Cash Flows**

	<b>Year Ended December 31,</b>			<b>Period from</b>
	<b>2008</b>	<b>2007</b>	<b>2006</b>	<b>March 13, 2003</b>
				<b>(Inception) to</b>
				<b>December 31,</b>
				<b>2008</b>
<b>Cash flows from operating activities</b>				
Net loss	\$ (51,064,241)	\$ (74,069,690)	\$ (63,511,168)	\$ (224,974,507)
Adjustments to reconcile net loss to net cash used in operating activities				
Depreciation and amortization	530,805	571,586	575,372	2,499,661
Stock-based compensation	13,387,789	19,622,814	6,131,827	44,323,312
(Loss) gain on disposal of assets	(174)	28,713	29,528	57,458
Accretion of discount on investments	(235,162)	(1,571,905)	(378,739)	(2,227,320)
Changes in assets and liabilities:				
Prepaid expenses and other current assets	495,200	168,987	270,745	(1,287,400)
Deposits	150,000		690,000	
Accounts payable	(2,475,697)	204,029	526,711	512,382
Accrued expenses	(6,892,577)	3,465,028	3,811,373	2,898,417
Deferred grant revenue		(147,464)		
Deferred rent and other liabilities	148,728	86,644	234,833	502,770
Net cash used in operating activities	(45,955,329)	(51,641,258)	(51,619,518)	(177,695,227)
<b>Cash flows from investing activities</b>				
Purchases of property and equipment	(943,659)	(279,433)	(1,354,156)	(4,381,391)
Proceeds from sale of property and equipment		200,179		200,179
Purchases of marketable securities	(14,786,080)	(138,953,879)	(102,232,608)	(267,818,742)
Proceeds from sale of marketable securities	11,258,094	3,577,859	82,137,888	96,973,843
Maturities of marketable securities	47,560,000	86,695,000	29,670,000	165,675,000
Investments in restricted cash				(430,230)
Net cash (used in) provided by investing activities	43,088,355	(48,760,274)	8,221,124	(9,781,341)
<b>Cash flows from financing activities</b>				
Proceeds from borrowings on note payable				515,147
			(1,540)	(91,796)

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Principal payments on obligations under capital lease				
Principal payments on note payable			(141,074)	(515,147)
Proceeds from the issuance of preferred stock, net of issuance costs				61,795,187
Proceeds from exercise of stock options and warrants		148,640	127,115	307,509
Proceeds from issuance of common stock, net of issuance costs		111,254,850	53,329,951	164,588,801
Net cash provided by financing activities		111,403,490	53,314,452	226,599,701
Effect of foreign currency translation	16,745	(1,320)	22	(43,829)
Net change in cash and cash equivalents	(2,850,229)	11,000,638	9,916,080	39,079,304
<b>Cash and cash equivalents</b>				
Beginning of period	41,929,533	30,928,895	21,012,815	
End of period	\$ 39,079,304	\$ 41,929,533	\$ 30,928,895	\$ 39,079,304
<b>Supplemental disclosure</b>				
Cash payments for interest	\$	\$	\$ 5,994	\$ 76,612
<b>Supplemental disclosure of non-cash financing activities</b>				
Equipment acquired through obligation under capital lease	\$	\$	\$	\$ 95,305

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

**Table of Contents**

**Vanda Pharmaceuticals Inc.  
(A development stage enterprise)**

**Notes to the Consolidated Financial Statements**

**1. Business organization and presentation**

***Business organization***

Vanda Pharmaceuticals Inc. (Vanda or the Company) is a biopharmaceutical company focused on the development and commercialization of small molecule therapeutics, with exclusive worldwide commercial rights to two product candidates in clinical development for various central nervous system disorders. Vanda commenced its operations in 2003. The Company's lead product candidate, iloperidone, is a compound for the treatment of schizophrenia. The Company submitted a New Drug Application (NDA) for iloperidone in schizophrenia to the United States Food and Drug Administration (FDA) on September 27, 2007. On November 27, 2007, the FDA accepted the NDA for iloperidone in schizophrenia. In July 2008, the Company announced that the FDA had determined that Vanda's NDA was not approvable and indicated, among other things, that the Company would have to conduct additional studies and submit that data before the FDA would approve iloperidone for commercial sale for the treatment of schizophrenia. In September 2008, the Company met with the FDA to discuss the FDA's determination. The FDA asked the Company to provide a complete response to the not-approvable letter, which the Company submitted on November 6, 2008. The FDA accepted the complete response for review and has set a new target action date of May 6, 2009. Pending the FDA's reply to the Company's complete response, the Company has suspended all non-essential iloperidone-related activities. The Company's second product candidate, tasimelteon, is a compound for the treatment of sleep and mood disorders. In November 2006, Vanda announced positive top-line results from the Phase III trial of tasimelteon in transient insomnia. In June 2008, the Company announced positive top-line results from the Phase III trial of tasimelteon in chronic primary insomnia. Tasimelteon is also ready for Phase II trials for the treatment of depression. The Company's rights to a third product candidate, VSF-173, a compound for the treatment of excessive sleepiness, were terminated as a result of the Company's failure to satisfy a specific development milestone within the time period specified in the license agreement pursuant to which the Company was granted such rights.

***Capital resources***

Since its inception, the Company has devoted substantially all of its efforts to business planning, research and development, market research, recruiting management and technical staff, acquiring operating assets and raising capital. Accordingly, the Company is considered to be in the development stage as defined in Statement of Financial Accounting Standards (SFAS) No. 7, *Accounting and Reporting by Development Stage Enterprises*.

The Company's activities will necessitate significant uses of working capital throughout 2009 and beyond. Additionally, the Company's capital requirements will depend on many factors, including the success of the Company's research and development efforts, payments received under contractual agreements with other parties, if any, and the status of competitive products. The Company plans to continue financing its operations with cash received from financing activities. Based on its current operating plans, the Company believes that its existing cash, cash equivalents and marketable securities will be sufficient to meet the Company's anticipated operating needs through the second quarter of 2010, and after that time Vanda will require additional capital. In budgeting for its activities, the Company has relied on a number of assumptions, including assumptions that the Company will not conduct any additional clinical trials for either the oral or injectable formulations of iloperidone, that it will not engage in any further commercial activities related to iloperidone, that it will not engage in further in-licensing activities, that it will not receive any proceeds from potential partnerships, that it will not conduct additional trials for tasimelteon, that it will be able to retain its key personnel, that we will continue to seek FDA approval of iloperidone, that it will continue to

evaluate clinical and pre-clinical compounds for potential development, and that it will not incur any significant contingent liabilities.

**Table of Contents**

**Vanda Pharmaceuticals Inc.  
(A development stage enterprise)**

**Notes to the Consolidated Financial Statements (Continued)**

The Company may need to raise additional funds if one or more of its assumptions proves to be incorrect or if it chooses to resume its commercialization efforts with respect to iloperidone, expand its product development efforts, conduct additional clinical trials for one or more of its product candidates or seek to acquire additional product candidates, and the Company may decide to raise additional funds even before they are needed if the conditions for raising capital are favorable. However, the Company may not be able to raise additional funds on acceptable terms, or at all. If the Company is unable to secure sufficient capital to fund its research and development activities, the Company may not be able to continue operations, or the Company may have to enter into collaboration agreements that could require the Company to share commercial rights to its products to a greater extent or at earlier stages in the drug development process than is currently intended. These collaborations, if consummated prior to proof-of-efficacy or safety of a given product candidate, could impair the Company's ability to realize value from that product candidate.

***Basis of presentation***

The accompanying consolidated financial statements have been prepared in accordance with accounting principles generally accepted in the United States of America. The consolidated financial statements include the accounts of the Company and its wholly-owned Singapore subsidiary that ceased operations during 2007. All inter-company balances and transactions have been eliminated.

