

NEUROCRINE BIOSCIENCES INC

Form 10-K

February 09, 2007

Table of Contents

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

**Form 10-K**

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

(Mark One)

- ANNUAL REPORT PURSUANT TO SECTION 13 OR 15(d)  
OF THE SECURITIES EXCHANGE ACT OF 1934  
For the fiscal year ended December 31, 2006**
- OR**
- TRANSITION REPORT PURSUANT TO SECTION 13 OR 15(d)  
OF THE SECURITIES EXCHANGE ACT OF 1934  
For the transition period from        to**

**Commission file number: 0-22705**

**NEUROCRINE BIOSCIENCES, INC.**

*(Exact name of registrant as specified in its charter)*

**Delaware**

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

**12790 El Camino Real, San Diego, CA**

*(Address of principal executive office)*

**33-0525145**

*(I.R.S. Employer  
Identification Number)*

**92130**

*(Zip Code)*

**Registrant's telephone number, including area code:**

**(858) 617-7600**

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

<b>Title of Each Class</b>	<b>Name of Each Exchange on Which Registered</b>
Common Stock, \$0.001 par value	The NASDAQ Stock Market
Preferred Share Purchase Rights	

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

Edgar Filing: NEUROCRINE BIOSCIENCES INC - Form 10-K

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 Act. Yes  No

Note Checking the box above will not relieve any registrant required to file reports pursuant to Section 13 or 15(d) of the Exchange Act from their obligations under those Sections.

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 the 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, or a non-accelerated filer. See definition of "accelerated filer and large accelerated filer" in Rule 12b-2 of the Exchange Act. (Check one):

Large accelerated filer

Accelerated filer

Non-accelerated filer

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

The aggregate market value of the common equity held by non-affiliates of the Registrant as of June 30, 2006 totaled approximately \$344,302,321 based on the closing price for the Registrant's Common Stock on that day as reported by the Nasdaq National Market. Such value excludes Common Stock held by executive officers, directors and 10% or greater stockholders as of June 30, 2006. Ten percent or greater stockholders as of June 30, 2006 is based on 13G and amended 13G reports publicly filed before June 30, 2006. This calculation does not reflect a determination that such parties are affiliates for any other purposes.

As of February 1, 2007, there were 37,905,988 shares of the Registrant's Common Stock outstanding.

#### DOCUMENTS INCORPORATED BY REFERENCE

##### Document Description

##### 10-K Part

Portions of the Registrant's notice of annual meeting of stockholders and proxy statement III, ITEMS 10, 11, 12, to be filed pursuant to Regulation 14A within 120 days after Registrant's fiscal year end of 13, 14 December 31, 2006 are incorporated by reference into Part III of this report.

---

## TABLE OF CONTENTS

	<b>Page</b>
<b><u>PART I</u></b>	
<u>Item 1.</u> <u>Business</u>	3
<u>Item 1A.</u> <u>Risk Factors</u>	17
<u>Item 1B.</u> <u>Unresolved Staff Comments</u>	29
<u>Item 2.</u> <u>Properties</u>	29
<u>Item 3.</u> <u>Legal Proceedings</u>	29
<u>Item 4.</u> <u>Submission of Matters to a Vote of Security Holders</u>	29
<b><u>PART II</u></b>	
<u>Item 5.</u> <u>Market for Registrant's Common Equity, Related Stockholder Matters and Issuer Purchases of Equity Securities</u>	30
<u>Item 6.</u> <u>Selected Financial Data</u>	31
<u>Item 7.</u> <u>Management's Discussion and Analysis of Financial Condition and Results of Operations</u>	32
<u>Item 7A.</u> <u>Quantitative and Qualitative Disclosures about Market Risk</u>	41
<u>Item 8.</u> <u>Financial Statements and Supplementary Data</u>	41
<u>Item 9.</u> <u>Changes in and Disagreements with Accountants on Accounting and Financial Disclosure</u>	41
<u>Item 9A.</u> <u>Controls and Procedures</u>	41
<u>Item 9B.</u> <u>Other Information</u>	44
<b><u>PART III</u></b>	
<u>Item 10.</u> <u>Directors, Executive Officers and Corporate Governance</u>	44
<u>Item 11.</u> <u>Executive Compensation</u>	44
<u>Item 12.</u> <u>Security Ownership of Certain Beneficial Owners and Management and Related Stockholder Matters</u>	44
<u>Item 13.</u> <u>Certain Relationships and Related Transactions, and Director Independence</u>	44
<u>Item 14.</u> <u>Principal Accountant Fees and Services</u>	44
<b><u>PART IV</u></b>	
<u>Item 15.</u> <u>Exhibits and Financial Statement Schedules</u>	45
<u>EXHIBIT 10.35</u>	
<u>EXHIBIT 21.1</u>	
<u>EXHIBIT 23.1</u>	
<u>EXHIBIT 31.1</u>	
<u>EXHIBIT 31.2</u>	
<u>EXHIBIT 32</u>	

---

**Table of Contents**

**PART I**

**FORWARD-LOOKING STATEMENTS**

This Annual Report on Form 10-K and the information incorporated herein by reference contain forward-looking statements that involve a number of risks and uncertainties. Although our forward-looking statements reflect the good faith judgment of our management, these statements can only be based on facts and factors currently known by us. Consequently, these forward-looking statements are inherently subject to risks and uncertainties, and actual results and outcomes may differ materially from results and outcomes discussed in the forward-looking statements.

Forward-looking statements can be identified by the use of forward-looking words such as believes, expects, hopes, may, will, plan, intends, estimates, could, should, would, continue, seeks, pro forma, or antic words (including their use in the negative), or by discussions of future matters such as the development of new products, technology enhancements, possible changes in legislation and other statements that are not historical. These statements include but are not limited to statements under the captions Risk Factors, Management's Discussion and Analysis of Financial Condition and Results of Operations and Business as well as other sections in this report. You should be aware that the occurrence of any of the events discussed under the heading Item 1A. Risk Factors and elsewhere in this report could substantially harm our business, results of operations and financial condition and that if any of these events occurs, the trading price of our common stock could decline and you could lose all or a part of the value of your shares of our common stock.

The cautionary statements made in this report are intended to be applicable to all related forward-looking statements wherever they may appear in this report. We urge you not to place undue reliance on these forward-looking statements, which speak only as of the date of this report. Except as required by law, we assume no obligation to update our forward-looking statements, even if new information becomes available in the future.

**ITEM 1. BUSINESS**

We were originally incorporated in California in January 1992 and were reincorporated in Delaware in May 1996.

We discover, develop and intend to commercialize drugs for the treatment of neurological and endocrine-related diseases and disorders. Our product candidates address some of the largest pharmaceutical markets in the world, including insomnia, anxiety, depression, various female and male health disorders, diabetes and other neurological and endocrine related diseases and disorders. We currently have nine programs in various stages of research and development, including six programs in clinical development. While we independently develop many of our product candidates, we have entered into a collaboration for one of our programs. Our lead clinical development program, indiplon, is a drug candidate for the treatment of insomnia.

**Table of Contents****Our Product Pipeline**

The following table summarizes our most advanced product candidates currently in clinical development and those currently in research, and is followed by detailed descriptions of each program:

<b>Program</b>	<b>Target Indication</b>	<b>Status</b>	<b>Commercial Rights</b>
<b><i>Products under clinical development:</i></b>			
Indiplon	Insomnia	Registration	Neurocrine
GnRH Antagonist	Endometriosis	Phase II	Neurocrine
CRF R <sub>1</sub> Antagonist	Mood Disorders, Irritable Bowel Syndrome	Phase II	GlaxoSmithKline/ Neurocrine
CRF R <sub>2</sub> Peptide Agonist Urocortin 2	Cardiovascular	Phase II	Neurocrine
Selective norepinephrine reuptake inhibitor (sNRI)	Neuropathic Pain	Phase I	Neurocrine
GnRH Antagonist	Benign Prostatic Hyperplasia	Phase I	Neurocrine
<b><i>Research:</i></b>			
sNRI	Depression, Stress, Urinary Incontinence	Research	Neurocrine
Glucose Dependent Insulin Secretagogues	Type II Diabetes	Research	Neurocrine
GnRH Antagonist	Endometriosis, Benign Prostatic Hyperplasia	Research	Neurocrine
Adenosine <sub>2A</sub> Receptor Antagonists	Parkinson's Disease	Research	Neurocrine/Almirall
Ion Channel Blocker	Chronic Pain	Research	Neurocrine

Registration indicates that we or our collaborators have submitted a New Drug Application (NDA) to the U.S. Food and Drug Administration (FDA) for regulatory approval of the drug candidate.

Phase II indicates that we or our collaborators are conducting clinical trials on groups of patients afflicted with a specific disease in order to determine preliminary efficacy, optimal dosages and expanded evidence of safety.

Phase I indicates that we or our collaborators are conducting clinical trials with a smaller number of patients to determine early safety profile, maximally tolerated dose and pharmacological properties of the product in human volunteers.

Research indicates identification and evaluation of compound(s) in laboratory and preclinical models.

R<sub>1</sub> and R<sub>2</sub> refer to two CRF receptor subtypes.

**Products Under Clinical Development*****Indiplon***

Insomnia is a neurological disorder with approximately 86 million adults in the United States reporting trouble sleeping a few nights per week or more, according to a 2006 report from Mattson Jack (an epidemiological database used to determine the prevalence of a disease or disorder). Mattson Jack also reports that approximately 26 million adults in the United States experience chronic insomnia, having trouble sleeping every night or almost every night. In addition, according to the National Sleep Foundation (2003), frequent sleep problems in individuals that are 55 to 84 years old, if ignored, can complicate the treatment of other medical conditions, including arthritis, diabetes, heart and lung disease and depression. According to a 2006 report from IMS Health, the United States insomnia pharmaceutical market was \$2.8 billion in 2005 and is expected to exceed \$3.1 billion in 2006.

## **Table of Contents**

Researchers have found that insomnia can be treated by drugs that interact with the site of action of a natural brain chemical involved in promoting and maintaining sleep. This chemical is called gamma amino-butyric acid, or GABA, and the site of action is called the GABA<sub>A</sub> receptor. During the 1980s, drugs that non-selectively target the GABA<sub>A</sub> receptor, known as benzodiazepines, were used as sedatives to treat insomnia. This class of drugs produces several undesirable side effects, including negative interactions with other central nervous system depressants, such as alcohol, the development of tolerance upon repeat dosing, and rebound insomnia, or the worsening of insomnia following discontinuation of dosing. Additional side effects, due to the long half-life, or the duration of action of a compound, associated with this class of drugs include next-day residual sedation effects and impairment of coordination and memory.

During the late 1980s, a class of drugs known as non-benzodiazepines was developed to target a specific site on the GABA<sub>A</sub> receptor. The non-benzodiazepines have a reduced incidence of side effects that are believed to be attributable to binding more selectively on a GABA<sub>A</sub> receptor subtype than the benzodiazepines. The most commonly prescribed of the non-benzodiazepines in the United States are Ambien<sup>®</sup>, Ambien CR<sup>®</sup>, Sonata<sup>®</sup> and Lunesta<sup>®</sup>. According to IMS Health, Ambien<sup>®</sup> is the current market leader in the United States, with sales of \$2.1 billion in 2005.

We obtained the rights to indiplon for the treatment of insomnia through an exclusive worldwide sublicense agreement that we entered into with DOV Pharmaceutical, Inc. (DOV) in June 1998. Indiplon is a non-benzodiazepine GABA<sub>A</sub> receptor agonist which acts via the same mechanism as the currently marketed non-benzodiazepine therapeutics. However, preclinical studies suggest that indiplon has fewer side effects than currently marketed non-benzodiazepines, including Ambien<sup>®</sup> and Sonata<sup>®</sup>. In our Phase II and III clinical studies, indiplon demonstrated efficacy with no significant next-day residual sedation effects at clinically relevant doses.

We have developed indiplon in both a short acting capsule formulation and a longer acting tablet formulation. To develop these two different formulations, we have capitalized on important features of indiplon, its rapid absorption and its short half-life in the body. Based on our clinical studies, we have determined that the concentration of indiplon in the bloodstream reaches levels high enough to induce sedation approximately 15 minutes after the patient takes the pill. Indiplon is then rapidly metabolized and eliminated. The result for the patient is rapid sleep onset followed by rapid elimination of the drug from the body, reducing the risk of next-day residual sedation effects.

We believe that indiplon will address the most prevalent forms of insomnia—difficulty falling asleep; difficulty staying asleep; and difficulty getting back to sleep after middle of the night awakenings. Both forms are intended to improve sleep quality without creating drug induced impairment upon awakening. Our indiplon program is one of the most comprehensive clinical programs addressing the multiple needs of both younger and older adult patients with various forms of insomnia such as sleep initiation, sleep maintenance and middle of the night awakening.

Based on the results of preclinical studies and Phase I, Phase II and Phase III clinical trials on indiplon, as well as a non-clinical data package related to indiplon manufacturing, formulation and commercial product development, we assembled and filed NDAs with the FDA for both indiplon capsules and indiplon tablets. On May 15, 2006, we received two complete responses from the FDA regarding our indiplon capsule and tablet NDAs. These responses indicated that indiplon 5 mg and 10 mg capsules were approvable (FDA Approvable Letter) and that the 15 mg tablets were not approvable (FDA Not Approvable Letter).

The FDA Approvable Letter requested that we reanalyze data from certain preclinical and clinical studies to support approval of indiplon 5 mg and 10 mg capsules for sleep initiation and middle of the night dosing. The FDA Approvable Letter also requested reexamination of the safety analyses. We held an end-of-review meeting with the FDA related to the FDA Approvable Letter in August 2006. This meeting was specifically focused on determining the



actions needed to bring indiplon capsules from Approvable to Approval in the resubmission of the NDA for indiplon capsules. At the meeting the FDA requested that the resubmission include further analyses and modifications of analyses previously submitted to address questions raised by the FDA in the initial review. This reanalysis has been substantially completed. The FDA also requested, and we have completed, a supplemental pharmacokinetic/food effect profile of indiplon capsules including several meal types. The NDA for indiplon

## **Table of Contents**

capsules is currently being updated to include responses to the FDA requests and is targeted to be resubmitted to the FDA by the end of the second quarter of 2007.

The FDA Not Approvable Letter requested that we reanalyze certain safety and efficacy data and questioned the sufficiency of the objective sleep maintenance clinical data with the 15 mg tablet in view of the fact that the majority of our indiplon tablet studies were conducted with doses higher than 15 mg. We held an end-of-review meeting with the FDA related to the FDA Not Approvable Letter in October 2006. This meeting was specifically focused on determining the actions needed to bring indiplon tablets from Not Approvable to Approval in the resubmission of the NDA for indiplon tablets. The FDA has requested additional long-term safety and efficacy data with the 15 mg dose for the adult population and the development of a separate dose for the elderly population. In discussions, we and the FDA noted positive efficacy data for sleep maintenance with both indiplon capsules and tablets. On the basis of these discussions, we are formulating a strategy to pursue a sleep maintenance claim for indiplon. The evaluation of indiplon for sleep maintenance is ongoing and includes both indiplon capsules and tablets.

### ***Gonadotropin-Releasing Hormone (GnRH) Antagonist***

Gonadotropin-releasing hormone, or GnRH, is a peptide that stimulates the secretion of the pituitary hormones that are responsible for sex steroid production and normal reproductive function. Researchers have found that chronic administration of GnRH agonists reversibly shuts down this transmitter pathway and is clinically useful in treating hormone-dependent diseases such as endometriosis, uterine fibroids and benign prostatic hyperplasia (BPH). Several companies have developed peptide GnRH agonists on this principle, such as Lupron<sup>®</sup> and Zoladex<sup>®</sup>, and according to their manufacturers, their annual worldwide sales in 2005 totaled \$2.5 billion (EvaluatePharma.com). However, since they are peptides, they must be injected via a depot formulation rather than the preferred oral route of administration. In addition, GnRH agonists can take up to several weeks to exert their effect, a factor not seen with the use of GnRH antagonists. More importantly, until their effects are maximal, they have shown a tendency to exacerbate the condition via a hormone flare, and lead to the loss of bone density.

Orally active, nonpeptide GnRH antagonists potentially offer several advantages over injectable GnRH peptide drugs, including rapid onset of hormone suppression without a hormonal flare. Also, injection site reactions commonly observed in peptide depots are avoided and dosing can be rapidly discontinued if necessary—a clinical management option not available with long-acting depot injections. Importantly, using orally active antagonists, it may be possible to alter the level of pituitary suppression by varying dosage and thereby titrating circulating estrogen levels. Using this approach, an oral GnRH antagonist may provide patients relief from the painful symptoms of endometriosis while avoiding the need for the active management of bone loss.

Mattson Jack (2006) estimates that there are approximately 6.0 million women in the United States who are clinically-recognized as having chronic endometriosis. Of those afflicted, approximately 200,000 patients are treated in an inpatient setting, and approximately 250,000 are treated in an outpatient setting, according to a 1998 National Patient Profile audit (SMG Marketing Group). According to the American Academy of Family Physicians, endometriosis is believed to account for a significant proportion of infertility and greater than 90 percent of cases of chronic pelvic pain. The direct medical costs of endometriosis are estimated at \$2.8 billion annually. We believe that the availability of an oral treatment, lacking the side effect profile of the currently available peptide agonists, may be an alternative to current therapies and ultimately encourage a higher treatment rate.

Several Phase I clinical trials of our GnRH candidate for endometriosis have been completed. These studies demonstrated that our GnRH antagonist was safe and well tolerated, and a dose-dependent suppression of estradiol with once a day dosing was observed with doses between 50mg and 200mg /day. The reduction in estradiol has been correlated with a reduction in pain and other symptoms of endometriosis and is a useful biomarker. Based on the results of these Phase I trials, we completed two separate three-month Phase II trials in endometriosis patients to

establish efficacy and tolerability of our lead endometriosis drug candidate during 2006. Efficacy in these Phase II studies was assessed by the Composite Pelvic Sign and Symptoms Score (CPSSS) and Visual Analog Scale (VAS) industry-standard and validated measures utilized for evaluating pain reduction in endometriosis patients. In addition to the standard clinical and laboratory assessments of safety, a biomarker for bone turnover (n-telopeptide) was also measured to assess potential impact on bone mineral density.

## **Table of Contents**

Preliminary results were reported in mid-2006 for the first study of 75 mg and 150 mg given once daily. The second Phase II study in patients with endometriosis was initiated in December 2005 to more fully explore dose response at 50 mg twice daily and 100 mg twice daily. Preliminary results from this trial were reported in January 2007. Taken together, these trials indicate that a reduction in pain associated with endometriosis, as measured by CPSSS and VAS, is possible with benefit occurring within the first two weeks for some women. The magnitude of pain reduction is roughly comparable to that seen with Depo-Provera® and Lupron® although direct comparison to these treatments was not part of these early Phase II trials. Average estradiol levels were reduced in a dose-related manner and, most importantly, do not fall into the post-menopausal range associated with GnRH agonist treatments. Furthermore, no increase in bone turnover was evident as shown by stable mean n-telopeptide levels.

We initiated a Phase IIb study in the fourth quarter of 2006 in which 240 patients with endometriosis will be treated over a 6-month treatment period. This multi-center, randomized, double-blind, study includes three treatment groups, with two doses of GnRH, 150mg once a day and 75mg twice daily, and an active comparator. In addition to confirming the effect of GnRH on endometriosis symptoms, this study is designed primarily to assess the impact of longer treatment on bone mineral density as measured by DEXA scan (X-Ray) at the conclusion of dosing and at 6-months and 12-months post treatment. These results, together with data from the previous two Phase II studies, are intended to provide the basis for securing agreement to a registration plan acceptable to the FDA.

BPH is defined by the enlargement of the prostate gland. In BPH, as the prostate grows larger and presses against the urethra, normal flow of urine is hindered. Researchers have determined that dihydrotestosterone (DHT), a derivative of testosterone, is the primary cause of prostate enlargement. Equally important, men who do not generate DHT do not develop BPH. Accordingly, by using a small molecule GnRH antagonist, one could block the production of testosterone, and indirectly DHT, and thus ameliorate the symptoms of BPH.

Moderate to severe BPH affects an estimated 21 million men in the United States (Mattson Jack 2006). Additionally, more than 40% of all men over the age of 60 suffer from the symptoms of BPH (Mattson Jack 2006). Worldwide sales of current treatments for BPH exceeded \$3 billion in 2005 (EvaluatePharma.com). During 2004, we conducted a Phase I single dose study to assess the safety, tolerability, pharmacokinetics and pharmacodynamics of our GnRH antagonist in healthy males. The results of this trial demonstrated that our GnRH antagonist effectively reduced testosterone production when compared to placebo. In 2005, we filed an Investigational New Drug application to initiate a multiple dose Phase I study in males. The study was completed in 2006 and the results demonstrate that a dose-related reduction of testosterone was achieved and that two weeks of GnRH antagonist treatment is generally safe and well tolerated in healthy males.

### ***Corticotropin-Releasing Factor (CRF) R<sub>1</sub> Antagonist***

According to Mattson Jack (2006), the lifetime prevalence of major depressive disorder exceeds 22 million in the United States and 12 million suffer from less severe forms of depression. The National Institute of Mental Health also indicated that in 2006 over 19 million Americans suffered from a debilitating anxiety disorder. In 2005, the branded worldwide market for depression therapeutics was in excess of \$12 billion (EvaluatePharma.com).

*Depression.* Depression is one of a group of neuropsychiatric disorders that is characterized by extreme feelings of elation and despair, loss of body weight, decreased aggressiveness and sexual behavior, and loss of sleep. Researchers believe that depression results from a combination of environmental factors, including stress, as well as an individual's biochemical vulnerability, which is genetically predetermined. The most frequently prescribed antidepressant therapies are selective serotonin reuptake inhibitors such as Zoloft®, Paxil®, Lexapro® and Prozac®, as well as certain generic equivalents, that act to increase the levels of serotonin and several other chemicals in the brain. However, because these drugs affect a wide range of neurotransmitters, they have been associated with a number of adverse side

effects. While newer, more selective drugs offer some safety improvement, side effects remain problematic. In addition, one of the biggest limitations of most existing antidepressant therapies is their slow onset of action.

*Anxiety.* Anxiety is among the most commonly observed group of central nervous system disorders, which includes phobias or irrational fears, panic attacks, and other syndromes. Of the pharmaceutical agents that other

## **Table of Contents**

companies currently market for the treatment of anxiety disorders, benzodiazepines, such as Valium® and Xanax®, and the anxiolytics BuSpar® and Effexor® as well as certain generic equivalents are the most frequently prescribed. Several side effects, however, limit the utility of these anti-anxiety drugs. Most problematic among these are drowsiness, memory difficulties, drug dependency and withdrawal reactions following the termination of therapy.

Researchers have identified what they believe to be the central mediator of the body's stress responses or stress-induced disorders (including depression and anxiety). This mediator is a brain chemical known as corticotropin-releasing factor, or CRF. CRF is overproduced in clinically depressed patients and individuals with anxiety disorders. Current research indicates that clinically depressed patients and patients with anxiety experience dysfunction of the hypothalamic-pituitary-adrenal axis, the system that manages the body's overall response to stress. This amplifies production of CRF, and induces the physical effects that are associated with stress that can lead to depression or anxiety. The novelty and specificity of the CRF mechanism of action and the prospect of improving upon selective serotonin reuptake inhibitor therapy represents a market opportunity both to better serve patients and expand overall treatment of depression. We also believe that CRF offers a novel mechanism of action that may offer the advantage of being more selective, thereby providing increased efficacy with reduced side effects in anxiety as compared to benzodiazepines.

We have a strategic position in the CRF field through our intellectual property portfolio and relationship with experts in the neuropsychiatric field. We have further characterized the CRF receptor system and have identified additional members of the CRF receptor family. We have patent rights on two receptor subtypes called CRF R<sub>1</sub> and CRF R<sub>2</sub>, and we have pending patent applications on small molecule organic compounds modulating the CRF receptors.

The first clinical trial to offer evidence of proof of concept of CRF antagonists in addressing depression (and anxiety as a co-examined variable) was a Phase IIa open label trial we conducted in 1999 pursuant to collaborations with Janssen in the field of CRF antagonists. Results from this trial indicated that the drug candidate was safe and well tolerated and demonstrated anti-depressant activity as measured by a widely-accepted depression scale known as the Hamilton Depression Scores. In this trial, the drug candidate was administered to 20 patients with major depressive disorders. Results from the trial, as reported in the Journal of Psychiatric Research, showed that treatment response, as defined by more than a 50% reduction in Hamilton Depression Scores, occurred in 50% of the patients in the low dose group and 80% of the patients in the higher dose group. Additionally, the drug candidate demonstrated a reduction in Hamilton Anxiety Scores from baseline in both treatment groups at all times after dosing. While development of our first generation CRF antagonist was discontinued for safety reasons by our collaborator Janssen, we were encouraged by these results which we believe support the hypothesized mechanism of action. Our CRF antagonist research collaboration with Janssen was terminated in March 2002.

In July 2001, we announced our second CRF antagonist collaboration, a worldwide collaboration with GlaxoSmithKline (GSK), to develop and commercialize CRF antagonists for psychiatric, neurological and gastrointestinal diseases. Under the terms of this agreement, GSK sponsored and we jointly conducted a collaborative research program and collaborated in the development of our current lead compounds, as well as novel back-up candidates and second generation compounds identified through the collaborative research. The sponsored research portion of the collaboration was completed in 2005.

During 2004, GSK advanced one of the lead CRF R<sub>1</sub> receptor antagonist drug candidates arising out of our collaboration into Phase I clinical trials. The trial was a double-blind, placebo-controlled, single-dose study to evaluate safety and pharmacokinetics of a range of escalating doses. This study dose was followed by the successful completion of a placebo-controlled double blind multiple dose Phase I study. In late 2006, GSK initiated Phase II proof of concept clinical trials with a lead CRF R<sub>1</sub> receptor antagonist compound for two indications, social anxiety disorder (SocAD) and irritable bowel syndrome (IBS).

The first proof of concept trial is a Phase II double-blind, randomized, placebo controlled, multiple dose study to evaluate the safety and efficacy of the CRF antagonist compound in patients with SocAD. The four-arm study will include more than 200 adult subjects with Generalized Social Anxiety Disorder/Social Phobia. Efficacy, safety, tolerability and pharmacokinetics will be assessed. The clinical endpoints of the study include validated scales for assessment of anxiety disorders including the Liebowitz Social Anxiety Scale and the Social Avoidance and Distress Scale.

## **Table of Contents**

GSK has also advanced an additional lead CRF receptor antagonist into a Phase I single-dose study in the first quarter of 2006 and this compound is now in a Phase I multi-dose study.

*Irritable Bowel Syndrome.* Research has also suggested that CRF plays a role in the control or modulation of the gastrointestinal system. Studies have demonstrated that central administration of CRF acts in the brain to inhibit emptying of the stomach while stimulating bowel activity, and suggest that overproduction of CRF in the brain may be a main contributor to stress-related gastrointestinal disorders.

IBS is a gastrointestinal inflammatory disease that affects approximately 30 million people in the United States (Mattson Jack, 2006), accounting for over \$25 billion in direct and indirect costs each year, according to the International Foundation for Functional Gastrointestinal Disorders. IBS can be a lifelong, intermittent disease, involving chronic or recurrent abdominal pain and frequent diarrhea or constipation. Some patients with IBS report the onset of symptoms of the disease following a major life stress event, such as death in the family, which suggests that the causes of IBS may be related to stress. In addition, most IBS sufferers also experience anxiety and depression.

The second proof of concept trial is a Phase II double-blind, randomized, placebo controlled study to evaluate the safety and efficacy of this compound in patients with IBS. Approximately 100 patients meeting established diagnostic criteria for IBS will be entered into this cross-over design trial. Standard assessments of safety, tolerability and pharmacokinetics will be conducted. The clinical endpoints reflect change in symptom frequency and severity via validated scales for IBS.

### ***CRF R<sub>2</sub> Peptide Agonist (Urocortin 2)***

Congestive heart failure (CHF) is a condition where the heart cannot pump enough blood to supply all of the body's organs. It is a result of narrowing of the arteries combined with high blood pressure, which results in increased respiration as well as edema from water retention. In the case of acute symptomology, CHF patients will eventually experience a rapid deterioration and require urgent treatment in the hospital. According to 2005 data from the American Heart Association, nearly 5 million people experience CHF and about 550,000 new cases are diagnosed each year in the United States. CHF becomes more prevalent with age and the number of cases is expected to grow as the overall age of the population increases. Current treatment options include a cocktail of drugs consisting of diuretics to remove excess water, beta blockers and digitalis to improve heart muscle contraction, and/or ACE inhibitors and vasodilators to expand blood vessels. There are in excess of one million hospitalizations each year in the United States for CHF (Mattson Jack, 2006).

Urocortin 2 is a recently discovered endogenous peptide ligand of the CRF R<sub>2</sub> receptor present in the cardiovascular system, notably the heart and cerebral arterial system. Urocortin 2 plays a role in the control of the hormonal, cardiovascular, gastrointestinal, and behavioral responses to stress, and has an array of effects on the cardiovascular system and metabolism. Based on preclinical efficacy and safety data, together with its known role in human physiology, we believe that urocortin 2 may have positive hemodynamic effects on cardiac output and blood pressure which may benefit patients with acute CHF.

During 2005, we completed a Phase II placebo controlled dose-escalation study to evaluate the safety, pharmacokinetics and pharmacodynamics of two dose levels of urocortin 2 in patients with stable CHF. Results of this study demonstrated a dose-related increase in cardiac output of up to 50% with only a modest increase (6%) in heart rate. We completed an additional Phase II study evaluating urocortin 2 over four hour infusions in patients with stable CHF in the first half of 2006. The treatments were generally well tolerated without serious adverse events, abnormalities in electrocardiograms or significant changes in renal function. Positive hemodynamic effects were noted in virtually all patients with increases in cardiac output ranging from 6% to 54%.



Our intent is to initiate additional Phase II studies with longer duration of infusion of up to 72 hours. However, additional preclinical studies are necessary to support this longer period of infusion. We expect to complete these preclinical studies in 2007.

## **Table of Contents**

### ***Selective Norepinephrine Reuptake Inhibitor (sNRI)***

In 2006, there were approximately 8 million chronic neuropathic pain sufferers (painful diabetic neuropathy) in the United States alone (National Institute of Arthritis and Musculoskeletal and Skin Diseases), representing over \$2 billion in branded neuropathic pain product sales (Med Ad News).

The rationale for the role of a selective norepinephrine reuptake inhibitor (sNRI) in treating neuropathic pain (NP) includes anatomical and neurochemical evidence for the role of both norepinephrine and serotonin (5-HT) in modulation of endogenous analgesic systems. While selective serotonin reuptake inhibitors (SSRIs) are generally ineffective in treating neuropathic pain, our lead sNRI development candidate has been efficacious in multiple preclinical models of neuropathic pain including the formalin model for persistent pain and the spinal nerve ligation test for mechanical hyperalgesia. Due to its specificity and selectivity, it is hypothesized that the orally-available small molecule may have advantages in the area of safety/tolerability and may also be used synergistically with other classes of compounds used in the treatment of NP, such as gabapentin. A Phase I study is currently being conducted to assess the safety, tolerability, and pharmacokinetics/pharmacodynamics for our sNRI drug candidate. The study design is a double-blind, placebo-controlled, single-dose, dose escalation in healthy male volunteers.

### **Research and Development**

Our research and development focus is on addressing diseases and disorders of the central nervous system and endocrine system, which include therapeutic categories ranging from diabetes to stress-related disorders and neurodegenerative diseases. Central nervous system and endocrinology drug therapies are among the largest therapeutic categories, accounting for over \$60 billion in worldwide drug sales in 2005 according to Med Ad News.

### ***GnRH Antagonists***

As previously mentioned, GnRH antagonists may be useful in treating certain hormone dependent diseases. Our discovery work in GnRH antagonists continues to focus on endometriosis and benign prostatic hyperplasia as we continue to search for additional candidates for preclinical and clinical trials.

### ***Selective Norepinephrine Reuptake Inhibitors***

As described above, sNRI may be useful in treating a variety of diseases. Our research in sNRI continues to focus on neuropathic pain as well as complimentary therapeutic categories such as major depressive disorders, stress and urinary incontinence as we continue to search for additional candidates for preclinical and clinical trials.

### ***Adenosine<sub>2A</sub>(A<sub>2A</sub>) Receptor Antagonists***

In October 2004, we entered into a licensing agreement with Almirall Prodesfarma, S.A. (Almirall) for the development of adenosine A<sub>2A</sub> receptor antagonists for Parkinson's disease. A<sub>2A</sub> receptor antagonists have been shown to be effective in both pre-clinical models of Parkinson's disease and in clinical trials with Parkinson's disease patients. This subtype of receptors for the neuromodulator adenosine is selectively localized on neurons in the brain that also express dopamine D2 receptors. The function of these neurons is impaired due to dopamine depletion that occurs in Parkinson's disease and antagonism of A<sub>2A</sub> receptors appears to help restore normal function. We are in the process of identifying a development candidate from this research program. In response to a Therapeutics Development Initiative by the Michael J. Fox Foundation to promote preclinical industry-initiated Parkinson's Disease research, we applied and were awarded a 2-year grant beginning in early 2007 to study the neuroprotective effects of A<sub>2A</sub> antagonists in motor function and dyskinesia.

***Glucose Dependent Insulin Secretagogues***

Type II diabetes affects more than 19 million Americans (Mattson Jack 2006), and is growing at epidemic proportions world-wide. The disease is characterized by reduced ability to secrete and respond to insulin. Drugs which can enhance the secretion of insulin in response to rising blood glucose levels can improve blood glucose control without increased risk of hypoglycemia. Our scientists are optimizing small molecule compounds that act in this way in order to discover novel oral therapies for glucose control in diabetes.

## **Table of Contents**

### ***Ion Channel Blockers***

Capitalizing on our expertise in the area of neurology and pain management in small molecule therapeutics, we have initiated a new program focused on a novel target for the treatment of chronic pain. The target is an ion channel present on sensory nerve fibers that plays a role in transmitting pain signals to the central nervous system. Our scientists hypothesize that blocking this channel could provide alleviation of chronic pain.

### **Our Discovery Technology**

We utilize a proprietary approach to small molecule drug design that we refer to as multi-channel technology.

*Multi-Channel Discovery*<sup>tm</sup>. The advent of molecular biology, culminating in the cloning of the human genome, has opened up a vast array of receptors as potential targets for drug discovery. Numerous new technologies have been developed to try to speed the identification of small molecule drugs. These technologies have mainly relied on the creation of large chemical libraries utilizing combinatorial chemistry, automated synthesis of compounds and ultra-high throughput screening machines to test hundreds of thousands of compounds against a particular receptor. While we utilize all of these technologies, we have taken the science to the next step, which we call Multi-Channel Discovery, or MCD<sup>tm</sup>.

MCD is driven by the power of traditional medicinal chemistry accelerated by a suite of computational methodologies that guide the synthesis of highly active small molecules. At the core of MCD is our development of a virtual library containing over 100 million molecules. Utilizing this universe of compounds our chemists sequentially apply computer generated molecular screens to filter compounds that will bind to the desired receptor. The unique feature of MCD is that chemists are no longer constrained by the physical properties of a particular compound but rather are free to work with thousands of shapes and charges to design compounds that will fit onto the receptor target.

The power of MCD, however, lies not in its application to a single receptor as a drug target but in the database of compounds that are characterized and isolated for the next target from the same class of receptors. Our current focus is on G-protein-coupled receptors. MCD is not a static process, but one that becomes more powerful, more predictive, and more efficient with each subsequent use. It is an artificial intelligence system applied to drug design. More recent enhancements using commercially available software now allow us to grow new molecules from an initial seed template that satisfy predetermined arrays of features often 2-D or 3-D pharmacophore. This generates new ideas that the medicinal chemist may not have originally considered and therefore offers another option when engaged in lead-hopping activities.

In connection with our multi-channel technology, we utilize other advanced technologies to enhance our drug discovery capabilities and to accelerate the drug development process. These technologies include:

*High-Throughput Screening.* We have assembled a chemical library of diverse, low molecular weight organic molecules for lead compound identification and we have implemented robotics screening capabilities linked to our library of compounds that facilitate the rapid identification of new drug candidates for multiple drug targets. We believe that our utilization of high-throughput screening and medicinal and peptide chemistry will enable us to rapidly identify and optimize lead molecules. Our chemical library is enhanced annually by computational selection of commercially available chemical libraries and further diversity is obtained through strategic collaborations.

*Molecular Biology.* Our scientists utilize novel techniques to examine gene expression in a variety of cellular systems. We have developed a sophisticated technique to evaluate the type and quantity of genes in various cellular systems prior to the isolation of genes. We have also developed unique expression vectors and cell lines that allow for

the highly efficient protein expression of specific genes.

Our drug discovery program creates a significant amount of genetic sequence information. We have developed a bioinformatics system, which we believe will allow us to identify novel genes involved in neurodegeneration. We collect data with automated instruments, and we store and analyze the data using customized computational tools.

*Gene Sequencing.* We apply integrated automated DNA sequencing and gene identification technology in our drug discovery program, enabling us to perform extended gene analysis in a rapid, high-throughput format with

## **Table of Contents**

independent linkage into a sequence identification database. We have optimized gene sequencing instrumentation for differential display, a technique that may facilitate the rapid identification of novel genes.