**2. Summary of significant accounting policies**

***Use of estimates***

The preparation of financial statements in conformity with accounting principles generally accepted in the United States of America requires management to make estimates that affect the reported amounts of assets and liabilities at the date of the financial statements, disclosure of contingent assets and liabilities, and the reported amounts of revenue and expenses during the reporting period. Actual results could differ from those estimates.

***Cash and cash equivalents***

For purposes of the consolidated balance sheets and consolidated statements of cash flows, cash equivalents represent highly-liquid investments with a maturity date of three months or less at the date of purchase.

***Marketable securities***

The Company classifies all of its marketable securities as available-for-sale securities. The Company's investment policy requires the selection of high-quality issuers, with bond ratings of AAA to A1+/P1. Available-for-sale securities are carried at fair market value, with unrealized gains and losses reported as a component of stockholders equity in accumulated other comprehensive income/loss. Interest and dividend income is recorded when earned and included in interest income. Premiums and discounts on marketable securities are amortized and accreted, respectively, to maturity and included in interest income. The Company uses the specific identification method in computing realized gains and losses on the sale of investments, which would be included in the consolidated statements of operations when generated. Marketable securities with a maturity of more than one year as of the balance sheet date are classified as long-term securities.

***Concentrations of credit risk***

Financial instruments which potentially subject the Company to significant concentrations of credit risk consist primarily of cash, cash equivalents and marketable securities. The Company places its cash, cash

**Table of Contents**

**Vanda Pharmaceuticals Inc.  
(A development stage enterprise)**

**Notes to the Consolidated Financial Statements (Continued)**

equivalents and marketable securities with highly-rated financial institutions and does not hold any investment securities as of December 31, 2008 that have been affected by the recent credit crisis. At December 31, 2008, the Company maintained all of its cash, cash equivalents and marketable securities in three financial institutions. Deposits held with these institutions may exceed the amount of insurance provided on such deposits. Generally, these deposits may be redeemed upon demand, and the Company believes there is minimal risk of losses on such balances.

***Fair value of financial instruments***

The carrying amounts of the Company's financial instruments, which include cash and cash equivalents, marketable securities, restricted cash, and accounts payable, approximate their fair values due to their short maturities.

***Property and equipment***

Property and equipment are stated at cost less accumulated depreciation and amortization. Depreciation of property and equipment is provided on a straight-line basis over the estimated useful lives of the assets. Amortization of leasehold improvements is provided on a straight-line basis over the shorter of their estimated useful life or the lease term. The costs of additions and improvements are capitalized, and repairs and maintenance costs are charged to operations in the period incurred.

Upon retirement or disposition of property and equipment, the cost and accumulated depreciation and amortization are removed from the accounts and any resulting gain or loss is reflected in the statement of operations for that period.

***Foreign currency translation***

The functional currency of the Company's wholly-owned foreign subsidiary located in Singapore is the local currency. Assets and liabilities of the Company's foreign subsidiary are translated to United States dollars based on exchange rates at the end of the reporting period. Income and expense items are translated at weighted average exchange rates prevailing during the reporting period. Translation adjustments are accumulated in a separate component of stockholders' equity. Translation gains or losses are included in the determination of operating results. The wholly-owned Singapore subsidiary ceased operations during 2007.

***Comprehensive income (loss)***

SFAS No. 130, *Reporting Comprehensive Income*, requires a full set of general-purpose financial statements to include the reporting of comprehensive income. Comprehensive loss is composed of two components, net loss and other comprehensive income/(loss). For the years ended December 31, 2008, 2007 and 2006, other comprehensive income/(loss) consists of cumulative translation adjustments due to the Company's foreign subsidiary and unrealized gains/(losses) on marketable securities.

***Accrued expenses***

Management is required to estimate accrued expenses as part of the process of preparing financial statements. The estimation of accrued expenses involves identifying services that have been performed on the Company's behalf, and



then estimating the level of service performed and the associated cost incurred for such services as of each balance sheet date in the financial statements. Accrued expenses include professional service fees, such as lawyers and accountants, contract service fees, such as those under contracts with clinical monitors, data management organizations and investigators in conjunction with clinical trials, fees to contract manufacturers in conjunction with the production of clinical materials, fees for marketing and other

**Table of Contents**

**Vanda Pharmaceuticals Inc.  
(A development stage enterprise)**

**Notes to the Consolidated Financial Statements (Continued)**

commercialization activities, and severance related costs due to the Company's workforce reduction. Pursuant to management's assessment of the services that have been performed on clinical trials and other contracts, the Company recognizes these expenses as the services are provided. Such management assessments include, but are not limited to: (1) an evaluation by the project manager of the work that has been completed during the period, (2) measurement of progress prepared internally and/or provided by the third-party service provider, (3) analyses of data that justify the progress, and (4) management's judgment.

***Research and development expenses***

The Company's research and development expenses consist primarily of fees for services provided by third parties in connection with the clinical trials, costs of contract manufacturing services, milestone license fees, costs of materials used in clinical trials and research and development, depreciation of capital resources used to develop products, related facilities costs, and salaries, other employee related costs and stock-based compensation for the research and development personnel. The Company expenses research and development costs as they are incurred, including payments made to date under the license agreements. Manufacturing-related costs are also included in research and development expenses as the Company does not yet have FDA approval for any of its product candidates. Costs related to the acquisitions of intellectual property have been expensed as incurred since the underlying technology associated with these acquisitions were made in connection with the Company's research and development efforts and have no alternative future use. Milestone payments are accrued in accordance with SFAS No. 5, *Accounting for Contingencies*, when it is deemed probable that the milestone event will be achieved.

***General and administrative expenses***

General and administrative expenses consist primarily of salaries, other employee related costs and stock-based compensation for personnel serving executive, business development, marketing, finance, accounting, information technology and human resource functions, facility costs not otherwise included in research and development expenses, insurance costs and professional fees for legal, accounting and other professional services. General and administrative expenses also include third party expenses incurred to support business development, marketing and other business activities related to our product candidate iloperidone.

***Accounting for stock-based compensation***

The Company accounts for the stock-based compensation expenses in accordance with the Financial Accounting Standards Board (FASB) revised SFAS No. 123, *Share-Based Payment* (SFAS 123(R)) adopted on January 1, 2006. Accordingly, compensation costs for all stock-based awards to employees and directors are measured based on the grant date fair value of those awards and recognized over the period during which the employee or director is required to perform service in exchange for the award. The Company generally recognizes the expense over the award's vesting period.

Prior to January 1, 2006, the Company accounted for stock-based compensation in accordance with Accounting Principles Board Opinion No. 25, *Accounting for Stock Issued to Employees* (APB 25) and FASB Interpretation No. 28, *Accounting for Stock Appreciation Rights and Other Variable Stock Option Plan or Award Plans* (FIN 28). Under APB 25, the stock-based compensation expense was recognized over the vesting period of the option to the

extent that the fair value of the stock exceeded the exercise price of the stock at the date of grant.

The Company adopted SFAS 123(R) using the modified prospective transition method. The valuation provisions of SFAS 123(R) apply to new stock-based awards and to stock-based awards that were outstanding at the effective date and subsequently modified or cancelled. Estimated compensation expense for stock-based awards outstanding at the effective date have been recognized over the remaining service period using the

**Table of Contents**

**Vanda Pharmaceuticals Inc.**  
**(A development stage enterprise)**

**Notes to the Consolidated Financial Statements (Continued)**

compensation cost calculated for pro forma disclosure purposes under FASB Statement No. 123, *Accounting for Stock-Based Compensation* (SFAS 123). In accordance with the modified prospective transition method, the Company's consolidated financial statements for prior periods were not restated to reflect, and do not include, the impact of SFAS 123(R).