### **Our Business Strategy**

Our goal is to become the leading biopharmaceutical company focused on neurological and endocrine-related diseases and disorders. The following are the key elements of our business strategy:

*Completing the Development, Commercialization, and Partnering of Our Lead Product Candidate, indiplon.* We are currently assembling the NDA resubmission for indiplon capsules and plan to file the resubmission by the end of the second quarter of 2007. We will continue to evaluate indiplon for sleep maintenance for both indiplon capsules and tablets. We will seek a partner, at an appropriate time, to assist us in the worldwide development and commercialization of indiplon.

*Continuing to Advance and Build Our Product Portfolio Focused on Neurological and Endocrine-Related Diseases and Disorders.* We believe that by continuing to advance and build our product pipeline, we can mitigate some of the clinical development risks associated with drug development. We currently have nine programs in various stages of research and development, including six programs in clinical development. We take a portfolio approach to managing our pipeline that balances the size of the market opportunities with clear and defined clinical and regulatory paths to approval. We do this to ensure that we focus our internal development resources on innovative therapies with improved probabilities of technical and commercial success.

*Identifying Novel Drug Targets to Address Large Unmet Market Opportunities.* We seek to identify and validate novel drug targets for internal development or collaboration. For example, the novel drug candidates we have identified to regulate CRF, which is believed to be the central mediator of the body's stress response, may represent the first new breakthrough for anxiety and depression in over 25 years. GnRH antagonists, compounds designed to reduce the secretions of sex steroids, may represent the first novel non-injectible means of treatment of endometriosis. The creativity and productivity of our discovery research group will continue to be a critical component for our continued success. Our team of approximately 137 biologists and chemists has a goal of delivering one innovative clinical compound each year to fuel our research and development pipeline. Research and development costs were \$97.7 million, \$106.6 million and \$115.1 million for the years ended December 31, 2006, 2005 and 2004, respectively.

*Selectively Establishing Corporate Collaborations with Global Pharmaceutical Companies to Assist in the Development of Our Products and Mitigate Financial Risk while Retaining Significant Commercial Upside.* We leverage the development, regulatory and commercialization expertise of our corporate collaborators to accelerate the development of certain of our potential products, while typically retaining co-promotional rights, and at times commercial rights, in North America. We intend to further leverage our resources by selectively entering into additional strategic alliances to enhance our internal development and commercialization capabilities by licensing our technology.

*Acquiring Rights to Complementary Drug Candidates and Technologies.* We plan to continue to selectively acquire rights to products in various stages of development to take advantage of our drug development capabilities. For example, in June 1998, we licensed exclusive worldwide commercial rights for indiplon from DOV. Additionally, during 2003, we licensed our urocortin 2 product candidate from the Research Development Foundation, and in 2004 we licensed adenosine<sub>2A</sub> receptor antagonist technology from Almirall.

### **Our Corporate Collaborations and Strategic Alliances**

One of our business strategies is to utilize strategic alliances to enhance our development and commercialization capabilities. The following is a summary of our significant collaborations/alliances:

*Pfizer.* In December 2002, we announced an exclusive worldwide collaboration with Pfizer to develop and commercialize indiplon. Under the terms of the agreement, Pfizer made an upfront payment to us of \$100 million and was responsible for all future third-party development, marketing and commercialization costs, with the exception of \$30 million for specified development costs that we contributed towards development of indiplon during 2003 and 2004. During 2005, Pfizer began to pay for and support a 200-person Neurocrine sales force to

## **Table of Contents**

promote Pfizer's leading antidepressant drug, Zoloft®, to psychiatrists in the United States. As of December 31, 2006, we had recorded revenues of \$100.0 million in license fees, \$90.5 million in milestones, \$127.9 million in sponsored development, and \$38.5 million in sales force allowance over the life of the agreement.

On June 22, 2006 we and Pfizer agreed to terminate our collaboration and license agreements to develop and co-promote indiplon effective December 19, 2006. As a result, we reacquired all worldwide rights for indiplon capsules and tablets and are responsible for any costs associated with development, registration, marketing and commercialization of indiplon.

*GlaxoSmithKline (GSK)*. In July 2001, we announced a worldwide collaboration with an affiliate of GSK to develop and commercialize CRF antagonists for psychiatric, neurological and gastrointestinal diseases. Under the terms of this agreement, we and GSK will conduct a collaborative research program and collaborate in the development of our current lead compounds, as well as novel back-up candidates and second generation compounds identified through the collaborative research. In addition, we will be eligible to receive milestone payments as compounds progress through the research and development process, royalties on future product sales and co-promotion rights in the U.S. in some circumstances. GSK may terminate the agreement at its discretion upon 90 days prior written notice to us. In such event, we may be entitled to specified payments and all product rights would revert to us. As of December 31, 2006, we had recorded revenues of \$4.5 million in license fees, \$28.8 million in milestone payments, \$19.5 million in sponsored research and \$1.2 million in reimbursement of development costs, over the life of the agreement. The sponsored research portion of this collaboration agreement concluded in 2005. In 2006, GSK initiated Phase II proof of concept clinical trials with a lead CRF antagonist compound for two indications, SocAD and IBS. We recognized \$8.0 million in milestones from GSK upon initiation of these two Phase II clinical trials during the year ended December 31, 2006.

## **Intellectual Property**

We seek to protect our lead compounds, compound libraries, expressed proteins, synthetic organic processes, formulations, assays, cloned targets, screening technology and other technologies by filing, or by causing to be filed on our behalf, patent applications in the United States and abroad. These applications have resulted in the issuance of approximately 61 United States patents. Additionally, we have licensed from institutions such as The Salk Institute, DOV, Almirall, Research Development Foundation and others the rights to issued United States patents, pending United States patent applications, and issued and pending foreign filings. We face the risk that one or more of the above patent applications may be denied. We also face the risk that issued patents that we own or license may be challenged or circumvented or may otherwise not provide protection for any commercially viable products we develop.

The technologies we use in our research, as well as the drug targets we select, may infringe the patents or violate the proprietary rights of third parties. If this occurs, we may be required to obtain licenses to patents or proprietary rights of others in order to continue with the commercialization of our products. We are aware of a patent application controlled by another company, which if granted in its broadest scope and held to be valid, could impact the commercialization of our tablet insomnia formulation in the United States unless we obtain a license, which may not be available to us. Based on information available from the United States Patent and Trademark Office (USPTO), we have learned that the USPTO has examined the pending claims of this application two times and that both times it has rejected all the pending claims. We are also aware that the corresponding patent application in Europe has issued as a patent, and we have filed an opposition against the issued European patent.

Indiplon is covered in an issued United States patent, which we sublicensed from DOV. The term of the United States patent is due to expire in 2020. Additional United States patents covering synthesis, formulations and forms of indiplon have been issued with expirations ranging from 2020 to 2023. We intend to seek additional protection of this



compound through United States and foreign patent applications directed to the synthesis, formulations and various forms of indiplon. We face the risk that these patents may not issue, or may subsequently be challenged successfully. In addition to the granted and potential patent protection, the United States, the European Union and Japan all provide data protection for new medicinal compounds. If this protection is available, no competitor may use the original applicant's data as the basis of a generic marketing application during the period

## **Table of Contents**

of data protection. This period of exclusivity is five years in the United States, six years in Japan and six to ten years in the European Union, measured from the date of FDA, or corresponding foreign, approval.

## **In-Licensed Technology**

We have in-licensed the following technologies to complement our ongoing clinical and research programs. Most of these licenses extend for the term of the related patent and contain customary royalty, termination and other provisions.

In January 2006, we licensed exclusive rights to a series of small molecule Adenosine receptor modulators from Universiteit Leiden.

In October 2004, we licensed non-exclusive rights to Almirall's small molecule Adenosine<sub>2A</sub> receptor antagonists for the treatment of Parkinson's Disease.

In October 2003, we licensed non-exclusive rights to CRF R<sub>2</sub> deficient mice from Research Development Foundation.

In June 2003, we licensed a non-exclusive rights to Cav3.1 human cDNA expressing cell line from University of Virginia Patent Foundation.

In May 2003, we entered into a collaboration and license agreement with Bicoll GmbH relating to GPCR targets.

In March 2003, we licensed a non-exclusive right to certain green fluorescent proteins.

In January 2003, we licensed exclusive rights to urocortin 2 from Research Development Foundation.

In December 2002, we entered into a collaboration and license agreement with Biosite Incorporated relating to high affinity antibodies.

In December 2002, we licensed knock-out mice to certain target genes from Deltagen, Inc.

In March 2001, we licensed non-exclusive rights to a saoS-2 cell line from The Sloan-Kettering Institute for Cancer Research.

In March 2001, we licensed a HERG cell line from Wisconsin Alumni Research Foundation.

In August 2000, we licensed non-exclusive rights to CRF R<sub>1</sub> deficient mice from the Research Development Foundation.

In August 1999, we licensed non-exclusive rights to the human gonadotropin-releasing hormone receptor from Mount Sinai School of Medicine.

In June 1998, we licensed exclusive worldwide rights to indiplon, from DOV.

## **Manufacturing and Distribution**

We currently rely on, and will continue to rely on, contract manufacturers to produce sufficient quantities of our product candidates for use in our preclinical and anticipated clinical trials. In addition, we intend to rely on third parties to manufacture any products that we may commercialize in the future. We have established an internal pharmaceutical development group to develop manufacturing methods for our product candidates, to optimize manufacturing processes, and to select and transfer these manufacturing technologies to our suppliers. We continue to contract with multiple manufacturers to ensure adequate product supply and to mitigate risk.

There currently are a limited number of these manufacturers. Furthermore, some of the contract manufacturers that we have identified to date only have limited experience at manufacturing, formulating, analyzing and packaging our product candidates in quantities sufficient for conducting clinical trials or for commercialization.

We currently have no distribution capabilities. In order to independently commercialize any of our product candidates, we must either internally develop distribution capabilities or make arrangements with third parties to perform these services.

## **Table of Contents**

### **Marketing and Sales**

We currently have limited experience in marketing or selling pharmaceutical products. Under our collaboration agreement with GSK we may have the opportunity to co-promote any products resulting from the collaboration in the United States. To market any of our other products independently would require us to develop a sales force with technical expertise along with establishing commercial infrastructure and capabilities.

### **Medical Affairs**

Our Medical Affairs department supports our drug development activities via the generation, communication and dissemination of clinical data and scientific information. Our field based scientific team is currently focused on educational activities related to treatment of insomnia and dissemination of scientific data via presentations at key Congresses and in publications.

### **Government Regulation**

Regulation by government authorities in the United States and foreign countries is a significant factor in the development, manufacture and marketing of our proposed products and in our ongoing research and product development activities. All of our products will require regulatory approval by government agencies prior to commercialization. In particular, human therapeutic products are subject to rigorous preclinical studies and clinical trials and other approval procedures of the FDA and similar regulatory authorities in foreign countries. Various federal and state statutes and regulations also govern or influence testing, manufacturing, safety, labeling, storage and record-keeping related to such products and their marketing. The process of obtaining these approvals and the subsequent compliance with appropriate federal and state statutes and regulations require the expenditure of substantial time and financial resources.

Preclinical studies generally are conducted in laboratory animals to evaluate the potential safety and the efficacy of a product. Drug developers submit the results of preclinical studies to the FDA as a part of an IND application that must be approved before clinical trials can begin in humans. Typically, clinical evaluation involves a time consuming and costly three-phase process.

- |           |  |
|-----------|--|
| Phase I   | Clinical trials are conducted with a small number of patients to determine the early safety profile, maximum tolerated dose and pharmacological properties of the product in human volunteers.   |
| Phase II  | Clinical trials are conducted with groups of patients afflicted with a specific disease in order to determine preliminary efficacy, optimal dosages and expanded evidence of safety.   |
| Phase III | Large-scale, multi-center, comparative clinical trials are conducted with patients afflicted with a specific disease in order to determine safety and efficacy as primary support for regulatory approval by the FDA to market a product candidate for a specific disease. |

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. To date, we have also conducted some of our clinical trials in Europe, Oceania, and South Africa. Clinical trials conducted in foreign countries may also be subject to oversight by regulatory authorities in those countries.

Once Phase III trials are completed, drug developers submit the results of preclinical studies and clinical trials to the FDA in the form of an NDA or a biologics licensing application for approval to commence commercial sales. In

response, the FDA may grant marketing approval, request additional information or deny the application if the FDA determines that the application does not meet regulatory approval criteria. FDA approvals may not be granted on a timely basis, or at all. Furthermore, the FDA may prevent a drug developer from marketing a product under a label for its desired indications, which may impair commercialization of the product.

If the FDA approves the NDA, the drug becomes available for physicians to prescribe in the United States. After approval, the drug developer must submit periodic reports to the FDA, including descriptions of any adverse reactions reported. The FDA may request additional studies, known as Phase IV, to evaluate long-term effects.

## **Table of Contents**

In addition to studies requested by the FDA after approval, a drug developer may conduct other trials and studies to explore use of the approved compound for treatment of new indications. The purpose of these trials and studies and related publications is to broaden the application and use of the drug and its acceptance in the medical community.

We will also have to complete an approval process similar to that in the United States in virtually every foreign target market for our products in order to commercialize our product candidates in those countries. The approval procedure and the time required for approval vary from country to country and may involve additional testing. Foreign approvals may not be granted on a timely basis, or at all. In addition, regulatory approval of prices is required in most countries other than the United States. The resulting prices may not be sufficient to generate an acceptable return to us or our corporate collaborators.

## **Competition**

The biotechnology and pharmaceutical industries are subject to rapid and intense technological change. We face, and will continue to face, competition in the development and marketing of our product candidates from biotechnology and pharmaceutical companies, research institutions, government agencies and academic institutions. Competition may also arise from, among other things:

other drug development technologies;

methods of preventing or reducing the incidence of disease, including vaccines; and

new small molecule or other classes of therapeutic agents.

Developments by others may render our product candidates or technologies obsolete or noncompetitive. We are performing research on or developing products for the treatment of several disorders including insomnia, anxiety, depression, endometriosis, diabetes, irritable bowel syndrome, and other CNS related disorders.

We are developing indiplon for the treatment of insomnia. Ambien<sup>®</sup>, Sonata<sup>®</sup>, Lunesta<sup>®</sup>, and Rozerem<sup>®</sup> are already marketed for the treatment of insomnia by Sanofi-Aventis, King Pharmaceuticals, Inc., Sepracor, Inc., and Takeda Pharmaceutical Company, respectively. Recently, in anticipation of the near-term generic entrant of Ambien<sup>®</sup> or zopliedem, Sanofi-Aventis launched a controlled-release formulation of Ambien<sup>®</sup> called Ambien CR<sup>®</sup>. H. Lundbeck A/S and Merck & Co. are developing gaboxadol, a GABA agonist, for sleep disorders, which is currently in Phase III clinical trials. Somaxon Pharmaceuticals is developing doxepine, a H1 antagonist, for the treatment of insomnia, which is currently in Phase III clinical trials.

In the area of anxiety disorders, our product candidates will compete with well-established products such as Valium<sup>®</sup>, marketed by Hoffman-La Roche, Xanax<sup>®</sup>, marketed by Pfizer, BuSpar<sup>®</sup>, marketed by Bristol-Myers Squibb, Zolof<sup>®</sup> marketed by Pfizer, Wellbutrin<sup>®</sup> marketed by GlaxoSmithKline and Effexor<sup>®</sup> marketed by Wyeth, among others, as well as any generic alternatives for each of these products.

We are also developing products for depression, which will compete with well-established products in the antidepressant class, including Prozac<sup>®</sup> and Cymbalta<sup>®</sup>, marketed by Eli Lilly, Zolof<sup>®</sup>, marketed by Pfizer, Paxil<sup>®</sup>, marketed by GlaxoSmithKline, Effexor<sup>®</sup>, marketed by Wyeth, and Lexapro<sup>®</sup>, marketed by Forest Laboratories, among others. Some technologies under development by other pharmaceutical companies could result in additional commercial treatments for depression and anxiety. In addition, a number of companies also are conducting research on molecules to block CRF, which is the same mechanism of action employed by our compounds.

There are a number of competitors to other potential products in our pipeline. Lupron Depot<sup>®</sup>, marketed by TAP Pharmaceuticals, and Synarel<sup>®</sup> and Depo-Provera<sup>®</sup>, marketed by Pfizer, are gonadotropin-releasing hormone peptide agonists that have been approved for the treatment of endometriosis, infertility, and central precocious puberty. Additionally, Proscar<sup>®</sup>, an enzyme inhibitor marketed by Merck, and Flomax<sup>®</sup>, an alpha blocker marketed by Boehringer Ingelheim Pharmaceuticals, are both used in the treatment of benign prostatic hyperplasia. These drugs may compete with any small molecule gonadotropin-releasing hormone antagonists we develop for these indications. If one or more of these products or programs are successful, it may reduce or eliminate the market for our products.

## **Table of Contents**

Compared to us, many of our competitors and potential competitors have substantially greater:

capital resources;

research and development resources, including personnel and technology;

regulatory experience;

preclinical study and clinical testing experience;

manufacturing and marketing experience; and

production facilities.

Any of these competitive factors could harm our business, prospects, financial condition and results of operations, which could negatively affect our stock price.

## **Employees**

As of December 31, 2006, we had 267 employees, consisting of 261 full-time and 6 part-time employees. Of the full-time employees, approximately 82 hold Ph.D., M.D. or equivalent degrees. None of our employees are represented by a collective bargaining arrangement, and we believe our relationship with our employees is good. Recruiting and retaining qualified scientific personnel to perform research and development work in the future will be critical to our success. We may not be able to attract and retain personnel on acceptable terms given the competition among biotechnology, pharmaceutical and health care companies, universities and non-profit research institutions for experienced scientists. In addition, we rely on a number of consultants to assist us in formulating our research and development strategies.

## **Insurance**

We maintain product liability insurance for our clinical trials. We intend to expand our insurance coverage to include the sale of commercial products if marketing approval is obtained for products in development. However, insurance coverage is becoming increasingly expensive, and we may not be able to maintain insurance coverage at a reasonable cost or in sufficient amounts to protect us against losses due to liability. In addition, we may not be able to obtain commercially reasonable product liability insurance for any products approved for marketing.

## **Available Information**

Our Annual Report on Form 10-K, Quarterly Reports on Form 10-Q, Current Reports on Form 8-K and amendments to reports filed pursuant to Sections 13(a) and 15(d) of the Securities Exchange Act of 1934, as amended, are available on our website at [www.neurocrine.com](http://www.neurocrine.com), when such reports are available on the Securities and Exchange Commission website.

Additionally, copies of our annual report will be made available, free of charge, upon written request.