For stock awards granted in 2008, 2007 and 2006, the fair value of these awards are amortized using the accelerated attribution method. For stock awards granted prior to January 1, 2006, expenses are amortized under the accelerated attribution method for options that were modified after the original grant date and under the straight-line attribution method for all other options. As stock-based compensation expense recognized in the consolidated statements of operations is based on awards ultimately expected to vest, it has been reduced for estimated forfeitures. SFAS 123(R) requires forfeitures to be estimated at the time of grant and revised, if necessary, in subsequent periods if actual forfeitures differ from those estimates. Pre-vesting forfeitures on the options granted during 2008, 2007 and 2006, were estimated to be approximately 2% based on the Company's historical experience. In the pro forma information required under SFAS 123 for the periods prior to January 1, 2006, the Company accounted for forfeitures as they occurred. At no time was the cumulative expense recognized less than the fair value of the vested options. The cumulative effect adjustment of adopting the change in estimating forfeitures was not considered material to the Company's financial statements for periods prior to January 1, 2006 upon implementation of SFAS 123(R).

The fair value of each option award is estimated on the date of grant using the Black-Scholes-Merton option pricing model that uses the assumptions noted in the following table. Expected volatility rates are based on historical volatility of the common stock of comparable entities due to the lack of historic information of the Company's publicly traded common stock. The expected term of options granted is based on the transition approach provided by Staff Accounting Bulletin (SAB) No. 107 as the options meet the plain vanilla criteria required by this guidance. The risk-free interest rates are based on the U.S. Treasury yield for a period consistent with the expected term of the option in effect at the time of the grant. The Company has not paid dividends to its stockholders since its inception and does not plan to pay dividends in the foreseeable future.

The weighted average grant date fair value of options granted during the years ended December 31, 2008 and December 31, 2007 was \$3.05 per share and \$18.99 per share, respectively. As of December 31, 2008, approximately \$9.8 million of total unrecognized compensation costs related to non-vested awards is expected to be recognized over a weighted average period of 1.17 years.

Assumptions used in the Black-Scholes-Merton model for employee and director options granted during the years ended December 31, 2008 and 2007 were as follows:

	<b>Year Ended December 31,</b>		
	<b>2008</b>	<b>2007</b>	<b>2006</b>
Expected dividend yield	0%	0%	0%
Weighted average expected volatility	68%	68%	73%
Weighted average expected term (years)	6.18	6.25	6.14
Weighted average risk-free rate	3.27%	4.10%	4.66%



**Table of Contents**

**Vanda Pharmaceuticals Inc.**  
**(A development stage enterprise)**

**Notes to the Consolidated Financial Statements (Continued)**

Total stock-based compensation expense, related to the Company's stock-based awards to employees and directors, recognized during the years ended December 31, 2008, 2007 and 2006 and for the period from March 13, 2003 (inception) to December 31, 2008 was comprised of the following:

	Year Ended December 31,			Period from
	2008	2007	2006	March 13, 2003 (Inception) to December 31, 2008
Research and development	\$ 1,747,863	\$ 4,259,315	\$ 742,048	\$ 7,540,189
General and administrative	11,667,598	15,227,529	5,350,291	36,635,339
Stock-based compensation expense	\$ 13,415,461	\$ 19,486,844	\$ 6,092,339	\$ 44,175,528
Stock-based compensation expense per basic and diluted share of common stock	\$ 0.50	\$ 0.74	\$ 0.38	

Since the Company had a net operating loss carryforward as of December 31, 2008, no excess tax benefits for the tax deductions related to stock-based awards were recognized in the consolidated statements of operations. Additionally, no incremental tax benefits were recognized from stock options exercised in 2008 or 2007 which would have resulted in a reclassification to reduce net cash used in operating activities with an offsetting increase in net cash provided by financing activities.

**Income taxes**

The Company accounts for income taxes under the liability method in accordance with the provisions of SFAS No. 109, *Accounting for Income Taxes* (SFAS 109), which requires companies to account for deferred income taxes using the asset and liability method. Under the asset and liability method, current income tax expense or benefit is the amount of income taxes expected to be payable or refundable for the current year. A deferred income tax asset or liability is recognized for future tax consequences attributable to differences between the financial statement carrying amounts of existing assets and liabilities and their respective tax bases and tax credits and loss carryforwards. Deferred tax assets are reduced by a valuation allowance when, in the opinion of management, it is more likely than not that some portion or all of the deferred tax assets will not be realized. Tax rate changes are reflected in income during the period such changes are enacted. Changes in ownership may limit the amount of net operating loss carryforwards that can be utilized in the future to offset taxable income.

On January 1, 2007, the Company adopted the provisions of Financial Accounting Standards Board Interpretation (FIN) No. 48, *Accounting for Uncertainty in Income Taxes*. The adoption of FIN No. 48 did not have a material effect on the Company's financial position or results of operations.

The Company recognizes interest and penalties accrued related to unrecognized tax benefits as a component of the income tax provision. For the year ended December 31, 2008, there have been no interest and penalties recorded as a component of the income tax provision. The Company's open tax years under FIN 48 are 2005 through 2008.

*Segment information*

Management has determined that the Company operates in one business segment which is the development and commercialization of pharmaceutical products.

**Table of Contents**

**Vanda Pharmaceuticals Inc.  
(A development stage enterprise)**

**Notes to the Consolidated Financial Statements (Continued)**

***Recent accounting pronouncements***

In December 2007, the FASB issued SFAS No. 141(R), a revision of SFAS No. 141, *Business Combinations*. The revision is intended to simplify existing guidance and converge rulemaking under U.S. generally accepted accounting principles with international accounting standards. This statement applies prospectively to business combinations where the acquisition date is on or after the beginning of the first annual reporting period beginning on or after December 15, 2008. Early adoption is prohibited. The implementation of this standard will not have a material impact on our consolidated financial position and results of operations.

In June 2008, the FASB issued FSP EITF 03-6-1, *Determining Whether Instruments Granted in Share-Based Payment Transactions Are Participating Securities* (FSP EITF 03-6-1). FSP EITF 03-6-1 clarified that all outstanding unvested share-based payment awards that contain rights to nonforfeitable dividends participate in undistributed earnings with common shareholders. Awards of this nature are considered participating securities and the two-class method of computing basic and diluted earnings per share must be applied. FSP EITF 03-6-1 is effective for fiscal years beginning after December 15, 2008. The implementation of this standard will not have a material impact on our consolidated financial position and results of operations.

In November 2008, the FASB ratified EITF Issue No. 08-6, *Equity method Investment Accounting Considerations* (EITF 08-6). EITF 08-6 addresses a number of matters associated with the impact of SFAS No. 141R and SFAS No. 160 on the accounting for equity method investments including initial recognition and measurement and subsequent measurement issues. EITF 08-6 is effective, on a prospective basis, for fiscal years beginning after December 15, 2008 and interim periods within those fiscal years. The implementation of this standard will not have a material impact on our consolidated financial position and results of operations.

***Certain risks and uncertainties***

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

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

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

**3. Earnings per share**



Net loss attributable to common stockholders per share is calculated in accordance with SFAS No. 128, *Earnings per Share*, and Staff Accounting Bulletin (SAB) No. 98. Basic earnings per share (EPS) is calculated by dividing the net loss attributable to common stockholders by the weighted average number of common shares outstanding, reduced by the weighted average unvested common shares subject to repurchase.

Diluted EPS is computed by dividing the net loss attributable to common stockholders by the weighted average number of other potential common stock outstanding for the period. Other potential common stock include stock options, warrants and restricted stock units but only to the extent that their inclusion is dilutive.

Table of Contents

**Vanda Pharmaceuticals Inc.**  
**(A development stage enterprise)**

**Notes to the Consolidated Financial Statements (Continued)**

The Company incurred a net loss in all periods presented, causing inclusion of any potentially dilutive securities to have an anti-dilutive affect, resulting in dilutive loss per share attributable to common stockholders and basic loss per share attributable to common stockholders being equivalent. The Company did not have any common shares issued for nominal consideration as defined under the terms of SAB No. 98, which would be included in EPS calculations.