## **ITEM 1A. RISK FACTORS**

### **Risks Related to Our Company**



***Our near-term success is dependent on the success of our lead product candidate, indiplon, and we may not receive regulatory approvals for it or our other product candidates or approvals may be delayed.***

Based on the results of preclinical studies and Phase I, Phase II and Phase III clinical trials on indiplon, as well as a non-clinical data package related to indiplon manufacturing, formulation and commercial product development, we assembled and filed with the FDA New Drug Applications (NDAs) for both indiplon capsules and indiplon tablets. On May 15, 2006, we received two complete responses from the FDA regarding our indiplon capsule and tablet NDAs. These responses indicated that indiplon 5 mg and 10 mg capsules were approvable (FDA Approvable Letter) and that the 15 mg tablets were not approvable (FDA Not Approvable Letter).

**Table of Contents**

The FDA Approvable Letter requested that we reanalyze data from certain preclinical and clinical studies to support approval of indiplon 5 mg and 10 mg capsules for sleep initiation and middle of the night dosing. The FDA Approvable Letter also requested reexamination of the safety analyses. We held an end-of-review meeting with the FDA related to the FDA Approvable Letter in August 2006. This meeting was specifically focused on determining the actions needed to bring indiplon capsules from Approvable to Approval in the resubmission of the NDA for indiplon capsules. At the meeting the FDA requested that the resubmission include further analyses and modifications of analyses previously submitted to address questions raised by the FDA in the initial review. This reanalysis has been substantially completed. The FDA also requested, and we have completed, a supplemental pharmacokinetic/food effect profile of indiplon capsules including several meal types. The NDA for indiplon capsules is currently being updated to include responses to the FDA requests and is targeted to be resubmitted to the FDA by the end of the second quarter of 2007.

The FDA Not Approvable Letter requested that we reanalyze certain safety and efficacy data and questioned the sufficiency of the objective sleep maintenance clinical data with the 15 mg tablet in view of the fact that the majority of our indiplon tablet studies were conducted with doses higher than 15 mg. We held an end-of-review meeting with the FDA related to the FDA Not Approvable Letter in October 2006. This meeting was specifically focused on determining the actions needed to bring indiplon tablets from Not Approvable to Approval in the resubmission of the NDA for indiplon tablets. The FDA has requested additional long-term safety and efficacy data with the 15 mg dose for the adult population and the development of a separate dose for the elderly population. In discussions, we and the FDA noted positive efficacy data for sleep maintenance with both indiplon capsules and tablets. On the basis of these discussions, we are formulating a strategy to pursue a sleep maintenance claim for indiplon. The evaluation of indiplon for sleep maintenance is ongoing and includes both indiplon capsules and tablets.

If we are unable to conduct the clinical trials or if these clinical trials do not demonstrate the safety and efficacy of indiplon tablets, we may not be able to resubmit the NDA for indiplon tablets. If we do obtain positive results from these clinical trials, we would then refile the NDA for indiplon tablets.

The process of preparing and resubmitting the NDAs will require significant resources and could be time consuming and subject to unanticipated delays and cost. Upon resubmission, the FDA could again refuse to approve one or both NDAs, or could still require additional data analysis or clinical trials, which would require substantial expenditures by us and could further delay the approval process. Even if our indiplon NDAs are approved, the FDA may determine that our data do not support elements of the labeling we have requested. In such a case, the labeling actually granted by the FDA could limit the commercial success of the product. The FDA could also require Phase IV, or post-marketing, trials to study the long-term effects of indiplon and could withdraw its approval based on the results of those trials. We face the risk that for any of the reasons described above, as well as other reasons set forth herein, indiplon may never be approved by the FDA or commercialized anywhere in the world.

If we are unable to refile one or both NDAs, or the FDA refuses to accept or approve the resubmitted NDAs for any reason or we experience a significant delay in approval and subsequent commercialization of indiplon, our business and reputation would be harmed and our stock price would decline.

***If we cannot raise additional funding, we may be unable to complete development of our product candidates.***

We may require additional funding to continue our research and product development programs, including preclinical testing and clinical trials of our product candidates, for operating expenses and to pursue regulatory approvals for product candidates, such as indiplon. We also may require additional funding to establish manufacturing and marketing capabilities in the future. We believe that our existing capital resources, together with interest income, and future payments due under our strategic alliances, will be sufficient to satisfy our current and projected funding

requirements for at least the next 12 months. However, these resources might be insufficient to conduct research and development programs as planned. If we cannot obtain adequate funds, we may be required to curtail significantly one or more of our research and development programs or obtain funds through additional arrangements with corporate collaborators or others that may require us to relinquish rights to some of our technologies or product candidates.

**Table of Contents**

Our future capital requirements will depend on many factors, including:

- continued scientific progress in our research and development programs;
- the magnitude of our research and development programs;
- progress with preclinical testing and clinical trials;
- the time and costs involved in obtaining regulatory approvals;
- the costs involved in filing and pursuing patent applications and enforcing patent claims;
- competing technological and market developments;
- the establishment of additional strategic alliances;
- the cost of commercialization activities and arrangements, including manufacturing of our product candidates; and
- the cost of product in-licensing and any possible acquisitions.

We intend to seek additional funding through strategic alliances, and may seek additional funding through public or private sales of our securities, including equity securities. In addition, we have financed capital purchases and may continue to pursue opportunities to obtain additional debt financing in the future. However, additional equity or debt financing might not be available on reasonable terms, if at all. Any additional equity financings will be dilutive to our stockholders and any additional debt financings may involve operating covenants that restrict our business.

***Because of the termination of our collaboration with Pfizer to develop and co-promote indiplon, we must identify a new partner and enter into a collaboration agreement with them or develop, commercialize, market and sell indiplon by ourselves.***

On June 22, 2006, we announced that the Company and Pfizer Inc. (Pfizer) had agreed to terminate our collaboration and license agreements to develop and co-promote indiplon. Under the collaboration, Pfizer had agreed to:

- fund substantially all third-party costs related to future indiplon development, manufacturing and commercialization activities;
- fund a 200-person Neurocrine sales force that would initially promote Zoloft® and, upon approval of the indiplon NDAs, co-promote indiplon in the United States;
- be responsible for obtaining all regulatory approvals outside of the United States and regulatory approvals in the United States after approval of the first indiplon NDA; and
- be responsible for sales and marketing of indiplon worldwide.

As a result of termination of this collaboration, we reacquired all worldwide rights for indiplon capsules and tablets. We received reimbursement of certain indiplon expenses incurred or committed prior to the June 22, 2006 notice date as well as certain ongoing expenses through December 19, 2006, the effective date of termination. We are responsible

for any costs associated with additional data or clinical trials that may be required for resubmission of the indiplon NDAs.

We will seek another partner or partners, at an appropriate time, to assist us in the worldwide development and commercialization of indiplon or develop, commercialize, market and sell indiplon by ourselves. We face competition in our search for partners with whom we may collaborate. As a result, we may not be successful in finding another collaboration partner on favorable terms, or at all, and any failure to obtain a new partner on favorable terms could adversely affect indiplon development, commercialization and future sales, which would harm our business. Identifying a new partner and entering into a collaboration agreement with them or developing the necessary infrastructure to commercialize, market and sell indiplon ourselves could cause delays in obtaining regulatory approvals and commercialization of indiplon, which would negatively impact our business. If we choose

**Table of Contents**

to commercialize, market and sell indiplon ourselves, we will be required to substantially increase our internal sales, distribution and marketing capabilities. The development of the infrastructure necessary to commercialize, market and sell indiplon will require substantial resources and may divert the attention of our management and key personnel and negatively impact our other product development efforts. Moreover, we may not be able to hire a sales force that is sufficient in size or has adequate expertise.

Pursuant to the collaboration agreement with Pfizer, our sales force ceased detailing Pfizer's antidepressant Zoloft® to psychiatrists as of June 30, 2006, the date of expiration of Zoloft® patent exclusivity. Pfizer notified us that as of July 1, 2006, Pfizer will no longer reimburse or support our sales force. Consequently, we terminated the entire sales force in July 2006 and incurred expenses of approximately \$5.9 million in the third quarter of 2006 related to salary continuation, outplacement services, and other costs related to eliminating the sales force. We cannot assure you that we will be able to successfully rebuild the sales force in a timely manner, or at all, should indiplon be approved by the FDA.

***We may become involved in securities class action litigation that could divert management's attention and harm our business.***

The market price of our common stock has declined significantly since our May 16, 2006 announcement of the FDA's action letters with respect to indiplon. In the past, following periods of volatility in the market price of a particular company's securities, securities class action litigation has often been brought against the company. We may become involved in this type of litigation in the future, which would be expensive and divert management's attention and resources from operating the business. Additionally, we may not be successful in having any such suit dismissed or settled within the limits of our insurance.

***Even if we ultimately receive an approval letter for indiplon or any other product, we may be unable to commercialize such products immediately upon receipt of such letter.***

Commercialization of a product for which we have received an approval letter from the FDA could be delayed for a number of reasons, some of which are outside of our control, including delays in the FDA's issuance of approvals for our trademarks or delays in the completion of required procedures by agencies other than the FDA, such as the Drug Enforcement Administration (DEA). For example, one of our competitors received an approval letter from the FDA for its proprietary product. In connection with the approval, the FDA recommended that the competitor's product be classified as a Schedule IV controlled substance by the DEA.

However, because the Federal government's administrative process for formally classifying the product as a Schedule IV controlled substance was not yet complete, the competitor's product launch was delayed several months. Indiplon, like the competitor's product, and like all non-benzodiazepine hypnotics, is expected to be a Schedule IV controlled substance requiring classification by the DEA. There can be no assurance that we will receive DEA scheduling promptly. If we receive an approval letter for indiplon and are unable to commercialize indiplon promptly thereafter, our business and financial position may be materially adversely affected due to reduced revenue from product sales during the period that commercialization is delayed. In addition, the exclusivity period, or the time during which the FDA will prevent generic pharmaceuticals from introducing a generic copy of the product, begins to run upon receipt of the approval letter from the FDA and, therefore, to the extent we are unable to commercialize a product upon receipt of an approval letter, our long-term product sales and revenues could be adversely affected.

***Our clinical trials may fail to demonstrate the safety and efficacy of our product candidates, which could prevent or significantly delay their regulatory approval.***

Any failure or substantial delay in completing clinical trials for our product candidates may severely harm our business. Before obtaining regulatory approval for the sale of any of our potential products, we must subject these product candidates to extensive preclinical and clinical testing to demonstrate their safety and efficacy for humans. Clinical trials are expensive, time-consuming and may take years to complete.

**Table of Contents**

In connection with the clinical trials of indiplon and our other product candidates, we face the risks that:

the product may not prove to be effective;

we may discover that a product candidate may cause harmful side effects;

the results may not replicate the results of earlier, smaller trials;

we or the FDA or similar foreign regulatory authorities may suspend the trials;

the results may not be statistically significant;

patient recruitment may be slower than expected; and

patients may drop out of the trials.

For example, we announced in 2006 that the results of our Phase II clinical trials using our altered peptide ligand (APL) technology did not meet their primary endpoints, although the products were safe and well tolerated. Based on these results, we discontinued the development of our APL programs.

Late stage clinical trials are often conducted with patients having the most advanced stages of disease. During the course of treatment, these patients can die or suffer other adverse medical effects for reasons that may not be related to the pharmaceutical agent being tested but which can nevertheless adversely affect clinical trial results.

***We have a history of losses and expect to incur losses and negative operating cash flows for the near future, and we may never achieve sustained profitability.***

Since our inception, we have incurred significant net losses, including net losses of \$107.2 million and \$22.2 million for the years ended December 31, 2006 and 2005, respectively. As a result of ongoing operating losses, we had an accumulated deficit of \$407.4 million and \$300.1 million as of December 31, 2006 and 2005, respectively. We do not expect to be profitable for the year ended December 31, 2007. Additionally, we will be responsible for any costs associated with additional data or clinical trials that may be required for resubmission of the indiplon NDAs.

We have not yet obtained regulatory approvals of any products and, consequently, have not generated revenues from the sale of products. Even if we succeed in developing and commercializing one or more of our drugs, we may not be profitable. We also expect to continue to incur significant operating and capital expenditures as we:

seek regulatory approvals for our product candidates;

develop, formulate, manufacture and commercialize our drugs;

in-license or acquire new product development opportunities;

implement additional internal systems and infrastructure; and

hire additional clinical, scientific and marketing personnel.



We also expect to experience negative cash flow for the near future as we fund our operating losses, in-licensing or acquisition opportunities, and capital expenditures. We will need to generate significant revenues to achieve and maintain profitability and positive cash flow. We may not be able to generate these revenues, and we may never achieve profitability in the future. Our failure to achieve or maintain profitability could negatively impact the market price of our common stock. Even if we become profitable, we cannot assure you that we would be able to sustain or increase profitability on a quarterly or annual basis.

***Because our operating results may vary significantly in future periods, our stock price may decline.***

Our quarterly revenues, expenses and operating results have fluctuated in the past and are likely to fluctuate significantly in the future. Our revenues are unpredictable and may fluctuate, among other reasons, due to our achievement of product development objectives and milestones, clinical trial enrollment and expenses, research and development expenses and the timing and nature of contract manufacturing and contract research payments. A high portion of our costs are predetermined on an annual basis, due in part to our significant research and development

**Table of Contents**

costs. Thus, small declines in revenue could disproportionately affect operating results in a quarter. Because of these factors, our operating results in one or more future quarters may fail to meet the expectations of securities analysts or investors, which could cause our stock price to decline.

***We depend on continuing our current collaboration and developing additional collaborations to develop and commercialize our product candidates.***

Our strategy for developing and commercializing our products is dependent upon maintaining our current arrangements and establishing new arrangements with research collaborators, corporate collaborators and others. We have an active collaboration agreement with GlaxoSmithKline and previously have had collaborations with Pfizer, Wyeth, Johnson & Johnson, and Eli Lilly and Company. We historically have been dependent upon these corporate collaborators to provide adequate funding for a number of our programs. Under these arrangements, our corporate collaborators are typically responsible for:

selecting compounds for subsequent development as drug candidates;

conducting preclinical studies and clinical trials and obtaining required regulatory approvals for these drug candidates; and

manufacturing and commercializing any resulting drugs.

Because we expect to continue to rely heavily on corporate collaborators including for the future worldwide development and commercialization of indiplon, the development of our projects would be substantially delayed if one or more of our current or future collaborators:

failed to select a compound that we have discovered for subsequent development into marketable products;

failed to gain the requisite regulatory approvals of these products;

did not successfully commercialize products that we originate;

did not conduct its collaborative activities in a timely manner;

did not devote sufficient time and resources to our partnered programs or potential products;

terminated its alliance with us;

developed, either alone or with others, products that may compete with our products;

disputed our respective allocations of rights to any products or technology developed during our collaborations;  
or

merged with a third party that wants to terminate the collaboration.

These issues and possible disagreements with current or future corporate collaborators could lead to delays in the collaborative research, development or commercialization of many of our product candidates. Furthermore, disagreements with these parties could require or result in litigation or arbitration, which would be time-consuming and expensive. If any of these issues arise, it may delay the development and commercialization of drug candidates and, ultimately, our generation of product revenues.

***We license some of our core technologies and drug candidates from third parties. If we default on any of our obligations under those licenses, we could lose our rights to those technologies and drug candidates.***

We are dependent on licenses from third parties for some of our key technologies. These licenses typically subject us to various commercialization, reporting and other obligations. If we fail to comply with these obligations, we could lose important rights. For example, we have licensed indiplon from DOV. In addition, we license some of the core technologies used in our collaborations from third parties, including the CRF receptor we license from The Salk Institute and use in our CRF program, Urocortin 2 which we license from Research Development Foundation, and the Adenosine<sub>2A</sub> receptor antagonist we license from Almirall. Other in-licensed technologies, such as the GnRH receptor we license from Mount Sinai School of Medicine, will be important for future collaborations for our GnRH program. If we were to default on our obligations under any of our licenses, we could lose some or all of our

## **Table of Contents**

rights to develop, market and sell products covered by these licenses. Likewise, if we were to lose our rights under a license to use proprietary research tools, it could adversely affect our existing collaborations or adversely affect our ability to form new collaborations. We also face the risk that our licensors could, for a number of reasons, lose patent protection or lose their rights to the technologies we have licensed, thereby impairing or extinguishing our rights under our licenses with them.

***Because the development of our product candidates is subject to a substantial degree of technological uncertainty, we may not succeed in developing any of our product candidates.***

All of our product candidates are in research, clinical development or in registration with the FDA. Only a small number of research and development programs ultimately result in commercially successful drugs. Potential products that appear to be promising at early stages of development may not reach the market for a number of reasons. These reasons include the possibilities that the potential products may:

be found ineffective or cause harmful side effects during preclinical studies or clinical trials;

fail to receive necessary regulatory approvals on a timely basis or at all;

be precluded from commercialization by proprietary rights of third parties;

be difficult to manufacture on a large scale; or

be uneconomical to commercialize or fail to achieve market acceptance.

If any of our products encounters any of these potential problems, we may never successfully market that product.

Since indiplon is our most advanced product program, our business and reputation would be particularly harmed, and our stock price likely would be harmed, if we fail to receive necessary regulatory approvals on a timely basis or achieve market acceptance.

***We have limited marketing experience, sales force or distribution capabilities, and if our products are approved, we may not be able to commercialize them successfully.***

Although we do not currently have any marketable products, our ability to produce revenues ultimately depends on our ability to sell our products if and when they are approved by the FDA. We currently have limited experience in marketing and selling pharmaceutical products. If we fail to establish successful marketing and sales capabilities or fail to enter into successful marketing arrangements with third parties, our product revenues will suffer.

***The independent clinical investigators and contract research organizations that we rely upon to conduct our clinical trials may not be diligent, careful or timely, and may make mistakes, in the conduct of our trials.***

We depend on independent clinical investigators and contract research organizations, or CROs, to conduct our clinical trials under their agreements with us. The investigators are not our employees, and we cannot control the amount or timing of resources that they devote to our programs. If independent investigators fail to devote sufficient time and resources to our drug development programs, or if their performance is substandard, it may delay or prevent the approval of our FDA applications and our introduction of new drugs. The CROs we contract with for execution of our clinical trials play a significant role in the conduct of the trials and the subsequent collection and analysis of data. Failure of the CROs to meet their obligations could adversely affect clinical development of our products. Moreover, these independent investigators and CROs may also have relationships with other commercial entities, some of which

may compete with us. If independent investigators and CROs assist our competitors at our expense, it could harm our competitive position.

**Table of Contents**

***We have no manufacturing capabilities. If third-party manufacturers of our product candidates fail to devote sufficient time and resources to our concerns, or if their performance is substandard, our clinical trials and product introductions may be delayed and our costs may rise.***

We have in the past utilized, and intend to continue to utilize, third-party manufacturers to produce the drug compounds we use in our clinical trials and for the potential commercialization of our future products. We have no experience in manufacturing products for commercial purposes and do not currently have any manufacturing facilities. Consequently, we depend on, and will continue to depend on, several contract manufacturers for all production of products for development and commercial purposes. If we are unable to obtain or retain third-party manufacturers, we will not be able to develop or commercialize our products. The manufacture of our products for clinical trials and commercial purposes is subject to specific FDA regulations. Our third-party manufacturers might not comply with FDA regulations relating to manufacturing our products for clinical trials and commercial purposes or other regulatory requirements now or in the future. Our reliance on contract manufacturers also exposes us to the following risks:

contract manufacturers may encounter difficulties in achieving volume production, quality control and quality assurance, and also may experience shortages in qualified personnel. As a result, our contract manufacturers might not be able to meet our clinical schedules or adequately manufacture our products in commercial quantities when required;

switching manufacturers may be difficult because the number of potential manufacturers is limited. It may be difficult or impossible for us to find a replacement manufacturer quickly on acceptable terms, or at all;

our contract manufacturers may not perform as agreed or may not remain in the contract manufacturing business for the time required to successfully produce, store or distribute our products; and

drug manufacturers are subject to ongoing periodic unannounced inspection by the FDA, the DEA, and corresponding state agencies to ensure strict compliance with good manufacturing practices and other government regulations and corresponding foreign standards. We do not have control over third-party manufacturers' compliance with these regulations and standards.

Our current dependence upon third parties for the manufacture of our products may harm our profit margin, if any, on the sale of our future products and our ability to develop and deliver products on a timely and competitive basis.

***Potential future impairments under SFAS 144 could adversely affect our future results of operations and financial position.***

In accordance with Statement of Financial Accounting Standards No. 144, Accounting for the Impairment or Disposal of Long-Lived Assets, we assess our long-lived assets for impairment quarterly or whenever events or changes in circumstances indicate that the carrying amount of an asset may not be recoverable. If indicators of impairment exist, we assess the recoverability of the affected long-lived assets by determining whether the carrying value of such assets can be recovered through undiscounted future operating cash flows. If the carrying amount is not recoverable, we measure the amount of any impairment by comparing the carrying value of the asset to the present value of the expected future cash flows (fair value) associated with the use of the asset. If the carrying amount of the asset were determined to be impaired, an impairment loss to write-down the carrying value of the asset to fair value would be required.

For example, our December 31, 2006 balance sheet reflects \$94.0 million of prepaid royalties related to our acquisition in February 2004 of Wyeth's financial interest in indiplon for approximately \$95.0 million, consisting of

\$50.0 million in cash and \$45.0 million in our common stock. This transaction decreased our overall royalty obligation on sales of indiplon from six percent to three and one-half percent.

This transaction has been recorded as a long-term asset and will be amortized over the commercialization period of indiplon, based primarily upon indiplon sales. Given the FDA letters we received on our NDA submissions for indiplon and the subsequent cancellation of the collaboration agreement with Pfizer, we determined that indicators of potential impairment existed. We performed the undiscounted cash flow analysis and determined that

**Table of Contents**

the carrying value of the prepaid royalty was recoverable as of December 31, 2006. However, events both within and outside of our control, such as competition from other insomnia therapeutic agents, disease prevalence, further FDA actions related to indiplon, our ability to partner indiplon, insomnia market dynamics and general market conditions may have an impact on our ability to recover the carrying value of this asset in the future.

If we determine that the sum of the expected future undiscounted cash flows relating to this prepaid royalty is less than the carrying amount of the asset, the asset would be impaired, and we would be required to record a non-cash impairment loss to write-down the carrying value of the asset to fair value. A material reduction in earnings resulting from such a charge could cause us to fail to be profitable in the period in which the charge is taken or otherwise to fail to meet the expectations of investors and securities analysts, which could cause the price of our stock to decline.

***If we are unable to retain and recruit qualified scientists or if any of our key senior executives discontinues his or her employment with us, it may delay our development efforts.***

We are highly dependent on the principal members of our management and scientific staff. The loss of any of these people could impede the achievement of our development objectives. Furthermore, recruiting and retaining qualified scientific personnel to perform research and development work in the future is critical to our success. We may be unable to attract and retain personnel on acceptable terms given the competition among biotechnology, pharmaceutical and health care companies, universities and non-profit research institutions for experienced scientists. In addition, we rely on a significant number of consultants to assist us in formulating our research and development strategy. All of our consultants are employed by employers other than us. They may have commitments to, or advisory or consulting agreements with, other entities that may limit their availability to us.

***We may be subject to claims that we or our employees have wrongfully used or disclosed alleged trade secrets of their former employers.***

As is commonplace in the biotechnology industry, we employ individuals who were previously employed at other biotechnology or pharmaceutical companies, including our competitors or potential competitors. Although no claims against us are currently pending, we may be subject to claims that these employees or we have inadvertently or otherwise used or disclosed trade secrets or other proprietary information of their former employers. Litigation may be necessary to defend against these claims. Even if we are successful in defending against these claims, litigation could result in substantial costs and be a distraction to management.

***Governmental and third-party payors may impose sales and pharmaceutical pricing controls on our products that could limit our product revenues and delay profitability.***

The continuing efforts of government and third-party payors to contain or reduce the costs of health care through various means may reduce our potential revenues. These payors' efforts could decrease the price that we receive for any products we may develop and sell in the future. In addition, third-party insurance coverage may not be available to patients for any products we develop. If government and third-party payors do not provide adequate coverage and reimbursement levels for our products, or if price controls are enacted, our product revenues will suffer.

***If physicians and patients do not accept our products, we may not recover our investment.***

The commercial success of our products, if they are approved for marketing, will depend upon the acceptance of our products as safe and effective by the medical community and patients.

The market acceptance of our products could be affected by a number of factors, including:



the timing of receipt of marketing approvals;

the safety and efficacy of the products;

**Table of Contents**

the success of existing products addressing our target markets or the emergence of equivalent or superior products; and

the cost-effectiveness of the products.

In addition, market acceptance depends on the effectiveness of our marketing strategy, and, to date, we have very limited sales and marketing experience or capabilities. If the medical community and patients do not ultimately accept our products as being safe, effective, superior and/or cost-effective, we may not recover our investment.

***Compliance with changing regulation of corporate governance and public disclosure may result in additional expenses.***

Changing laws, regulations and standards relating to corporate governance and public disclosure, including the Sarbanes-Oxley Act of 2002, new SEC regulations and Nasdaq rules, are creating uncertainty for companies such as ours. These new or changed laws, regulations and standards are subject to varying interpretations in many cases due to their lack of specificity, and as a result, their application in practice may evolve over time as new guidance is provided by regulatory and governing bodies, which could result in continuing uncertainty regarding compliance matters and higher costs necessitated by ongoing revisions to disclosure and governance practices. We are committed to maintaining high standards of corporate governance and public disclosure. As a result, our efforts to comply with evolving laws, regulations and standards have resulted in, and are likely to continue to result in, increased general and administrative expenses and management time related to compliance activities. In particular, our efforts to comply with Section 404 of the Sarbanes-Oxley Act of 2002 and the related regulations regarding our required assessment of our internal controls over financial reporting and our independent registered public accounting firm's audit of that assessment requires the commitment of significant financial and managerial resources. We expect these efforts to require the continued commitment of significant resources. If we fail to comply with new or changed laws, regulations and standards, our reputation may be harmed and we might be subject to sanctions or investigation by regulatory authorities, such as the Securities and Exchange Commission. Any such action could adversely affect our financial results and the market price of our common stock.

***The price of our common stock is volatile.***

The market prices for securities of biotechnology and pharmaceutical companies historically have been highly volatile, and the market has from time to time experienced significant price and volume fluctuations that are unrelated to the operating performance of particular companies. Over the course of the last 12 months, the price of our common stock has ranged from approximately \$8 per share to approximately \$73 per share. The market price of our common stock may fluctuate in response to many factors, including:

developments related to the FDA approval process for indiplon;

the results of our clinical trials;

developments concerning our strategic alliance agreements;

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

developments in patent or other proprietary rights;

future sales of our common stock by existing stockholders;

comments by securities analysts;

general market conditions;

fluctuations in our operating results;

government regulation;

health care reimbursement;

**Table of Contents**

failure of any of our product candidates, if approved, to achieve commercial success; and

public concern as to the safety of our drugs.

**Risks Related to Our Industry**

*We may not receive regulatory approvals for our product candidates or approvals may be delayed.*

Regulation by government authorities in the United States and foreign countries is a significant factor in the development, manufacture and marketing of our proposed products and in our ongoing research and product development activities. Any failure to receive the regulatory approvals necessary to commercialize our product candidates would harm our business. The process of obtaining these approvals and the subsequent compliance with federal and state statutes and regulations require spending substantial time and financial resources. If we fail or our collaborators or licensees fail to obtain or maintain, or encounter delays in obtaining or maintaining, regulatory approvals, it could adversely affect the marketing of any products we develop, our ability to receive product or royalty revenues, our recovery of prepaid royalties, and our liquidity and capital resources. All of our products are in research and development, and we have not yet received regulatory approval to commercialize any product from the FDA or any other regulatory body. In addition, we have limited experience in filing and pursuing applications necessary to gain regulatory approvals, which may impede our ability to obtain such approvals.

In particular, human therapeutic products are subject to rigorous preclinical testing and clinical trials and other approval procedures of the FDA and similar regulatory authorities in foreign countries. The FDA regulates, among other things, the development, testing, manufacture, safety, efficacy, record keeping, labeling, storage, approval, advertising, promotion, sale and distribution of biopharmaceutical products. Securing FDA approval requires the submission of extensive preclinical and clinical data and supporting information to the FDA for each indication to establish the product candidate's safety and efficacy. The approval process may take many years to complete and may involve ongoing requirements for post-marketing studies. Any FDA or other regulatory approval of our product candidates, once obtained, may be withdrawn. If our potential products are marketed abroad, they will also be subject to extensive regulation by foreign governments.

*We face intense competition, and if we are unable to compete effectively, the demand for our products, if any, may be reduced.*

The biotechnology and pharmaceutical industries are subject to rapid and intense technological change. We face, and will continue to face, competition in the development and marketing of our product candidates from academic institutions, government agencies, research institutions and biotechnology and pharmaceutical companies.

Competition may also arise from, among other things:

other drug development technologies;

methods of preventing or reducing the incidence of disease, including vaccines; and

new small molecule or other classes of therapeutic agents.

Developments by others may render our product candidates or technologies obsolete or noncompetitive.

We are performing research on or developing products for the treatment of several disorders including insomnia, anxiety, depression, endometriosis, irritable bowel syndrome, pain, Parkinson's Disease, and other neuro-endocrine related diseases and disorders, and there are a number of competitors to products in our research pipeline. If one or more of our competitors' products or programs are successful, the market for our products may be reduced or eliminated.

Compared to us, many of our competitors and potential competitors have substantially greater:

capital resources;

research and development resources, including personnel and technology;

**Table of Contents**

regulatory experience;

preclinical study and clinical testing experience;

manufacturing and marketing experience; and

production facilities.

***If we are unable to protect our intellectual property, our competitors could develop and market products based on our discoveries, which may reduce demand for our products.***

Our success will depend on our ability to, among other things:

obtain patent protection for our products;

preserve our trade secrets;

prevent third parties from infringing upon our proprietary rights; and

operate without infringing upon the proprietary rights of others, both in the United States and internationally.

Because of the substantial length of time and expense associated with bringing new products through the development and regulatory approval processes in order to reach the marketplace, the pharmaceutical industry places considerable importance on obtaining patent and trade secret protection for new technologies, products and processes. Accordingly, we intend to seek patent protection for our proprietary technology and compounds. However, we face the risk that we may not obtain any of these patents and that the breadth of claims we obtain, if any, may not provide adequate protection of our proprietary technology or compounds.

We also rely upon unpatented trade secrets and improvements, unpatented know-how and continuing technological innovation to develop and maintain our competitive position, which we seek to protect, in part, through confidentiality agreements with our commercial collaborators, employees and consultants. We also have invention or patent assignment agreements with our employees and some, but not all, of our commercial collaborators and consultants. However, if our employees, commercial collaborators or consultants breach these agreements, we may not have adequate remedies for any such breach, and our trade secrets may otherwise become known or independently discovered by our competitors.

In addition, although we own a number of patents, the issuance of a patent is not conclusive as to its validity or enforceability, and third parties may challenge the validity or enforceability of our patents. We cannot assure you how much protection, if any, will be given to our patents if we attempt to enforce them and they are challenged in court or in other proceedings. It is possible that a competitor may successfully challenge our patents or that challenges will result in limitations of their coverage. Moreover, competitors may infringe our patents or successfully avoid them through design innovation. To prevent infringement or unauthorized use, we may need to file infringement claims, which are expensive and time-consuming. In addition, in an infringement proceeding a court may decide that a patent of ours is not valid or is unenforceable, or may refuse to stop the other party from using the technology at issue on the grounds that our patents do not cover its technology. Interference proceedings declared by the United States Patent and Trademark Office (USPTO) may be necessary to determine the priority of inventions with respect to our patent applications or those of our licensors. Litigation or interference proceedings may fail and, even if successful, may result in substantial costs and be a distraction to management. We cannot assure you that we will be able to prevent

misappropriation of our proprietary rights, particularly in countries where the laws may not protect such rights as fully as in the United States.

*The technologies we use in our research as well as the drug targets we select may infringe the patents or violate the proprietary rights of third parties.*

We cannot assure you that third parties will not assert patent or other intellectual property infringement claims against us or our collaborators with respect to technologies used in potential products. We are aware of a patent application controlled by another company, which if granted in its broadest scope and held to be valid, could impact the commercialization of our indiplon tablets in the United States unless we obtain a license, which may not be available to us. Based on information available from the USPTO, we have learned that the USPTO has examined the

## **Table of Contents**

pending claims of this application two times and that both times it has rejected all the pending claims. We are also aware that the corresponding patent application in Europe has issued as a patent, and we have filed an opposition against the issued European patent. Even if we were to prevail, any litigation could be costly and time-consuming and could divert the attention of our management and key personnel from our business operations. If a patent infringement suit were brought against us or our collaborators, we or our collaborators could be forced to stop or delay developing, manufacturing or selling potential products that are claimed to infringe a third party's intellectual property unless that party grants us or our collaborators rights to use its intellectual property. In such cases, we could be required to obtain licenses to patents or proprietary rights of others in order to continue to commercialize our products. However, we may not be able to obtain any licenses required under any patents or proprietary rights of third parties on acceptable terms, or at all. Even if our collaborators or we were able to obtain rights to the third party's intellectual property, these rights may be non-exclusive, thereby giving our competitors access to the same intellectual property. Ultimately, we may be unable to commercialize some of our potential products or may have to cease some of our business operations as a result of patent infringement claims, which could severely harm our business.

### ***We face potential product liability exposure far in excess of our limited insurance coverage.***

The use of any of our potential products in clinical trials, and the sale of any approved products, may expose us to liability claims. These claims might be made directly by consumers, health care providers, pharmaceutical companies or others selling our products. We have obtained limited product liability insurance coverage for our clinical trials in the amount of \$10 million per occurrence and \$10 million in the aggregate. However, our insurance may not reimburse us or may not be sufficient to reimburse us for any expenses or losses we may suffer. Moreover, insurance coverage is becoming increasingly expensive, and we may not be able to maintain insurance coverage at a reasonable cost or in sufficient amounts to protect us against losses due to liability. We intend to expand our insurance coverage to include the sale of commercial products if we obtain marketing approval for product candidates in development, but we may be unable to obtain commercially reasonable product liability insurance for any products approved for marketing. On occasion, juries have awarded large judgments in class action lawsuits based on drugs that had unanticipated side effects. A successful product liability claim or series of claims brought against us would decrease our cash reserves and could cause our stock price to fall.

### ***Our activities involve hazardous materials, and we may be liable for any resulting contamination or injuries.***

Our research activities involve the controlled use of hazardous materials. We cannot eliminate the risk of accidental contamination or injury from these materials. If an accident occurs, a court may hold us liable for any resulting damages, which may harm our results of operations and cause us to use a substantial portion of our cash reserves, which would force us to seek additional financing.

## **ITEM 1B. UNRESOLVED STAFF COMMENTS**

None.

## **ITEM 2. PROPERTIES**

We own our facility which has approximately 200,000 square feet of laboratory and office space in San Diego, California, of which approximately 85% is allocated to research and development activities. There is currently a mortgage loan outstanding on the facility of approximately \$48.3 million. We believe that our property and equipment are generally well maintained and in good operating condition.

## **ITEM 3. LEGAL PROCEEDINGS**



We are not currently a party to any material legal proceedings.

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

Not applicable.

**Table of Contents****PART II****ITEM 5. MARKET FOR REGISTRANT'S COMMON EQUITY, RELATED STOCKHOLDER MATTERS AND ISSUER PURCHASES OF EQUITY SECURITIES**

Our common stock is traded on the Nasdaq Global Select Market under the symbol NBIX. The following table sets forth for the periods indicated the high and low sale price for our common stock. These prices do not include retail markups, markdowns or commissions.

	<b>High</b>	<b>Low</b>
<b>Year Ended December 31, 2005</b>		
1st Quarter	\$ 50.10	\$ 36.58
2nd Quarter	44.09	33.86
3rd Quarter	52.90	41.20
4th Quarter	65.70	43.31
<b>Year Ended December 31, 2006</b>		
1st Quarter	\$ 73.13	\$ 57.45
2nd Quarter	65.13	8.61
3rd Quarter	11.75	8.57
4th Quarter	13.05	7.51

As of January 31, 2007, there were approximately 72 stockholders of record of our common stock. We have not paid any cash dividends on our common stock since inception and do not anticipate paying cash dividends in the foreseeable future.

Information about our equity compensation plans is incorporated by reference in Item 12 of Part III of this Annual Report on Form 10-K.

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

The following selected financial data have been derived from our audited financial statements. The information set forth below is not necessarily indicative of the results of future operations and should be read in conjunction with Management's Discussion and Analysis of Financial Condition and Results of Operations and the financial statements and notes thereto appearing elsewhere in this Annual Report on Form 10-K.