	<b>Year Ended December 31,</b>		
	<b>2008</b>	<b>2007</b>	<b>2006</b>
Numerator:			
Net loss attributable to common stockholders	\$ (51,064,241)	\$ (74,069,690)	\$ (63,511,168)
Denominator:			
Weighted average common shares outstanding	26,652,867	26,370,485	16,040,425
Weighted average unvested common shares subject to repurchase	(2,741)	(10,308)	(38,610)
Denominator for basic and diluted net loss per share	26,650,126	26,360,177	16,001,815
Basic and diluted net loss per share attributable to common stockholders	\$ (1.92)	\$ (2.81)	\$ (3.97)
Historical outstanding anti-dilutive securities not included in diluted net loss per share calculation:			
Options to purchase common stock	4,453,629	2,938,160	1,706,732

#### 4. Marketable securities

The following is a summary of the Company's available-for-sale marketable securities as of December 31, 2008:

	<b>Amortized Cost</b>	<b>Gross Unrealized Gains</b>	<b>Gross Unrealized Losses</b>	<b>Fair Market Value</b>
Short-term:				
U.S. Treasury and government agencies	\$ 1,992,452	\$ 7,408	\$	\$ 1,999,860
U.S. corporate debt	5,279,828	2,336	(29,818)	5,252,346
U.S. asset-based securities	126,547	45		126,592
	\$ 7,398,827	\$ 9,789	\$ (29,818)	\$ 7,378,798



**Table of Contents**

**Vanda Pharmaceuticals Inc.**  
**(A development stage enterprise)**

**Notes to the Consolidated Financial Statements (Continued)**

The following is a summary of the Company's available-for-sale marketable securities as of December 31, 2007:

	<b>Amortized Cost</b>	<b>Gross Unrealized Gains</b>	<b>Gross Unrealized Losses</b>	<b>Fair Market Value</b>
Short-term:				
U.S. Treasury and government agencies	\$ 3,980,732	\$	\$ (897)	\$ 3,979,835
U.S. corporate debt	33,301,950	48,247	(11,417)	33,338,780
U.S. asset-based securities	5,920,992	4,353		5,925,345
	\$ 43,203,674	\$ 52,600	\$ (12,314)	\$ 43,243,960
Long-term:				
U.S. Treasury and government agencies	\$ 1,999,104	\$ 2,844	\$	\$ 2,001,948
U.S. corporate debt	1,988,637		(18,597)	1,970,040
U.S. asset-based securities	4,003,480	3,863		4,007,343
	\$ 7,991,221	\$ 6,707	\$ (18,597)	\$ 7,979,331

## 5. Fair Value Measurements

In September 2006, the FASB issued Statement No. 157, "Fair Value Measurements" (SFAS 157). SFAS 157 defines fair value, establishes a framework for measuring fair value in accordance with GAAP, and expands disclosures about fair value measurements. In February 2008, the FASB agreed to delay the effective date of SFAS 157 for all nonfinancial assets and nonfinancial liabilities, except those that are recognized or disclosed at fair value in the financial statements on a recurring basis, to fiscal years beginning after November 15, 2008. The Company has adopted the provisions of SFAS 157 as of January 1, 2008, for financial instruments. Although the adoption of SFAS 157 did not materially impact its financial condition, results of operations, or cash flow, the Company is now required to provide additional disclosures as part of its financial statements. Under FAS No. 159, entities are permitted to choose to measure many financial instruments and certain other items at fair value. The Company did not elect the fair value measurement option under FAS No. 159, "The Fair Value Option for Financial Assets and Financial Liabilities" including an amendment to FAS 115 (SFAS 159), for any of its financial assets or liabilities.

SFAS 157 establishes a three-tier fair value hierarchy, which prioritizes the inputs used in measuring fair value. These tiers include:

Level 1 defined as observable inputs such as quoted prices in active markets

Level 2 defined as inputs other than quoted prices in active markets that are either directly or indirectly observable

Level 3 defined as unobservable inputs in which little or no market data exists, therefore requiring an entity to develop its own assumptions

As of December 31, 2008, the Company held certain assets that are required to be measured at fair value on a recurring basis. The Company currently does not have non-financial assets and non-financial liabilities that are required to be measured at fair value on a recurring basis.

Table of Contents

**Vanda Pharmaceuticals Inc.**  
**(A development stage enterprise)**

**Notes to the Consolidated Financial Statements (Continued)**

**Fair Value Measurements at Reporting Date Using  
Quoted Prices  
in**

	<b>December 31, 2008</b>	<b>Active Markets for Identical Assets (Level 1)</b>	<b>Significant Other Observable Inputs (Level 2)</b>	<b>Significant Unobservable Inputs (Level 3)</b>
Description :				
Available-for-sale securities	\$ 7,378,798	\$ 1,999,860	\$ 5,378,938	\$
Total	\$ 7,378,798	\$ 1,999,860	\$ 5,378,938	\$

#### 6. Prepaid expenses and other current assets

The following is a summary of the Company's prepaid expenses and other current assets:

	<b>December 31,</b>	
	<b>2008</b>	<b>2007</b>
Current deposits with vendors	\$ 210,000	\$ 455,000
Prepaid insurance	282,391	395,203
Prepaid research and development expenses	221,690	175,955
Accrued interest income	53,378	603,556
Other prepaid expenses	104,511	146,771
Other receivables	415,430	5,396
Total prepaid expenses and other current assets	\$ 1,287,400	\$ 1,781,881

#### 7. Property and equipment

Property and equipment at cost:

<b>Estimated Useful Life (Years)</b>	<b>December 31,</b>	
	<b>2008</b>	<b>2007</b>

Laboratory equipment	5	\$ 1,348,098	\$ 1,281,877
Computer equipment	3	776,921	758,776
Furniture and fixtures	7	705,784	187,317
Leasehold improvements	10	844,158	505,684
		3,674,961	2,733,654
Less accumulated depreciation and amortization		(1,916,850)	(1,387,809)
		\$ 1,758,111	\$ 1,345,845

Depreciation and amortization expense for the years ended December 31, 2008, 2007 and 2006 was \$530,805, \$571,586 and \$575,372. Depreciation and amortization expense for the period from March 13, 2003 (inception) to December 31, 2008 was \$2,499,661.

#### **8. Restricted cash**

During 2005, in conjunction with the lease of the office and laboratory space building in Rockville, MD, the Company provided the landlord with a letter of credit, which was collateralized with a restricted cash

**Table of Contents**

**Vanda Pharmaceuticals Inc.**  
**(A development stage enterprise)**

**Notes to the Consolidated Financial Statements (Continued)**

deposit in the amount of \$430,230. The deposit is recorded as non-current restricted cash at December 31, 2008 since the letter of credit is required until the lease expires in 2016.

**9. Accrued liabilities**

Accrued liabilities consist of the following:

	<b>December 31,</b>	
	<b>2008</b>	<b>2007</b>
Accrued research and development expenses	\$ 925,124	\$ 7,151,360
Bonus accrual		957,035
Accrued consulting and other professional fees	233,829	1,307,650
Employee benefits	126,816	168,275
Lease abandonment		84,617
Other accrued expenses		120,801
Accrued severance	1,612,648	
Total accrued liabilities	\$ 2,898,417	\$ 9,789,738

**10. Singapore research facility**

In May 2007, the Company initiated a plan to move its operations out of Singapore to consolidate its discovery research activities in its Rockville, Maryland facility. The consolidation was significantly completed by the end of 2007, and substantively all expenses of the move, including employee severance, loss on the sale of fixed assets and other related costs were recorded in the consolidated financial statements as of December 31, 2007. Total expenses relating to the consolidation of the discovery research activities were not material to the Company's consolidated financial statements. The Company recorded a final cumulative translation adjustment of \$16,220 as of December 31, 2008.