	<b>2006</b>	<b>2005</b>	<b>2004</b>	<b>2003</b>	<b>2002</b>
	<b>(In thousands, except for loss per share data)</b>				
<b>STATEMENT OF OPERATIONS DATA</b>					
Revenues:					
Sponsored research and development	\$ 6,716	\$ 9,187	\$ 27,156	\$ 96,699	\$ 12,364
Milestones and license fees	16,038	92,702	57,612	41,126	3,516
Sales force allowance	16,480	22,000			
Grant income and other revenues			408	1,253	2,165
Total revenues	39,234	123,889	85,176	139,078	18,045
Operating expenses:					
Research and development	97,678	106,628	115,066	177,271	108,939
Sales, general and administrative	54,873	42,333	22,444	20,594	12,721
Total operating expenses	152,551	148,961	137,510	197,865	121,660
Loss from operations	(113,317)	(25,072)	(52,334)	(58,787)	(103,615)
Other income:					
Gain on sale of property				17,946	
Interest income, net	6,112	2,881	6,640	10,743	9,079
Total other income	6,112	2,881	6,640	28,689	9,079
Loss before income taxes	(107,205)	(22,191)	(45,694)	(30,098)	(94,536)
Income taxes			79	158	
Net loss	\$ (107,205)	\$ (22,191)	\$ (45,773)	\$ (30,256)	\$ (94,536)
Net loss per common share:					
Basic and diluted	\$ (2.84)	\$ (0.60)	\$ (1.26)	\$ (0.93)	\$ (3.10)
Shares used in calculation of net loss per common share:					
Basic and diluted	37,722	36,763	36,201	32,374	30,488
<b>BALANCE SHEET DATA</b>					
Cash, cash equivalents and short-term investments	\$ 182,604	\$ 273,068	\$ 301,129	\$ 453,168	\$ 244,710

Edgar Filing: NEUROCRINE BIOSCIENCES INC - Form 10-K

Working capital	173,542	245,617	254,230	361,797	215,615
Total assets	389,677	483,123	519,217	554,955	266,539
Long-term debt	49,152	53,590	59,452	32,473	5,277
Accumulated deficit	(407,351)	(300,146)	(277,955)	(232,182)	(201,926)
Total stockholders equity	314,716	390,104	393,827	391,120	224,254

**Table of Contents**

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

*The following Management's Discussion and Analysis of Financial Condition and Results of Operations section contains forward-looking statements pertaining to, among other things, the expected continuation of our collaborative agreements, the receipt of research and development payments thereunder, the future achievement of various milestones in product development and the receipt of payments related thereto, the potential receipt of royalty payments, pre-clinical testing and clinical trials of potential products, the period of time that our existing capital resources will meet our funding requirements, and our financial results of operations. Our actual results could differ materially from those anticipated in these forward-looking statements as a result of various risks and uncertainties, including those set forth in this Annual Report on Form 10-K under the heading Item 1A. Risk Factors. See Forward-Looking Statements in Part I of this Annual Report on Form 10-K.*

**Overview**

We discover, develop and intend to commercialize drugs for the treatment of neurological and endocrine-related diseases and disorders. Our product candidates address some of the largest pharmaceutical markets in the world, including insomnia, anxiety, depression, endometriosis, irritable bowel syndrome, pain, diabetes and other neurological and endocrine related diseases and disorders. To date, we have not generated any revenues from the sale of products, and we do not expect to generate any revenues from product sales until indiplon receives regulatory approval and is commercialized. We have funded our operations primarily through private and public offerings of our common stock and payments received under research and development agreements. We are developing certain products with corporate collaborators and will rely on existing and future collaborators to meet funding requirements. We expect to generate future net losses due to increases in operating expenses as product candidates are advanced through the various stages of clinical development. As of December 31, 2006, we had incurred a cumulative deficit of \$407.4 million and expect to incur operating losses in the near future, which may be greater than losses in prior years. We currently have nine programs in various stages of research and development, including six programs in clinical development. While we independently develop many of our product candidates, we are in a collaboration for one of our programs. Our lead clinical development program, indiplon, is a drug candidate for the treatment of insomnia.

On May 15, 2006, we received two complete responses from the FDA regarding our indiplon capsule and tablet NDAs. These responses indicated that indiplon 5 mg and 10 mg capsules were approvable (FDA Approvable Letter) and that the 15 mg tablets were not approvable (FDA Not Approvable Letter).

The FDA Approvable Letter requested that we reanalyze data from certain preclinical and clinical studies to support approval of indiplon 5 mg and 10 mg capsules for sleep initiation and middle of the night dosing. The FDA Approvable Letter also requested reexamination of the safety analyses. We held an end-of-review meeting with the FDA related to the FDA Approvable Letter in August 2006. This meeting was specifically focused on determining the actions needed to bring indiplon capsules from Approvable to Approval in the resubmission of the NDA for indiplon capsules. At the meeting the FDA requested that the resubmission include further analyses and modifications of analyses previously submitted to address questions raised by the FDA in the initial review. This reanalysis has been substantially completed. The FDA also requested, and we have completed, a supplemental pharmacokinetic/food effect profile of indiplon capsules including several meal types. The NDA for indiplon capsules is targeted to be resubmitted to the FDA by the end of the second quarter of 2007.

The FDA Not Approvable Letter requested that we reanalyze certain safety and efficacy data and questioned the sufficiency of the objective sleep maintenance clinical data with the 15 mg tablet in view of the fact that the majority

of our indiplon tablet studies were conducted with doses higher than 15 mg. We held an end-of-review meeting with the FDA related to the FDA Not Approvable Letter in October 2006. This meeting was specifically focused on determining the actions needed to bring indiplon tablets from Not Approvable to Approval in the resubmission of the NDA for indiplon tablets. The FDA has requested additional long-term safety and efficacy data with the 15 mg dose for the adult population and the development of a separate dose for the elderly population. In discussions, we and the FDA noted positive efficacy data for sleep maintenance with both indiplon capsules and tablets. On the basis of these discussions, we are formulating a strategy to pursue a sleep maintenance claim for

## **Table of Contents**

indiplon. The evaluation of indiplon for sleep maintenance is ongoing and includes both indiplon capsules and tablets.

On June 22, 2006, we and Pfizer agreed to terminate our collaboration and license agreements to develop and co-promote indiplon effective December 19, 2006. As a result, we reacquired all worldwide rights for indiplon capsules and tablets and are responsible for any costs associated with development, registration, marketing and commercialization of indiplon.

In July 2006 and August 2006, we announced a restructuring program to prioritize research and development efforts and implement cost containment measures. As a result, we terminated our entire sales force in July 2006 and reduced our research and development and general and administrative staff in San Diego by approximately 100 employees in August 2006. In connection with this restructuring, we recorded a one-time charge of approximately \$9.5 million in the third quarter of 2006, of which \$2.8 million is included in research and development expense and \$6.7 million is included in sales, general and administrative expense. Restructuring charges are comprised of salary continuation, outplacement services, and other miscellaneous costs related to these reductions in force. Substantially all of these expenses were paid in cash during the third quarter of 2006. We expect these reductions to reduce expenses by approximately \$50.0 million in 2007.

On September 26, 2006, we completed a Tender Offer (Offer) to holders of outstanding options to purchase our common stock under our 2003 Incentive Stock Plan (2003 Plan), 1992 Incentive Stock Plan (the 1992 Plan) and 2001 Stock Option Plan, as amended (the 2001 Plan). The Offer was for holders of options under the 2003 Plan to cancel their options in exchange for a lesser number of new options (a two-for-one exchange ratio) to purchase shares of our common stock issued under the 2003 Plan and for holders of options under the 1992 Plan and 2001 Plan to cancel one-half of their options and amend their remaining options to purchase shares of our common stock. The Offer was open to eligible employees and active consultants who held options with an exercise price of \$20.00 or higher per share as of September 25, 2006. Certain executives and members of the Board of Directors were not eligible to participate in the Offer. Approximately 2.0 million options were exchanged or amended resulting in approximately 1.0 million new or amended option grants and approximately 1.0 million cancelled option grants at completion of the Offer. New or amended options under the Offer vest annually over a period of three years and have a weighted average exercise price of \$10.90. Unamortized share based compensation expense, net of forfeiture rate, related to the Offer totaled approximately \$8.7 million and will be amortized over 3 years.

## **Critical Accounting Policies**

Our discussion and analysis of our financial condition and results of operations is based upon financial statements that we have prepared in accordance with accounting principles generally accepted in the United States. The preparation of these financial statements requires management to make estimates and judgments that affect the reported amounts of assets, liabilities and expenses, and related disclosures. On an on-going basis, we evaluate these estimates, including those related to revenues under collaborative research agreements and grants, clinical trial accruals (research and development expense), debt, share-based compensation, investments, and fixed assets. Estimates are based on historical experience, information received from third parties and on various other assumptions that are believed to be reasonable under the circumstances, the results of which form the basis for making judgments about the carrying values of assets and liabilities that are not readily apparent from other sources. Actual results may differ from these estimates under different assumptions or conditions. The items in our financial statements requiring significant estimates and judgments are as follows:

### ***Revenue Recognition***

Revenues under collaborative research and development agreements are recognized as costs are incurred over the period specified in the related agreement or as the services are performed. These agreements are on a best-efforts

basis, and do not require scientific achievement as a performance obligation, and provide for payment to be made when costs are incurred or the services are performed. All fees are nonrefundable to the collaborators. Upfront, nonrefundable payments for license fees and advance payments for sponsored research revenues received in excess of amounts earned are classified as deferred revenue and recognized as income over the contract or development period. Estimating the duration of the development period includes continual assessment of development stages and



## **Table of Contents**

regulatory requirements. Milestone payments are recognized as revenue upon achievement of pre-defined scientific events, which requires substantive effort, and for which achievement of the milestone was not readily assured at the inception of the agreement. Revenues from grants are recognized based on a percentage-of-completion basis as the related costs are incurred.

### ***Clinical Trial Costs***

Research and development (R&D) expenses include related salaries, contractor fees, facilities costs, administrative expenses and allocations of corporate costs. All such costs are charged to R&D expense as incurred. These expenses result from our independent R&D efforts as well as efforts associated with collaborations, grants and in-licensing arrangements. In addition, we fund R&D and clinical trials at other companies and research institutions under agreements, which are generally cancelable. We review and accrue clinical trials expense based on work performed, which relies on estimates of total costs incurred based on patient enrollment, completion of studies and other events. We follow this method since reasonably dependable estimates of the costs applicable to various stages of a research agreement or clinical trial can be made. Accrued clinical costs are subject to revisions as trials progress to completion. Revisions are charged to expense in the period in which the facts that give rise to the revision become known. Historically, revisions have not resulted in material changes to R&D costs, however a modification in the protocol of a clinical trial or cancellation of a trial could result in a charge to our results of operations.

### ***Asset Impairment***

In accordance with Statement of Financial Accounting Standards No. 144 (SFAS 144), Accounting for the Impairment or Disposal of Long-Lived Assets, if indicators of impairment exist, we assess the recoverability of the affected long-lived assets by determining whether the carrying value of such assets can be recovered through undiscounted future operating cash flows. If impairment is indicated, we measure the amount of such impairment by comparing the carrying value of the asset to the estimated fair value of the related asset, which is generally determined based on the present value of the expected future cash flows.

During the second quarter of 2006, we received two letters from the FDA related to our NDA submissions for indiplon. These letters indicated that indiplon capsules were approvable and that indiplon tablets were not approvable. Additionally on June 22, 2006, we announced that we and Pfizer had agreed to terminate our collaboration and license agreements to develop and co-promote indiplon. These two events are indicators of potential impairment for our prepaid royalty, which is carried as a long-lived asset on our balance sheet. This prepaid royalty arose out of our acquisition, in February 2004, of Wyeth's financial interest in indiplon for approximately \$95.0 million, consisting of \$50.0 million in cash and \$45.0 million in our common stock. This transaction decreased our overall royalty obligation on sales of indiplon from six percent to three and one-half percent. In accordance with SFAS 144 we performed an analysis of the undiscounted cash flows related to this prepaid royalty. Based on our current expectations with respect to FDA approval, commercialization and our plan to partner indiplon, we have determined that the carrying value of this asset is fully recoverable, and we have not recognized any impairment charge to date. However, events both within and outside of our control, such as competition from other insomnia therapeutic agents, disease prevalence, further FDA actions related to indiplon, our ability to partner indiplon, insomnia market dynamics and general market conditions may have an impact on our ability to recover the carrying value of this asset in the future. In the event that either the tablet or capsule or both formulations of indiplon are further delayed, are not eventually approved by the FDA or are approved by the FDA but not successfully commercialized, an impairment charge would likely occur. We will continue to monitor this long-lived asset on a quarterly basis.

### ***Share Based Payments***

We grant stock options to purchase our common stock to our employees and directors under the 2003 Plan and grant stock options to certain employees pursuant to Employment Commencement Nonstatutory Stock Option Agreements. We also grant certain employees stock bonuses and restricted stock units under the 2003 Plan. Additionally, we have outstanding options that were granted under option plans from which we no longer make grants. The benefits provided under all of these plans are subject to the provisions of revised Statement of Financial

**Table of Contents**

Accounting Standards No. 123 (SFAS 123R), Share-Based Payment, which we adopted effective January 1, 2006. We elected to use the modified prospective application in adopting SFAS 123R and therefore have not restated results for prior periods. The valuation provisions of SFAS 123R apply to new awards and to awards that are outstanding on the adoption date and subsequently modified or cancelled. Our results of operations for fiscal 2006 were impacted by the recognition of non-cash expense related to the fair value of our share-based compensation awards. Share-based compensation expense recognized under SFAS 123R for the year ended December 31, 2006 was \$14.6 million.

Stock option awards and restricted stock units generally vest over a three to four year period and expense is ratably recognized over those same time periods. However, due to certain retirement provisions in our stock plans, share-based compensation expense may be recognized over a shorter period of time, and in some cases the entire share-based compensation expense may be recognized upon grant of the share-based compensation award. Employees who are age 55 or older and have five or more years of service with us are entitled to accelerated vesting of certain unvested share-based compensation awards upon retirement. This retirement provision leads to variability in the quarterly expense amounts recognized under SFAS 123R, and therefore individual share-based compensation awards may impact earnings disproportionately in any individual fiscal quarter.

The determination of fair value of stock-based payment awards on the date of grant using the Black-Scholes model is affected by our stock price, as well as the input of other subjective assumptions. These assumptions include, but are not limited to, the expected term of stock options and our expected stock price volatility over the term of the awards. Our stock options have characteristics significantly different from those of traded options, and changes in the assumptions can materially affect the fair value estimates.

SFAS 123R requires forfeitures to be estimated at the time of grant and revised, if necessary, in subsequent periods if actual forfeitures differ from those estimates. If actual forfeitures vary from our estimates, we will recognize the difference in compensation expense in the period the actual forfeitures occur or when options vest.

**Results of Operations for Years Ended December 31, 2006, 2005 and 2004**

The following table summarizes our primary sources of revenue during the periods presented:

	<b>Year Ended December 31,</b>		
	<b>2006</b>	<b>2005</b>	<b>2004</b>
	<b>(In thousands)</b>		
Revenues under collaboration agreements:			
Pfizer	\$ 29,660	\$ 121,397	\$ 76,939
GlaxoSmithKline (GSK)	9,074	2,492	7,829
Other	500		
Total revenue under collaboration agreements	39,234	123,889	84,768
Grant income			408
Total revenues	\$ 39,234	\$ 123,889	\$ 85,176

Our revenues for the year ended December 31, 2006 were \$39.2 million compared with \$123.9 million in 2005. This decrease in revenues is primarily due to milestones recognized in 2005 under our former collaboration agreement with Pfizer. During 2005, we recognized \$70.0 million in milestones from Pfizer related to the FDA's accepting for review

our NDA for indiplon capsules and tablets. License fees recognized under our Pfizer agreement decreased to \$6.5 million in 2006 compared to \$20.7 million in 2005. Sponsored development revenue from Pfizer declined to \$6.6 million in 2006 compared to \$8.7 million in 2005. We also recognized \$16.5 million in sales force allowance revenue from Pfizer in 2006 compared to \$22.0 million in 2005. Additionally, during 2006, we recognized \$9.0 million in milestones under our GSK collaboration agreement compared to \$2.0 million in 2005. The 2006 milestones recognized under the GSK agreement relate to clinical advancements and initiation of two Phase II proof of concept clinical trials for generalized social anxiety disorder and irritable bowel syndrome in our CRF program.

**Table of Contents**

Our revenues for the year ended December 31, 2005 were \$123.9 million compared with \$85.2 million in 2004. This increase in revenues is primarily due to milestones recognized under our collaboration agreement with Pfizer. Milestones received under the Pfizer collaboration agreement totaled \$70.0 million in 2005 related to the FDA's accepting for review our NDA for indiplon capsules and tablets, compared to \$20.5 million in milestones earned in 2004 under the Pfizer collaboration agreement for the successful completion of Phase III studies for long-term administration and sleep maintenance of indiplon during 2004. License fees recognized under our Pfizer agreement were \$20.7 million in 2005 compared to \$34.8 million in 2004. Sponsored development revenue decreased to \$8.7 million in 2005 compared to \$21.7 million in 2004, due to the continued winding down of our indiplon Phase III clinical program. During 2005, we also recognized \$22.0 million from Pfizer as a sales force allowance for the building and operation of our 200-person sales force. Additionally, during 2005 we received \$2.0 million in milestones under our GSK collaboration agreement, related to successful completion of the research portion of the agreement and selection of two drug candidates for clinical development. During 2004, we recognized \$5.5 million from GSK for sponsored research in our CRF program. The sponsored research portion of our collaboration agreement with GSK ended in 2005. We also earned \$1.5 million during 2004 from GSK related to milestones for selection and progress of development candidates.

We expect revenues to decrease significantly during 2007 compared to 2006 primarily due to the cancellation of our Pfizer collaboration agreement.

Research and development expenses decreased to \$97.7 million during 2006 compared to \$106.6 million in 2005. The \$8.9 million decrease in 2006 research and development expenses is primarily attributed to the completion and termination of our two Phase II APL programs in 2006 combined with a reduction in clinical trial costs as several Phase III clinical trials for indiplon were completed in 2005. External development costs related to indiplon in 2006 were \$4.2 million compared to \$12.8 million in 2005. External development costs related to our APL programs was \$2.7 million in 2006 compared to \$8.5 million in 2005. These decreases in 2006 were partially offset by increases related to our GnRH and sNRI programs. GnRH external development costs increased to \$11.1 million in 2006 from \$10.1 million in 2005 due to expansion of Phase II studies in endometriosis. External development costs related to sNRI increased to \$2.4 million in 2006 from \$0.2 million in 2005 due to product manufacturing and preclinical study costs. Additionally, scientific personnel costs increased to \$44.2 million in 2006 compared to \$36.0 million in 2005. The increase in scientific personnel costs was primarily due to expenses of \$6.3 million related to the adoption of SFAS 123R in 2006. Additionally, laboratory costs were lower by \$4.3 million in 2006 compared to 2005 primarily due to our reduction in force.

Research and development expenses decreased to \$106.6 million during 2005 compared to \$115.1 million in 2004. The \$8.5 million decrease from 2004 to 2005 relates primarily to the winding down of our Phase III program for indiplon. External development costs incurred related to indiplon were \$12.8 million in 2005 compared to \$26.5 million in 2004, primarily due to the tapering of our indiplon clinical program during 2005. This decrease was offset by an increase in external development expense under other clinical programs of approximately \$5.4 million. External development costs related to our GnRH program increased to \$10.1 million in 2005 from \$9.5 million in 2004, costs related to our multiple sclerosis program increased to \$4.7 million in 2005 from \$3.7 million in 2004, and costs in our H1 antagonist program increased to \$3.8 million in 2005 from \$1.7 million in 2004. Additionally, scientific personnel costs have increased to \$36.0 million in 2005 compared to \$32.9 million in 2004, and laboratory costs were \$2.1 million higher in 2005 than 2004. The increase in personnel costs and laboratory costs are related to efforts on advancing our research and development candidates. Costs related to in-licensing, scientific consultants, and milestone expenses were \$3.3 million in 2005 compared to \$8.9 million in 2004. This decrease is primarily due to milestone expenses and consultant expenses during 2004, related to the indiplon NDA filings.