In 2004 the Company's subsidiary in Singapore entered into an agreement with the Economic Development Board of Singapore (EDB) to provide a grant for a development project. During 2005, the Company received a payment from the EDB that was recorded as deferred grant revenue since under certain conditions the EDB could have reclaimed these funds. On September 19, 2007 the Company agreed with the EDB to pay back 50% of the grant and the remaining 50%, or \$71,345, was recognized as other income during the year ended December 31, 2007.

**11. Commitments*****Operating leases***



In 2003, the Company entered into a five-year non-cancelable operating lease agreement for office and laboratory space. In January 2006 the Company vacated and in September 2007 sublet the office space for the remaining term of the lease that expired in June 2008.

In August 2005, the Company entered into a ten-year, six-month non-cancelable operating lease agreement for office and laboratory space at a new office complex in Rockville, Maryland, which is renewable for an additional five-year period at the end of the original term. The lease expires in June 2016. The lease includes a rent abatement and scheduled base rent increases over the term of the lease.

The total amount of the base rent payments and rent abatement will be charged to expense on a straight-line method over the term of the lease. In conjunction with a letter of credit, the Company collateralized the

**Table of Contents**

**Vanda Pharmaceuticals Inc.**  
**(A development stage enterprise)**

**Notes to the Consolidated Financial Statements (Continued)**

operating lease with a restricted cash deposit in the amount of \$430,230, which is recorded as non-current restricted cash at December 31, 2008.

During the second quarter of 2007, the Company exercised an option to lease additional space in its current headquarters in Rockville, Maryland and the additional commitment is reflected in the following schedule of future minimum lease payments for non-cancelable operating leases as of December 31, 2008:

2009	685,270
2010	705,994
2011	726,992
2012	748,807
2013	771,440
Thereafter	2,034,404
	<b>\$ 5,672,907</b>

Rent expense for the years ended December 31, 2008, 2007 and 2006 was \$1,003,305, \$899,824 and \$902,729. Rent expense for the period from March 13, 2003 (inception) to December 31, 2008 was \$3,563,497.

***Consulting fees***

The Company has engaged a regulatory consultant to assist in the Company's efforts to obtain FDA approval of the iloperidone NDA. The Company has committed to initial consulting expenses in the aggregate amount of \$2.0 million pursuant to this engagement, which was expensed in 2008. In addition, the Company retained the services of the consultant on a monthly basis at a retainer fee of \$250,000 per month effective as of January 1, 2009. In the event that the iloperidone NDA is approved by the FDA, the Company will be obligated to pay the consultant a success fee of \$6.0 million, which amount will be offset by the aggregate amount of all monthly retainer fees previously paid to the consultant (Success Fee). In addition to these fees, the Company is obligated to reimburse the consultant for its ordinary and necessary business expenses incurred in connection with its engagement. The Company may terminate the engagement at any time; however, the Company will remain obligated to pay any remaining Success Fee if the iloperidone NDA is approved by the FDA following such termination.

***Accrued Severance***

On December 16, 2008, the Company committed to a plan of termination that resulted in a work force reduction of 17 employees, including two officers, in order to reduce operating costs. As of December 31, 2008, the Company employed 24 full-time employees. This represents approximately a 55% decrease from the 53 employees the Company had on August 1, 2008. The Company recorded a charge of \$1.6 million for severance costs related to salaries and benefits.



**Table of Contents**

**Vanda Pharmaceuticals Inc.**  
**(A development stage enterprise)**

**Notes to the Consolidated Financial Statements (Continued)**

The following table summarizes the activity in 2008 for the liability for the cash portion of severance costs related to the reductions-in-force:

	Beginning Balance	Year Ended December 31, 2008		Ending Balance
		Charge	Cash Paid	
Workforce Reduction:				
Research Development	\$	\$ 571,391	\$	\$ 571,391
General & Administrative		1,041,257		1,041,257
Total	\$	\$ 1,612,648	\$	\$ 1,612,648

***License agreements***

In June 2004, the Company acquired exclusive rights to develop and commercialize iloperidone through a sublicense agreement with Novartis AG (Novartis). In consideration for this license, the Company paid Novartis an initial license fee of \$500,000, which was immediately expensed to research and development expenses. The Company is obligated to make future milestone payments to Novartis of less than \$100 million in the aggregate (the majority of which are tied to sales milestones), as well as royalty payments to Novartis which, as a percentage of net sales, is in the mid-twenties. The Company's rights with respect to the patents to develop and commercialize iloperidone may terminate, in whole or in part, if we fail to meet certain development or commercialization milestones relating to the time it takes for us to launch iloperidone commercially following regulatory approval, and the time it takes for us to receive regulatory approval following our submission of an NDA or equivalent foreign filing. Additionally, the Company's rights may terminate in whole or in part if it does not meet certain other obligations under its sublicense agreement to make royalty and milestone payments, if it fails to comply with requirements in its sublicense agreement regarding its financial condition, or if it does not abide by certain restrictions in its sublicense agreement regarding other development activities.

In February 2004 the Company entered into a license agreement with Bristol-Myers Squibb Company (BMS) under which the Company received an exclusive worldwide license under certain patents and patent applications to develop and commercialize tasimelteon. In partial consideration for the license, the Company paid BMS an initial license fee of \$500,000, which was immediately expensed to research and development expenses. The Company is obligated to make future milestone payments to BMS of less than \$40 million in the aggregate (the majority of which are tied to sales milestones) as well as royalty payments based on the net sales of tasimelteon at a rate which, as a percentage of net sales, is in the low teens. The Company is also obligated under this agreement to pay BMS a royalty on certain payments (excluding royalties) that the Company receives from a third party in connection with any sublicensing arrangement, at a rate in the mid-twenties. If the Company has not agreed to one or more partnering arrangements to develop and commercialize tasimelteon in certain significant markets with one or more third parties after the completion of the Phase III program, BMS has the option to exclusively develop and commercialize tasimelteon on its own on pre-determined financial terms, including milestone and royalty payments. Either party may terminate the

agreement under certain circumstances, including a material breach of the agreement by the other.

In June 2004 the Company entered into a license agreement with Novartis under which the Company received an exclusive worldwide license to develop and commercialize VSF-173. In consideration for the license, the Company paid Novartis an initial license fee of \$500,000, which was immediately expensed to research and development expenses. The Company is also obligated to make future milestone payments to Novartis of less than \$50 million in the aggregate (the majority of which are tied to sales milestones) and royalty payments which, as a percentage of net sales, is in the low to mid teens. On November 3, 2008, the Company received written notice from Novartis that the license agreement had terminated in accordance with

**Table of Contents**

**Vanda Pharmaceuticals Inc.**  
**(A development stage enterprise)**

**Notes to the Consolidated Financial Statements (Continued)**

its terms as a result of the Company's failure to satisfy a specific development milestone within the time period specified in the license agreement. As a result, the Company no longer has any rights with respect to VSF-173 and Novartis has a non-exclusive worldwide license to all information and intellectual property generated by or on behalf of the Company related to its development of VSF-173. The Company is currently evaluating any options that it may have with respect to VSF-173, which may include the possibility of entering into a new license agreement or other arrangement with Novartis to allow the Company to resume its development of VSF-173; however, there can be no assurance that the Company will be able to enter into such an agreement or arrangement on acceptable terms, or at all.

During 2006, the Company met a clinical milestone under the tasimelteon agreement with BMS relating to the initiation of its first Phase III clinical trial and made an associated milestone payment of \$1.0 million. In November 2007, the Company met a milestone under this license agreement with Novartis relating to the acceptance of the NDA for iloperidone in schizophrenia and made a license payment of \$5.0 million to Novartis. In March 2007, the Company met its first milestone under this license agreement with Novartis relating to the initiation of the Phase II clinical trial for VSF-173, and made an associated milestone payment of \$1.0 million. The milestone license fees were expensed to research and development expenses.

No amounts were recorded as liabilities as of December 31, 2008, since the amount, timing and likelihood of these payments are unknown and will depend on the successful outcome of future clinical trials, regulatory filings, favorable FDA regulatory approvals, growth in product sales and other factors.

***Clinical agreements***

In course of its business the Company regularly enters into agreements with clinical organizations to provide services relating to clinical development and clinical manufacturing activities under fee service arrangements. The Company's current agreements for clinical services may be terminated on no more than 60 days notice without incurring additional charges, other than charges for work completed but not paid for through the effective date of termination and other costs incurred by the Company's contractors in closing out work in progress as of the effective date of termination.

***Guarantees and indemnifications***

The Company has entered into a number of standard intellectual property indemnification agreements in the ordinary course of its business. Pursuant to these agreements, the Company indemnifies, holds harmless, and agrees to reimburse the indemnified party for losses suffered or incurred by the indemnified party, generally the Company's business partners or customers, in connection with any U.S. patent or any copyright or other intellectual property infringement claim by any third party with respect to the Company's products. The term of these indemnification agreements is generally perpetual from the date of execution of the agreement. The maximum potential amount of future payments the Company could be required to make under these indemnification agreements is unlimited. Since inception, the Company has not incurred costs to defend lawsuits or settle claims related to these indemnification agreements. The Company also indemnifies its officers and directors for certain events or occurrences, subject to certain limits. The Company believes that the fair value of the indemnification agreements is minimal, and accordingly the Company has not recognized any liabilities relating to these agreements as of December 31, 2008.

**12. Equity incentive plans**

As of December 31, 2008 the Company had two equity incentive plans, the Second Amended and Restated Management Equity Plan adopted in December 2004 (the 2004 Plan) and the 2006 Equity Incentive Plan adopted in April 2006 (the 2006 Plan). An aggregate of 1,154,248 shares were subject to outstanding options granted under the 2004 Plan as of December 31, 2008, and no additional options will be granted under

**Table of Contents**

**Vanda Pharmaceuticals Inc.**  
**(A development stage enterprise)**

**Notes to the Consolidated Financial Statements (Continued)**

this plan. Reserved under the 2006 Plan as of December 31, 2008 are 4,516,639 shares of the Company's common stock of which 3,299,381 shares were subject to outstanding options as of December 31, 2008. On January 1 of each year, the number of shares reserved under the 2006 Plan is automatically increased by 4% of the total number of shares of common stock that are outstanding at that time, or, if less, by 1,500,000 shares (or such lesser number as may be approved by the Company's board of directors). As of January 1, 2009, the number of shares of common stock that may be issued under the 2006 Plan was automatically increased by 1,066,139 shares, representing 4% of the total number of shares of common stock outstanding on January 1, 2009, increasing the total number of shares of common stock available for issuance under the Plan to 5,582,778 shares.

Options are subject to terms and conditions established by the compensation committee of the board of directors. None of the stock-based awards are classified as a liability as of December 31, 2008. Option awards have 10-year contractual terms and all options granted prior to December 31, 2006 and options granted to new employees vest and become exercisable on the first anniversary of the grant date with respect to the 25% of the option awards. The remaining 75% of the option awards vest and become exercisable monthly in equal installments thereafter over three years. Option awards granted to existing employees after December 31, 2006 vest and become exercisable monthly in equal installments over four years. The initial stock options granted to directors upon their election vest and become exercisable in equal monthly installments over a period of four years, while the subsequent annual stock option grants to directors vest and become exercisable in equal monthly installments over a period of one year. A total of 1,209,125 option awards to executives outstanding as of December 31, 2008 provide for accelerated vesting if there is a change in control of the Company. When an option is exercised, the Company issues a new share of common stock.

In conjunction with the workforce reduction in December 2008, the company accelerated an additional three months of vesting from the date of termination and extended the exercisable term after termination of the terminated employees from three months to six months after termination date. Prior to the modification an option would have been exercisable with respect to the vested shares at any time until the date three months after the employee's termination date. However per the separation agreement, the terminated employees will receive three additional months of vesting and the options will be exercisable with respect to vested shares for six months. Options with respect to the unvested shares expired on the date of the employee's termination date. FAS 123R treats a modification of the terms or conditions of an equity award as an exchange of the original award for a new award. Incremental compensation cost is measured as the excess, if any, of the fair value of the modified award determined in accordance with the provisions of FAS 123R over the fair value of the original award immediately before its terms are modified, measured based on the share price and other pertinent factors at that date. As the modified options are significantly less than the fair market value, the additional compensation expense is immaterial and therefore no additional compensation expense was recognized.



**Table of Contents**

**Vanda Pharmaceuticals Inc.**  
**(A development stage enterprise)**

**Notes to the Consolidated Financial Statements (Continued)**

A summary of option activity for the 2004 Plan is presented below:

	Number of Shares	Weighted Average Exercise Price at Grant Date	Weighted Average Remaining Term (Years)	Aggregate Intrinsic Value
March 13, 2003 (inception)		\$		
Granted	333,602	0.33		
Cancelled	(18,639)	0.33		
Outstanding at December 31, 2004	314,963	0.33		
Granted	1,318,753	0.33		
Cancelled	(5,249)	0.33		
Exercised	(95,925)	0.33		\$ 456,857
Outstanding at December 31, 2005	1,532,542	1.39		
Granted	38,014	5.97		
Cancelled	(1,118)	0.33		
Exercised	(222,233)	0.33		\$ 5,096,166
Outstanding at December 31, 2006	1,347,205	1.69		
Cancelled	(14,276)	3.72		
Exercised	(162,954)	0.93		\$ 3,325,163
Outstanding at December 31, 2007	1,169,975	1.77	7.75	\$ 5,988,373
Forfeited	(4,849)	5.27		
Cancelled	(10,878)	5.84		
Outstanding at December 31, 2008	1,154,248	1.72	6.72	\$ 128,600
Exercisable at December 31, 2008	922,706	1.62	6.62	\$ 108,949

A summary of option activity for the 2006 Plan is presented below:

Number of	Weighted Average Exercise Price at	Weighted Average	Aggregate
-----------	--	---------------------	-----------

	<b>Shares</b>	<b>Grant Date</b>	<b>Remaining Term (Years)</b>	<b>Intrinsic Value</b>
Outstanding at January 1, 2006		\$		
Granted	359,527	20.21		
Outstanding at December 31, 2006	359,527	20.21		
Granted	1,451,801	27.60		
Forfeited	(41,391)	27.85		
Cancelled	(4,302)	28.44		
Outstanding at December 31, 2007	1,765,635	26.08	9.14	\$
Granted	1,412,250	4.75		
Forfeited	(19,903)	20.28		
Cancelled	(481,601)	9.89		
Outstanding at December 31, 2008	2,676,381	17.79	8.53	\$
Exercisable at December 31, 2008	1,140,847	21.22	8.34	\$

The Company received a total of \$0 and \$148,640 in cash from the exercises of options during the year ended December 31, 2008 and December 31, 2007, respectively.