We expect research and development expenses to decrease during 2007 compared to 2006, primarily due to cost savings related to our reduction in force that occurred in 2006. We expect research and development costs will

increase in 2008 compared to 2007 as our pipeline matures.

Sales, general and administrative expenses increased to \$54.9 million in 2006 compared to \$42.3 million during 2005 and \$22.4 million during 2004. The \$12.6 million increase in expenses from 2005 to 2006 resulted primarily from the adoption of SFAS 123R in 2006, which resulted in expense of approximately \$8.3 million, and severance costs of \$6.7 million. The \$19.9 million increase in expenses from 2004 to 2005 resulted primarily from

## **Table of Contents**

the implementation of our commercialization strategy, including the hiring, training and deployment of our 200-person sales force. This increase in sales costs was primarily offset by revenue recognized under our sales force allowance from Pfizer.

We expect sales, general and administrative expenses to decrease significantly during 2007 primarily due to the cost savings related to the reduction in force during 2006.

Other income increased to \$6.1 million in 2006 compared with \$2.9 million during 2005 and \$6.6 million during 2004. The increase in other income from 2005 to 2006 is due to lower interest expense and higher interest income. Interest expense decreased from \$4.2 million in 2005 to \$3.7 million in 2006, primarily due to maturity of debt obligations. The increase in interest income from 2005 to 2006 is primarily due to higher rate of return on our investment portfolio during 2006. The decrease in other income from 2005 to 2004 is a primarily due to increased interest expense and lower interest income. Interest expense increased from \$2.0 million in 2004 to \$4.2 million in 2005, primarily due to capitalization, in 2004, of approximately \$1.3 million in interest expense related to the construction of our corporate facility, and higher average debt balances in 2005. Our debt balance increased during 2004 as we incurred debt as needed to fund construction of our facility which was completed in 2004. The decrease in interest income from 2004 to 2005 is a result of lower average cash and investment balances, primarily due to operating losses.

Our net loss for 2006 was \$107.2 million, or \$2.84 per share, compared to \$22.2 million, or \$0.60 per share, in 2005 and \$45.8 million, or \$1.26 per share, in 2004. The increase in net loss from 2005 to 2006 was primarily the result of \$70.0 million in milestones recognized under the Pfizer collaboration agreement during 2005 combined with the adoption of SFAS 123R, which resulted in expense of \$14.6 million, and severance costs of \$9.5 million in 2006. These costs were partially offset by lower external development costs in 2006 of \$12.1 million. The decrease in net loss from 2004 to 2005 was primarily the result of \$70.0 million in milestones recognized under the Pfizer collaboration agreement in 2005, offset by higher non-indiplon related research and development costs in that year.

## **Liquidity and Capital Resources**

At December 31, 2006, our cash, cash equivalents, and short-term investments totaled \$182.6 million compared with \$273.1 million at December 31, 2005. This \$90.5 million decrease is primarily a result of our operating loss of \$107.2 million for the year ended December 31, 2006, offset by the receipt of \$15.8 million from stock option exercises. At December 31, 2005, our cash, cash equivalents, and short-term investments totaled \$273.1 million compared with \$301.1 million at December 31, 2004. This \$28.0 million decrease is primarily a result of our operating loss of \$22.2 million for the year ended December 31, 2005, and payments on long-term debt of \$6.7 million. We expect to use approximately \$80.0 million in cash during 2007 and end 2007 with at least \$100.0 million in cash.

Net cash used in operating activities during 2006 was \$99.3 million compared to \$30.8 million in 2005. This increase is primarily due to a loss of \$107.2 million compared to a net loss of \$22.2 million in 2005. Net cash used in operating activities during 2005 was \$30.8 million compared to \$100.0 million in 2004. The fluctuation between 2004 and 2005 is due to a loss of \$22.2 million in 2005 compared to a loss of \$45.8 million in 2004, and a reduction in payables of \$31.1 million in 2004, primarily due to paying accrued clinical trial costs for indiplon.

Net cash provided by investing activities during 2006 was \$120.3 million compared to \$9.4 million in 2005 and \$18.5 million in 2004. These fluctuations resulted primarily from timing differences in investment purchases, sales and maturities and the fluctuations in our portfolio mix between cash equivalents and short-term investment holdings. We expect similar fluctuations to continue in future periods. Capital equipment purchases for 2006, 2005, and 2004 were \$3.1 million, \$7.2 million and \$13.7 million, respectively. Capital equipment purchases for 2007 are expected to

be approximately \$2.0 million. During 2004, net cash provided by investing activities included construction costs of \$31.7 million. Additionally, we paid \$50.0 million in cash as part of our purchase of Wyeth's portion of the indiplon royalty stream.

On February 26, 2004, we entered into several agreements with Wyeth and DOV pursuant to which we acquired Wyeth's financial interest in indiplon for approximately \$95.0 million, consisting of \$50.0 million in cash and \$45.0 million in our common stock. Wyeth's financial interest in indiplon arose from a 1998 license agreement



## **Table of Contents**

between Wyeth and DOV whereby Wyeth licensed the indiplon technology to DOV in exchange for milestone payments and royalties on future sales of indiplon. We subsequently licensed the indiplon technology from DOV in exchange for milestones and royalties. The February 2004 agreements among us, Wyeth and DOV provide that we will make milestone and royalty payments to DOV net of amounts that DOV would have been obligated to pay to Wyeth such that we will retain all milestone, royalty and other payments on indiplon commercialization that would have otherwise been payable to Wyeth. This decreases our overall royalty obligation on sales of indiplon from six percent to three and one-half percent. This transaction has been recorded as a long-term asset (prepaid royalty), and this asset will be amortized over the commercialization period of indiplon, based primarily upon indiplon sales.

During 2003, we sold our former research and administrative facility and an undeveloped parcel of land adjacent to the facility for \$40.0 million and recognized a gain on the sale of these properties of approximately \$18.0 million. Additionally, during 2003, we acquired undeveloped real property in San Diego, California for approximately \$17.0 million to construct a new corporate facility. In January 2004, we purchased an additional parcel of land adjacent to the property for \$7.7 million. Construction of the new facility commenced in June 2003 and was completed in mid-2004.

The costs we incurred in connection with these two properties included design and construction costs as well as site improvements, equipment and construction financing costs for the facilities. These costs were approximately \$57.1 million. The land acquisition and construction costs were financed through the net proceeds of the sale of the former facility and a construction loan. The construction loan agreement was for an amount up to \$60.6 million and required us to place a \$17.5 million guaranty deposit with the lender for the term of the loan. The loan bore interest at the prime rate plus .75 percentage points. In October 2004, we repaid the outstanding amount under the construction loan of \$60.3 million, and our guaranty deposit was released by the lender. The construction loan was replaced with a \$49.5 million loan secured by a first mortgage on the property. The new loan bears interest at a rate of 6.48% per annum, and is being amortized over a period of thirty years, with a principal balloon payment of \$42.0 million due on the tenth anniversary of the loan. Additionally, we are required by the lender to maintain a \$5.0 million letter of credit with a local bank as security for the first mortgage loan. The letter of credit is secured by a \$5.2 million deposit with the same bank.

Net cash provided by financing activities during 2006 was \$10.1 million in 2006 compared to \$10.3 million in 2005 and \$36.7 million in 2004. In addition to the above mentioned fiscal 2004 debt transactions, cash proceeds from the issuance of common stock upon exercise of outstanding stock options and employee stock purchase plans were \$15.8 million, \$17.0 million and \$6.8 million in 2006, 2005 and 2004, respectively. We expect similar fluctuations to occur in the future, as the amount and frequency of stock-related transactions are dependent upon the market performance of our common stock.

## **Factors That May Affect Future Financial Condition and Liquidity**

We anticipate significant increases in expenditures as we continue to expand our research and development activities. Because of our limited financial resources, our strategies to develop some of our programs include collaborative agreements with major pharmaceutical companies and sales of our common stock in both public and private offerings. Our collaborative agreements typically include a partial recovery of our research costs through license fees, contract research funding and milestone revenues. Our collaborators are also financially and managerially responsible for clinical development and commercialization. In these cases, the estimated completion date would largely be under the control of the collaborator. We intend to seek a partner, at an appropriate time, to assist us in the worldwide development and commercialization of indiplon. We cannot forecast, with any degree of certainty, which other proprietary products or indications, if any, will be subject to future collaborative arrangements, in whole or in part, and how such arrangements would affect our capital requirements.

The following table summarizes our contractual obligations at December 31, 2006 and the effect such obligations are expected to have on our liquidity and cash flow in future periods. Our license, research and clinical development agreements are generally cancelable with written notice in 0-180 days. In addition to the minimum payments due under our license and research agreements, we may be required to pay up to \$33.5 million in

**Table of Contents**

milestone payments, plus sales royalties, in the event that all scientific research under these agreements is successful. Some of our clinical development agreements contain incentives for time-sensitive activities.

Contractual Obligations	Total	Less than	1 - 3	3 - 5	More than
		1	Years	Years	5
(In thousands)					
Debt	\$ 53,641	\$ 4,489	\$ 2,887	\$ 1,594	\$ 44,671
Operating leases	370	201	169		
License and research agreements	1,493	1,098	170	150	75
Clinical development agreements	15,562	11,375	4,187		
Total contractual obligations	\$ 71,066	\$ 17,163	\$ 7,413	\$ 1,744	\$ 44,746

The funding necessary to execute our business strategies is subject to numerous uncertainties, which may adversely affect our liquidity and capital resources. Completion of clinical trials may take several years or more, but the length of time generally varies substantially according to the type, complexity, novelty and intended use of a product candidate. It is also important to note that if a clinical candidate is identified, the further development of that candidate can be halted or abandoned at any time due to a number of factors. These factors include, but are not limited to, funding constraints, safety or a change in market demand.

An important element of our business strategy is to pursue the research and development of a diverse range of product candidates for a variety of disease indications. We pursue this goal through proprietary research and development as well as searching for new technologies for licensing opportunities. This allows us to diversify against risks associated with our research and development spending. To the extent we are unable to maintain a diverse and broad range of product candidates, our dependence on the success of one or a few product candidates would increase.

The nature and efforts required to develop our product candidates into commercially viable products include research to identify a clinical candidate, preclinical development, clinical testing, FDA approval and commercialization. This process may cost in excess of \$500 million and can take in excess of 10 years to complete for each product candidate.

We test our potential product candidates in numerous pre-clinical studies to identify disease indications for which our product candidates may show efficacy. We may conduct multiple clinical trials to cover a variety of indications for each product candidate. As we obtain results from trials, we may elect to discontinue clinical trials for certain product candidates or for certain indications in order to focus our resources on more promising product candidates or indications. The duration and the cost of clinical trials may vary significantly over the life of a project as a result of differences arising during the clinical trial protocol, including, among others, the following:

we or the FDA or similar foreign regulatory authorities may suspend the trials;

we may discover that a product candidate may cause harmful side effects;

patient recruitment may be slower than expected; and

patients may drop out of the trials.

For each of our programs, we periodically assess the scientific progress and merits of the programs to determine if continued research and development is economically viable. Certain of our programs have been terminated due to the lack of scientific progress and lack of prospects for ultimate commercialization. Because of the uncertainties associated with research and development of these programs, we may not be successful in achieving commercialization. As such, the ultimate timeline and costs to commercialize a product cannot be accurately estimated.

Our product candidates have not yet achieved FDA regulatory approval, which is required before we can market them as therapeutic products in the United States. In order to proceed to subsequent clinical trial stages and to ultimately achieve regulatory approval, the FDA must conclude that our clinical data establish safety and efficacy. We must satisfy the requirements of similar regulatory authorities in foreign countries in order to market products in those countries. The results from preclinical testing and early clinical trials may not be predictive of

**Table of Contents**

results in later clinical trials. It is possible for a candidate to show promising results in clinical trials, but subsequently fail to establish sufficient safety and efficacy data necessary to obtain regulatory approvals.

As a result of the uncertainties discussed above, among others, the duration and completion costs of our research and development projects are difficult to estimate and are subject to considerable variation. Our inability to complete our research and development projects in a timely manner or our failure to enter into collaborative agreements, when appropriate, could significantly increase our capital requirements and could adversely impact our liquidity. These uncertainties could force us to seek additional, external sources of financing from time to time in order to continue with our business strategy. Our inability to raise additional capital, or to do so on terms reasonably acceptable to us, would jeopardize the future success of our business.

We also may be required to make further substantial expenditures if unforeseen difficulties arise in other areas of our business. In particular, our future capital requirements will depend on many factors, including:

- continued scientific progress in our research and development programs;
- the magnitude of our research and development programs;
- progress with preclinical testing and clinical trials;
- the time and costs involved in obtaining regulatory approvals;
- the costs involved in filing and pursuing patent applications and enforcing patent claims;
- competing technological and market developments;
- the establishment of additional collaborations and strategic alliances;
- the cost of manufacturing facilities and of commercialization activities and arrangements; and
- the cost of product in-licensing and any possible acquisitions.

We believe that our existing capital resources, together with interest income and future payments due under our strategic alliances, will be sufficient to satisfy our current and projected funding requirements for at least the next 12 months. However, we cannot guarantee that our existing capital resources and anticipated revenues will be sufficient to conduct and complete all of our research and development programs as planned.

We will require additional funding to continue our research and product development programs, to conduct preclinical studies and clinical trials, for operating expenses, to pursue regulatory approvals for our product candidates, for the costs involved in filing and prosecuting patent applications and enforcing or defending patent claims, if any, for the cost of product in-licensing and for any possible acquisitions, and we may require additional funding to establish manufacturing and marketing capabilities in the future. We may seek to access the public or private equity markets whenever conditions are favorable. We may also seek additional funding through strategic alliances and other financing mechanisms. We cannot assure you that adequate funding will be available on terms acceptable to us, if at all. Any additional equity financings will be dilutive to our stockholders and any additional debt may involve operating covenants that may restrict our business. If adequate funds are not available through these means, we may be required to curtail significantly one or more of our research or development programs or obtain funds through arrangements with collaborators or others. This may require us to relinquish rights to certain of our technologies or product candidates. To the extent that we are unable to obtain third-party funding for such expenses, we expect that

increased expenses will result in increased losses from operations. We cannot assure you that we will successfully develop our products under development or that our products, if successfully developed, will generate revenues sufficient to enable us to earn a profit.

**Interest Rate Risk**

We are exposed to interest rate risk on our short-term investments. The primary objective of our investment activities is to preserve principal while at the same time maximizing yields without significantly increasing risk. To achieve this objective, we invest in highly liquid and high quality government and other debt securities. To minimize our exposure due to adverse shifts in interest rates, we invest in short-term securities and ensure that the maximum average maturity of our investments does not exceed 36 months. If a 10% change in interest rates were to have

**Table of Contents**

occurred on December 31, 2006, this change would not have had a material effect on the fair value of our investment portfolio as of that date. Due to the short holding period of our investments, we have concluded that we do not have a material financial market risk exposure.

**New Accounting Pronouncements**

In July 2006, the Financial Accounting Standards Board (FASB) issued FASB Interpretation No. 48, Accounting for Uncertainty in Income Taxes, an interpretation of FASB Statement No. 109 (FIN 48). FIN 48 clarifies the accounting for uncertainty in income taxes by prescribing the recognition threshold a tax position is required to meet before being recognized in the financial statements. It also provides guidance on derecognition, classification, interest and penalties, accounting in interim periods, disclosure, and transition. FIN 48 is effective for fiscal years beginning after December 15, 2006 and is required to be adopted by us in 2007. We do not expect the adoption of FIN 48 to have a material impact on our consolidated results of operations and financial condition.

In September 2006, the FASB issued SFAS No. 157, Fair Value Measurements (SFAS 157). SFAS 157 provides guidance for using fair value to measure assets and liabilities. It also responds to investors' requests for expanded information about the extent to which companies measure assets and liabilities at fair value, the information used to measure fair value, and the effect of fair value measurements on earnings. SFAS 157 applies whenever other standards required (or permit) assets or liabilities to be measured at fair value, and does not expand the use of fair value in any new circumstances. SFAS 157 is effective for financial statements issued for fiscal years beginning after November 15, 2007. We are currently evaluating the effect that the adoption of SFAS 157 will have on our consolidated results of operations and financial condition and is not yet in a position to determine such effects.

In September 2006, the Securities and Exchange Commission issued Staff Accounting Bulletin (SAB) No. 108, Considering the Effects of Prior Year Misstatements when Quantifying Misstatements in Current Year Financial Statements (SAB 108). SAB 108 provides guidance on the consideration of the effects of prior year misstatements in quantifying current year misstatements for the purpose of a materiality assessment. SAB 108 establishes an approach that requires quantification of financial statement errors based on the effects of each of the company's balance sheet and statement of operations and the related financial statement disclosures. Early application of the guidance in SAB 108 is encouraged in any report for an interim period of the first fiscal year ending after November 15, 2006, and will be adopted by us in the first quarter of fiscal 2007. We do not expect the adoption of SAB 108 to have a material impact on our consolidated results of operations and financial condition.

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

Information required by this item is contained in Item 7. Management's Discussion and Analysis of Financial Condition and Results of Operations - Interest Rate Risk. Such information is incorporated herein by reference.

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

Information required by this item is contained in Item 15 below. Such information is incorporated herein by reference.

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

Not applicable.

**ITEM 9A. CONTROLS AND PROCEDURES**

We maintain disclosure controls and procedures that are designed to ensure that information required to be disclosed in our Exchange Act reports is recorded, processed, summarized and reported within the timelines specified in the Securities and Exchange Commission's rules and forms, and that such information is accumulated and communicated to our management, including our Chief Executive Officer and Chief Financial Officer, as appropriate, to allow timely decisions regarding required disclosure. In designing and evaluating the disclosure



**Table of Contents**

controls and procedures, management recognized that any controls and procedures, no matter how well designed and operated, can only provide reasonable assurance of achieving the desired control objectives, and in reaching a reasonable level of assurance, management necessarily was required to apply its judgment in evaluating the cost-benefit relationship of possible controls and procedures.

As required by SEC Rule 13a-15(b), we carried out an evaluation, under the supervision and with the participation of our management, including our Chief Executive Officer and Chief Financial Officer, of the effectiveness of the design and operation of our disclosure controls and procedures as of the end of the year covered by this report. Based on the foregoing, our Chief Executive Officer and Chief Financial Officer concluded that our disclosure controls and procedures were effective at the reasonable assurance level.