**Table of Contents**

**Vanda Pharmaceuticals Inc.**  
**(A development stage enterprise)**

**Notes to the Consolidated Financial Statements (Continued)**

Restricted stock is a stock award that entitles the holder to receive shares of the Company's common stock as the award vests. The Company issued restricted stock to one employee in 2007 and restricted stock units (RSUs) to all employees who remained with the Company following the workforce reduction in December 2008 and three employees terminated as a result of the workforce reduction who entered into consulting agreements with the Company. The restricted stock issued in 2007 vested annually with respect to 25% of the shares each year after the grant. For the RSUs issued in 2008 to the retained employees, 50% of such shares vest upon approval by the FDA of the NDA for iloperidone, and 50% of such shares vest on December 31, 2009. Upon a change of control of Vanda Pharmaceuticals Inc., 100% of the unvested restricted stock units will vest. For the RSUs issued in 2008 to the terminated employees who entered into consulting agreements with the Company, 50% of the RSUs vest if the terminated employee is subsequently rehired by the Company and 50% of the RSUs vest on December 31, 2009, provided that the terminated employee has been rehired by the Company and remains employed by the Company at such date. The fair value of each restricted stock award is estimated using the intrinsic value method which is based on the closing price on the date of grant. As of December 31, 2008, there was approximately \$162,192 of total unrecognized compensation cost related to unvested restricted stock awards granted under the Company's stock incentive plans. The cost is expected to be recognized through December 2009.

A summary of restricted stock activity for the 2006 Plan is presented below:

	Number of Shares	Weighted Average Price/Share	Aggregate Intrinsic Value
Outstanding at January 1, 2007		\$	
Granted	3,000	16.24	
Unvested at December 31, 2007	3,000	16.24	\$ 20,640
Granted	623,000	0.57	
Vested	(750)	16.24	
Cancelled	(2,250)	16.24	
Unvested at December 31, 2008	623,000	0.57	\$ 311,500

### 13. Equity

#### *Public offerings and reverse stock split*

On April 18, 2006 the Company consummated its initial public offering, consisting of 5,750,000 shares of common stock. On April 21, 2006 the underwriters exercised an over-allotment option to purchase an additional 214,188 shares of the Company's common stock. Including the over-allotment shares, the offering totaled 5,964,188 shares at a public offering price of \$10.00 per share, resulting in net proceeds to the Company of approximately \$53.3 million after deducting payments of underwriters' discounts and commissions and offering expenses.

On January 19, 2007 the Company completed its follow-on offering, consisting of 3,800,000 shares of its common stock. On January 22, 2007 the underwriters exercised an over-allotment option to purchase an additional 570,000 shares of the Company's common stock. Including the over-allotment shares being purchased, the offering totaled 4,370,000 shares at a public offering price of \$27.29 per share, resulting in net proceeds to the Company of approximately \$111.3 million after deducting underwriting discounts and commissions and offering expenses.

In connection with the initial public offering, the Company effected a 1-for-3.309755 reverse stock split of the issued and outstanding common stock. Information relating to common stock and common stock-

**Table of Contents**

**Vanda Pharmaceuticals Inc.**  
**(A development stage enterprise)**

**Notes to the Consolidated Financial Statements (Continued)**

equivalents set forth in these financial statements (including the share numbers in the preceding paragraphs) has been restated to reflect this split for all periods presented. Upon consummation of the initial public offering, all shares of the Company's Series A preferred stock and Series B preferred stock were converted into an aggregate of 15,794,632 shares of common stock.

***Beneficial conversion feature Series B preferred stock***

In September 2005, the Company completed the sale of an additional 15,040,654 shares of Series B preferred stock for proceeds of approximately \$18.5 million. After evaluating the fair value of the Company's common stock obtainable upon conversion by the stockholders, the Company determined that the issuance of the Series B preferred stock sold in September 2005 resulted in a beneficial conversion feature calculated in accordance with EITF Issue No. 98-5, *Accounting for Convertible Securities with Beneficial Conversion Features or Contingently Adjustable Conversion Ratios*, (EITF 98-5) as interpreted by EITF Issue No. 00-27, *Application of Issue No. 98-5 to Certain Convertible Instruments*, (EITF 00-27) of approximately \$18.5 million which was fully accreted in September 2005 and is recorded as a deemed dividend to preferred stockholders for the year ended December 31, 2005.

In December 2005, the Company closed an additional private placement of 12,195,129 shares of Series B preferred stock for proceeds of approximately \$15.0 million. The Company evaluated the fair value of the Company's common stock obtainable upon conversion by the stockholders using EITF 98-5 and EITF 00-27 and determined that the issuance of the Series B preferred stock sold in December 2005 resulted in a beneficial conversion feature of approximately \$15.0 million that was fully accreted in December 2005 and recorded as a deemed dividend to preferred stockholders for the year ended December 31, 2005.

**14. Income taxes**

The tax provision is as follows:

	<b>December 31,</b>		
	<b>2008</b>	<b>2007</b>	<b>2006</b>
Current federal tax expense	\$	\$	\$
Current state tax expense			
Current foreign expense		9,879	549
Deferred tax expense			
Total tax expense	\$	\$ 9,879	\$ 549

**Table of Contents**

**Vanda Pharmaceuticals Inc.**  
**(A development stage enterprise)**

**Notes to the Consolidated Financial Statements (Continued)**

Deferred tax assets consist of the following:

	<b>December 31,</b>	
	<b>2008</b>	<b>2007</b>
<b>Deferred tax asset (liability)</b>		
Net operating loss carryforwards	\$ 48,781,358	\$ 40,772,613
Start-up costs	34,228,958	21,542,179
Stock-based compensation	2,330,260	1,725,983
Licensing agreements	2,925,575	3,076,083
Research and development credit	5,455,721	4,470,774
Depreciation and amortization	(10,179)	(33,797)
Amortization of warrants	12,422	12,162
Accrued and deferred expenses	263,343	57,200
Net deferred tax assets	93,987,458	71,623,197
Deferred tax asset valuation allowance	(93,987,458)	(71,623,197)
	\$	\$

Based on the Company's limited operating history and management's expectation of future profitability, management believes that the Company's deferred tax assets do not meet the criteria that they will be more likely than not realized. Accordingly, a valuation allowance for the entire deferred tax asset amount has been recorded.

The effective tax rate differs from the U.S. federal statutory tax rate of 34% due to the following:

	<b>December 31,</b>	
	<b>2008</b>	<b>2007</b>
Federal tax at statutory rate	34.0%	34.0%
State taxes	5.4%	4.6%
Change in valuation allowance	(41.1)%	(41.2)%
Research and development credit	1.9%	2.1%
Meals, entertainment and other non-deductable items	(0.2)%	0.5%
Effective tax rate	0.0%	0.0%

At December 31, 2008 and 2007, the Company had U.S. federal and state net operating loss carryforwards of approximately \$123.7 million and \$105.6 million, respectively available to reduce future taxable income, which will

begin to expire in 2023. At December 31, 2008 and 2007, the Company had approximately \$5.5 million and \$4.5 million of research and development credit, respectively which will begin to expire in 2023.

These net operating loss carryforwards may be used to offset future taxable income and thereby reduce our U.S. federal income taxes otherwise payable. Section 382 of the Internal Revenue Code of 1986, as amended ( the Code ), imposes an annual limit on the ability of a corporation that undergoes an ownership change to use its net operating loss carry forwards to reduce its tax liability. In the event of certain changes in our shareholder base, our ability to utilize certain net operating losses to offset future taxable income in any particular year will be limited pursuant to IRC Section 382.

In addition to our U.S. federal tax net operating loss carryforwards, we also had net operating loss carryforwards in a variety of states in which we operate. In the event of an ownership change, our ability to

**Table of Contents**

**Vanda Pharmaceuticals Inc.**  
**(A development stage enterprise)**

**Notes to the Consolidated Financial Statements (Continued)**

utilize state net operating losses will be limited by annual limitations similar to those described in Section 382 of the Code.

**15. Employee benefit plan**

The Company has a defined contribution plan under the Internal Revenue Code Section 401(k). This plan covers substantially all employees who meet minimum age and service requirements and allows participants to defer a portion of their annual compensation on a pre-tax basis. Currently, the Company matches 50 percent up to the first six percent of employee contributions. All matching contributions have been paid by the Company. The employer match vests over a 4 year period. The total employer match for the years ended December 31, 2008, 2007 and 2006 was \$127,728, \$120,306 and \$101,425.

**16. Quarterly financial data (unaudited)**

	<b>First Quarter</b>	<b>Second Quarter</b>	<b>Third Quarter</b>	<b>Forth Quarter</b>
<b>2008</b>				
Loss from operations	\$ (20,061,879)	\$ (13,935,894)	\$ (11,192,687)	\$ (7,654,661)
Net loss	(19,196,129)	(13,494,882)	(10,869,211)	(7,504,019)
Basic and diluted net loss per share attributable to common stockholders	(0.72)	(0.51)	(0.41)	(0.28)
<b>2007</b>				
Loss from operations	\$ (16,825,608)	\$ (17,643,200)	\$ (23,521,894)	\$ (22,047,673)
Net loss	(15,392,760)	(15,985,023)	(21,943,501)	(20,748,406)
Basic and diluted net loss per share attributable to common stockholders	(0.61)	(0.60)	(0.82)	(0.78)



**Table of Contents**

**VANDA PHARMACEUTICALS INC.  
EXHIBIT INDEX**

<b>Exhibit No.</b>	<b>Description</b>
3.8	Form of Amended and Restated Certificate of Incorporation of the registrant (filed as Exhibit 3.8 to Amendment No. 2 to the registrant's Registration Statement on Form S-1 (File No. 333-130759), as filed on March 17, 2006, and incorporated herein by reference)
3.10	Form of Certificate of Designation of Series A Junior Participating Preferred Stock (filed as Exhibit 3.10 to the registrant's current report on Form 8-K (File No. 001-34186) as filed on September 25, 2008 and incorporated herein by reference)
3.11	Second Amended and Restated Bylaws of the registrant, as amended and restated on December 16, 2008 (filed as Exhibit 3.11 to the registrant's current report on Form 8-K (File No. 001-34186) as filed on December 17, 2008 and incorporated herein by reference)
4.1	2004 Securityholder Agreement (as amended) (filed as Exhibit 4.1 to the registrant's Registration Statement on Form S-1 (File No. 333-130759), as originally filed on December 29, 2005, and incorporated herein by reference)
4.4	Specimen certificate representing the common stock of the registrant (filed as Exhibit 4.4 to Amendment No. 2 to the registrant's Registration Statement on Form S-1 (File No. 333-130759), as filed on March 17, 2006, and incorporated herein by reference)
4.5	Rights Agreement, dated as of September 25, 2008, between the registrant and American Stock Transfer & Trust Company, LLC, as Rights Agent (filed as Exhibit 4.5 to the registrant's current report on Form 8-K (File No. 001-34186) as filed on September 25, 2008 and incorporated herein by reference)
10.1	Registrant's Second Amended and Restated Management Equity Plan (filed as Exhibit 10.1 to the registrant's Registration Statement on Form S-1 (File No. 333-130759), as originally filed on December 29, 2005, and incorporated herein by reference)
10.2#	Sublicense Agreement between the registrant and Novartis Pharma AG dated June 4, 2004 (as amended) (relating to iloperidone) (filed as Exhibit 10.2 to Amendment No. 1 to the registrant's Registration Statement on Form S-1 (File No. 333-130759), as filed on February 16, 2006, and incorporated herein by reference)
10.3#	Amended and Restated License, Development and Commercialization Agreement by and between Bristol-Myers Squibb Company and the registrant dated July 24, 2005 (relating to tasimelteon) (filed as Exhibit 10.3 to Amendment No. 1 to the registrant's Registration Statement on Form S-1 (File No. 333-130759), as filed on February 16, 2006, and incorporated herein by reference)
10.7	Lease Agreement between the registrant and Red Gate III LLC dated June 25, 2003 (lease of Rockville, MD office space) (filed as Exhibit 10.7 to the registrant's Registration Statement on Form S-1 (File No. 333-130759), as originally filed on December 29, 2005, and incorporated herein by reference)
10.8	Amendment to Lease Agreement between the registrant and Red Gate III LLC dated September 27, 2003 (filed as Exhibit 10.8 to the registrant's Registration Statement on Form S-1 (File No. 333-130759), as originally filed on December 29, 2005, and incorporated herein by reference)
10.9	Lease Agreement between the registrant and MCC3 LLC (by Spaulding and Slye LLC) dated August 4, 2005 (filed as Exhibit 10.9 to the registrant's Registration Statement on Form S-1 (File No. 333-130759), as originally filed on December 29, 2005, and incorporated herein by reference)
10.10	Summary Plan Description provided for the registrant's 401(k) Profit Sharing Plan & Trust (filed as Exhibit 10.10 to the registrant's Registration Statement on Form S-1 (File No. 333-130759), as originally filed on December 29, 2005, and incorporated herein by reference)

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- 10.11 Form of Indemnification Agreement entered into by directors (filed as Exhibit 10.11 to the registrant's Registration Statement on Form S-1 (File No. 333-130759), as originally filed on December 29, 2005, and incorporated herein by reference)
- 10.17 2006 Equity Incentive Plan (filed as Exhibit 10.17 to Amendment No. 2 to the registrant's Registration Statement on Form S-1 (File No. 333-130759), as filed on March 17, 2006, and incorporated herein by reference)

**Table of Contents**

<b>Exhibit No.</b>	<b>Description</b>
10.19	Amendment to Lease Agreement between the registrant and MCC3 LLC (by Spaulding and Slye LLC) dated November 15, 2006 (filed as Exhibit 10.19 to the registrant's annual report on Form 10-K (File No. 000-51863) for the year ending December 31, 2006 and incorporated herein by reference)
10.21	Form of Tax Indemnity Agreement (filed as Exhibit 10.20 to the registrant's quarterly report on Form 10-Q (File No. 000-51863) for the period ending September 30, 2007 and incorporated herein by reference)
10.22	Second Amendment to Lease Agreement between the registrant and MCC3 LLC (by Spaulding and Slye MCC3 LLC) dated September 14, 2007 (filed as Exhibit 10.22 to the registrant's annual report on Form 10-K (File No. 000-51863) for the year ending December 31, 2007 and incorporated herein by reference)
10.23	Amended and Restated Employment Agreement for Mihael H. Polymeropoulos dated November 4, 2008
10.24	Amended and Restated Employment Agreement for William D. Clark dated November 4, 2008
10.25	Amended and Restated Employment Agreement for Steven A. Shallcross dated November 4, 2008
10.26	Amended and Restated Employment Agreement for Paolo Baroldi dated November 4, 2008
10.27	Amended and Restated Employment Agreement for Al Gianchetti dated November 4, 2008
10.28	Offer Letter for John Feeney originally dated September 17, 2007
10.29	Severance Protection Letter for Stephanie Irish dated December 17, 2008
10.30	Separation Agreement for Al Gianchetti dated December 1, 2008
10.31	Separation Agreement for Paolo Baroldi dated December 17, 2008
10.32	Separation Agreement for Steven A. Shallcross dated December 17, 2008
23.1	Consent of PricewaterhouseCoopers LLP, Independent Registered Public Accounting Firm
31.1	Certification of the Chief Executive Officer, as required by Section 302 of the Sarbanes-Oxley Act of 2002.
31.2	Certification of the Chief Financial Officer as required by Section 302 of the Sarbanes-Oxley Act of 2002.
32.1	Certifications of the Chief Executive Officer and Chief Financial Officer as required by 18 U.S.C. 1350.
32.2	Certifications of the Chief Executive Officer and Chief Financial Officer as required by 18 U.S.C. 1350.

# Application has been made to the Securities and Exchange Commission to seek confidential treatment of certain provisions. Omitted material for which confidential treatment has been requested has been filed separately with the Securities and Exchange Commission.