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

Internal control over financial reporting refers to the process designed by, or under the supervision of, our Chief Executive Officer and Chief Financial Officer, and effected by our board of directors, management and other personnel, 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, and includes those policies and procedures that:

- (1) Pertain to the maintenance of records that in reasonable detail accurately and fairly reflect the transactions and dispositions of our assets;
- (2) Provide reasonable assurance that transactions are recorded as necessary to permit preparation of financial statements in accordance with generally accepted accounting principles, and that our receipts and expenditures are being made only in accordance with authorization of our management and directors; and
- (3) Provide reasonable assurance regarding prevention or timely detection of unauthorized acquisition, use or disposition of our assets that could have a material effect on the financial statements.

Internal control over financial reporting cannot provide absolute assurance of achieving financial reporting objectives because of its inherent limitations. Internal control over financial reporting is a process that involves human diligence and compliance and is subject to lapses in judgment and breakdowns resulting from human failures. Internal control over financial reporting also can be circumvented by collusion or improper management override. Because of such limitations, there is a risk that material misstatements may not be prevented or detected on a timely basis by internal control over financial reporting. However, these inherent limitations are known features of the financial reporting process. Therefore, it is possible to design into the process safeguards to reduce, though not eliminate, this risk. Management is responsible for establishing and maintaining adequate internal control over financial reporting for the company.

Management has used the framework set forth in the report entitled *Internal Control-Integrated Framework* published by the Committee of Sponsoring Organizations of the Treadway Commission, known as COSO, to evaluate the effectiveness of our internal control over financial reporting. Based on this assessment, management has concluded that our internal control over financial reporting was effective as of December 31, 2006. Ernst & Young LLP, the independent registered public accounting firm that audited the consolidated financial statements included in this Annual Report on Form 10-K, has issued an attestation report on management's assessment of the effectiveness of our internal control over financial reporting as of December 31, 2006. This report which expresses an unqualified opinion on management's assessment of and the effectiveness of our internal controls over financial reporting as of December 31, 2006 is included herein.

There has been no change in our internal control over financial reporting during our most recent fiscal quarter that has materially affected, or is reasonably likely to materially affect, our internal control over financial reporting.

**Table of Contents**

**Report of Independent Registered Public Accounting Firm  
on Internal Control Over Financial Reporting**

The Board of Directors and Stockholders  
Neurocrine Biosciences, Inc.

We have audited management's assessment, included in the accompanying Management's Report on Internal Control Over Financial Reporting, that Neurocrine Biosciences, Inc. maintained effective internal control over financial reporting as of December 31, 2006, based on criteria established in Internal Control-Integrated Framework issued by the Committee of Sponsoring Organizations of the Treadway Commission (the COSO criteria). Neurocrine Biosciences' management is responsible for maintaining effective internal control over financial reporting and for its assessment of the effectiveness of internal control over financial reporting. Our responsibility is to express an opinion on management's assessment and an opinion on the effectiveness of the company's internal control over financial reporting based on our audit.

We conducted our audit in accordance with the standards of the Public Company Accounting Oversight Board (United States). Those standards require that we plan and perform the audit to obtain reasonable assurance about whether effective internal control over financial reporting was maintained in all material respects. Our audit included obtaining an understanding of internal control over financial reporting, evaluating management's assessment, testing and evaluating the design and operating effectiveness of internal control, and performing such other procedures as we considered necessary in the circumstances. We believe that our audit provides a reasonable basis for our opinion.

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 (1) pertain to the maintenance of records that, in reasonable detail, accurately and fairly reflect the transactions and dispositions of the assets of the company; (2) 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 (3) 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.

In our opinion, management's assessment that Neurocrine Biosciences, Inc. maintained effective internal control over financial reporting as of December 31, 2006, is fairly stated, in all material respects, based on the COSO criteria. Also, in our opinion, Neurocrine Biosciences, Inc. maintained, in all material respects, effective internal control over financial reporting as of December 31, 2006, based on the COSO criteria.

We also have audited, in accordance with the standards of the Public Company Accounting Oversight Board (United States), the consolidated balance sheets as of December 31, 2006 and 2005, and the related consolidated statements of operations, stockholders' equity and cash flows for each of the three years in the period ended December 31, 2006 of Neurocrine Biosciences, Inc. and our report dated February 2, 2007 expressed an unqualified opinion thereon.

/s/ ERNST & YOUNG LLP

San Diego, California  
February 2, 2007

**Table of Contents**

**ITEM 9B. *OTHER INFORMATION***

None

**PART III**

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

Information required by this item will be contained in our Definitive Proxy Statement for our 2007 Annual Meeting of Stockholders, to be filed pursuant to Regulation 14A with the Securities and Exchange Commission within 120 days of December 31, 2006. Such information is incorporated herein by reference.

We have adopted a code of ethics that applies to our Chief Executive Officer, Chief Financial Officer, and to all of our other officers, directors, employees and agents. The code of ethics is available at the Corporate Governance section of the Investor Relations page on our website at [www.neurocrine.com](http://www.neurocrine.com). We intend to disclose future amendments to, or waivers from, certain provisions of our code of ethics on the above website within four business days following the date of such amendment or waiver.

**ITEM 11. *EXECUTIVE COMPENSATION***

Information required by this item will be contained in our Definitive Proxy Statement for our 2007 Annual Meeting of Stockholders, to be filed pursuant to Regulation 14A with the Securities and Exchange Commission within 120 days of December 31, 2006. Such information is incorporated herein by reference.

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

Information required by this item will be contained in our Definitive Proxy Statement for our 2007 Annual Meeting of Stockholders, to be filed pursuant to Regulation 14A with the Securities and Exchange Commission within 120 days of December 31, 2006. Such information is incorporated herein by reference.

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

Information required by this item will be contained in our Definitive Proxy Statement for our 2007 Annual Meeting of Stockholders, to be filed pursuant to Regulation 14A, with the Securities and Exchange Commission within 120 days of December 31, 2006. Such information is incorporated herein by reference.

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

Information required by this item will be contained in our Definitive Proxy Statement for our 2007 Annual Meeting of Stockholders, to be filed pursuant to Regulation 14A, with the Securities and Exchange Commission within 120 days of December 31, 2006. Such information is incorporated herein by reference.

**Table of Contents**

**PART IV**

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

**(a) Documents filed as part of this report.**

1. List of Financial Statements. The following are included in this report:

Report of Independent Registered Public Accounting Firm

Consolidated Balance Sheets as of December 31, 2006 and 2005

Consolidated Statements of Operations for the years ended December 31, 2006, 2005 and 2004

Consolidated Statements of Stockholders' Equity for the years ended December 31, 2006, 2005 and 2004

Consolidated Statements of Cash Flows for the years ended December 31, 2006, 2005 and 2004

Notes to the Consolidated Financial Statements (includes unaudited Selected Quarterly Financial Data)

2. List of all Financial Statement schedules. All schedules are omitted because they are not applicable or the required information is shown in the Financial Statements or notes thereto.

3. List of Exhibits required by Item 601 of Regulation S-K. See part (b) below.

**(b) Exhibits.** The following exhibits are filed as part of, or incorporated by reference into, this report:

<b>Exhibit Number</b>	<b>Description</b>
3.1	Restated Certificate of Incorporation (1)
3.2	Certificate of Amendment to Certificate of Incorporation (22)
3.3	Bylaws (1)
3.4	Certificate of Amendment of Bylaws (8)
3.5	Certificate of Amendment of Bylaws (20)
4.1	Form of Common Stock Certificate (1)
4.2	Amended and Restated Preferred Shares Rights Agreement by and between the Registrant and American Stock Transfer & Trust Company, as Rights Agent, dated as of January 11, 2002 (9)
10.1	1992 Incentive Stock Plan, as amended (6)
10.2	1996 Director Stock Option Plan, as amended, and form of stock option agreement (1)
10.3	Form of Director and Officer Indemnification Agreement (1)
10.4	Employment Agreement dated March 1, 1997, between the Registrant and Gary A. Lyons, as amended May 24, 2000 (5)
10.5*	Research and License Agreement dated October 15, 1996, between the Registrant and Eli Lilly and Company (2)
10.6	

Edgar Filing: NEUROCRINE BIOSCIENCES INC - Form 10-K

Form of incentive stock option agreement and nonstatutory stock option agreement for use in connection with 1992 Incentive Stock Plan (25)

- 10.7\* Sub-License and Development Agreement dated June 30, 1998, by and between DOV Pharmaceutical, Inc. and the Registrant (3)
- 10.8\* Collaboration and License Agreement dated January 1, 1999, by and between American Home Products Corporation acting through its Wyeth Laboratories Division and the Registrant (4)
- 10.9 Employment Agreement dated October 1, 1998, between the Registrant and Margaret Valeur-Jensen, as amended May 24, 2000 (5)
- 10.10\* Collaboration and License Agreement between the Registrant and Glaxo Group Limited dated July 20, 2001 (7)
- 10.11 2001 Stock Option Plan, as amended August 6, 2002 and October 15, 2002 (10)
- 10.12 Neurocrine Biosciences, Inc. Nonqualified Deferred Compensation Plan, as amended (18)

**Table of Contents**

<b>Exhibit Number</b>	<b>Description</b>
10.13	Neurocrine Biosciences, Inc. 2003 Incentive Stock Plan, as amended and form of stock option agreement (18)
10.14	Employment Commencement Nonstatutory Stock Option Agreement between the Registrant and Wendell Wierenga (14)
10.15	Tax Indemnity Agreement between the Registrant and Gary Lyons (11)
10.16	Tax Indemnity Agreement between the Registrant and Paul W. Hawran (11)
10.17	Tax Indemnity Agreement between the Registrant and Margaret Valeur-Jensen (11)
10.18	Tax Indemnity Agreement between the Registrant and Kevin Gorman (11)
10.19	Tax Indemnity Agreement between the Registrant and Paul Conlon (11)
10.20	Employment Agreement dated October 27, 2003 between the Registrant and Kevin C. Gorman (13)
10.21	Promissory Note between Science Park Center LLC and Teachers Insurance and Annuity Association of America (15)
10.22	Deed of Trust, Assignment of Leases and Rents, Security Agreement and Fixture Filing by and between Science Park Center LLC, and Stewart Title Guaranty Company, as Trustee for the benefit of Teachers Insurance and Annuity Association of America (15)
10.23	Letter of Credit (15)
10.24	Assignment and License Agreement dated February 26, 2004 by and among Wyeth Holdings Corporation and the Registrant (12)
10.25	Stock Purchase Agreement dated February 25, 2004 by and among Wyeth Holdings Corporation and the Registrant (12)
10.26	Consent Agreement and Amendment dated February 25, 2004 by and among Wyeth Holdings Corporation, the Registrant and DOV Pharmaceutical, Inc. (12)
10.27	License Agreement dated March 15, 2004 by and among Wyeth Holdings Corporation and DOV Pharmaceutical, Inc. (12)
10.28	Employment Agreement dated June 20, 2005 between the Registrant and Richard Ranieri (16)
10.29	Employment Commencement Nonstatutory Stock Option Agreement between the Registrant and Richard Ranieri (16)
10.30	Employment Commencement Nonstatutory Stock Option Agreement between the Registrant and Christopher O Brien (17)
10.31	Amendment dated February 7, 2006 to Collaboration and License Agreement between the Registrant and Glaxo Group Limited (22)
10.32	Amended and Restated Employment Agreement dated September 18, 2006 between the Registrant and Paul W. Hawran (21)
10.33	Employment Agreement dated September 18, 2006 between the Registrant and Timothy P. Coughlin (21)
10.34	Form of Restricted Stock Unit Agreement (23)
10.35	Consulting Agreement dated November 15, 2006 between the Registrant and Wylie Vale
10.36	Consulting Agreement dated December 30, 2006 between the Registrant and Wendell Wierenga, Ph.D. (24)
21.1	Subsidiaries of the Registrant
23.1	Consent of Independent Registered Public Accounting Firm
31.1	Certification of Chief Executive Officer pursuant to Rules 13a-14 and 15d-14 promulgated under the Securities Exchange Act of 1934
31.2	Certification of Chief Financial Officer pursuant to Rules 13a-14 and 15d-14 promulgated under the Securities Exchange Act of 1934



32\*\* Certifications of Chief Executive Officer and Chief Financial Officer pursuant to 18 U.S.C.  
Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002  
46

---

**Table of Contents**

- (1) Incorporated by reference to the Company's Registration Statement on Form S-1 (Registration No. 333-03172)
- (2) Incorporated by reference to the Company's Annual Report on Form 10-K for the fiscal year ended December 31, 1996 filed on March 31, 1997
- (3) Incorporated by reference to the Company's Quarterly Report on Form 10-Q filed on August 14, 1998
- (4) Incorporated by reference to the Company's Annual Report on Form 10-K for the fiscal year ended December 31, 1998 filed on March 31, 1999
- (5) Incorporated by reference to the Company's Quarterly Report on Form 10-Q filed on August 11, 2000
- (6) Incorporated by reference to the Company's Registration Statement on Form S-8 filed on July 16, 2001
- (7) Incorporated by reference to the Company's Quarterly Report on Form 10-Q filed on August 14, 2001
- (8) Incorporated by reference to the Company's Annual Report on Form 10-K for the fiscal year ended December 31, 2007 filed on April 10, 1998
- (9) Incorporated by reference to the Company's Current Report on Form 8-K filed on January 14, 2002
- (10) Incorporated by reference to the Company's Annual Report on Form 10-K for the fiscal year ended December 31, 2002 filed on March 4, 2003
- (11) Incorporated by reference to the Company's Annual Report on Form 10-K for the fiscal year ended December 31, 2003 filed on March 15, 2004
- (12) Incorporated by reference to the Company's Report on Form 8-K filed on March 17, 2004, as amended
- (13) Incorporated by reference to the Company's Quarterly Report on Form 10-Q filed on May 10, 2004
- (14) Incorporated by reference to the Company's Registration Statement on Form S-8 filed on September 2, 2004
- (15) Incorporated by reference to the Company's Report on Form 8-K filed on October 29, 2004
- (16) Incorporated by reference to the Company's Report on Form 8-K filed on June 24, 2005
- (17) Incorporated by reference to the Company's Report on Form 8-K filed on November 1, 2005
- (18) Incorporated by reference to the Company's Report on Form 8-K filed on January 19, 2006
- (19) Incorporated by reference to the Company's Quarterly Report on Form 10-Q filed on August 9, 2006
- (20) Incorporated by reference to the Company's Quarterly Report on Form 10-Q filed on August 9, 2004
- (21) Incorporated by reference to the Company's Report on Form 8-K filed on September 19, 2006
- (22) Incorporated by reference to the Company's Report on Form 8-K filed on February 13, 2006

- (23) Incorporated by reference to the Company's Quarterly Report on Form 10-Q filed on November 9, 2006
- (24) Incorporated by reference to the Company's Report on Form 8-K filed on December 22, 2006.
- (25) Incorporated by reference to the Company's Registration Statement on Form S-8 filed on June 26, 1998.

\* Confidential treatment has been granted with respect to certain portions of the exhibit.

\*\* These certifications are being furnished solely to accompany this annual report pursuant to 18 U.S.C. Section 1350, and are not being filed for purposes of Section 18 of the Securities Exchange Act of 1934 and are not to be incorporated by reference into any filing of Neurocrine Biosciences, Inc., whether made before or after the date hereof, regardless of any general incorporation language in such filing.

(c) *Financial Statement Schedules. See Item 15(a)(2) above.*

**Table of Contents**

**SIGNATURES**

Pursuant to the requirements of Section 13 or 15(d) of the Securities Exchange Act of 1934, the Registrant has duly caused this report to be signed on its behalf by the undersigned, thereunto duly authorized.

NEUROCRINE BIOSCIENCES, INC.  
A Delaware Corporation

By: /s/ Gary A. Lyons

Gary A. Lyons  
President and Chief  
Executive Officer

Date: February 8, 2007

Pursuant to the requirements of the Securities Exchange Act of 1934, this report has been signed by the following persons on behalf of the Registrant and in the capacities and on the dates indicated:

<b>Signature</b>	<b>Title</b>	<b>Date</b>
/s/ Gary A. Lyons Gary A. Lyons	President, Chief Executive Officer and Director (Principal Executive Officer)	February 8, 2007
/s/ Timothy P. Coughlin Timothy P. Coughlin	Vice President and Chief Financial Officer (Principal Financial and Accounting Officer)	February 8, 2007
/s/ Joseph A. Mollica Joseph A. Mollica	Chairman of the Board of Directors	February 8, 2007
/s/ Adrian Adams Adrian Adams	Director	February 8, 2007
/s/ Corinne H. Lyle Corinne H. Lyle	Director	February 8, 2007
/s/ W. Thomas Mitchell W. Thomas Mitchell	Director	February 8, 2007
/s/ Richard F. Pops Richard F. Pops	Director	February 8, 2007

/s/ Stephen A. Sherwin

Director

February 8, 2007

Stephen A. Sherwin

/s/ Wylie W. Vale

Director

February 8, 2007

Wylie W. Vale

**Table of Contents**

**NEUROCRINE BIOSCIENCES, INC.**

**INDEX TO THE FINANCIAL STATEMENTS**

	<b>Page</b>
<u>Report of Independent Registered Public Accounting Firm</u>	F-2
<u>Consolidated Balance Sheets</u>	F-3
<u>Consolidated Statements of Operations</u>	F-4
<u>Consolidated Statements of Stockholders' Equity</u>	F-5
<u>Consolidated Statements of Cash Flows</u>	F-6
<u>Notes to the Consolidated Financial Statements</u>	F-7

F-1

---

**Table of Contents**

**REPORT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM**

The Board of Directors and Stockholders  
Neurocrine Biosciences, Inc.

We have audited the accompanying consolidated balance sheets of Neurocrine Biosciences, Inc. as of December 31, 2006 and 2005, and the related consolidated statements of operations, stockholders' equity, and cash flows for each of the three years in the period ended December 31, 2006. These financial statements are the responsibility of the Company's management. Our responsibility is to express an opinion on these financial statements based on our audits.

We conducted our audits in accordance with the standards of the Public Company Accounting Oversight Board (United States). Those standards require that we plan and perform the audit to obtain reasonable assurance about whether the financial statements are free of material misstatement. An audit includes examining, on a test basis, evidence supporting the amounts and disclosures in the financial statements. An audit also includes assessing the accounting principles used and significant estimates made by management, as well as evaluating the overall financial statement presentation. We believe that our audits provide a reasonable basis for our opinion.

In our opinion, the consolidated financial statements referred to above present fairly, in all material respects, the consolidated financial position of Neurocrine Biosciences, Inc. at December 31, 2006 and 2005, and the results of its consolidated operations and its cash flows for each of the three years in the period ended December 31, 2006, in conformity with U.S. generally accepted accounting principles.

We have also audited, in accordance with the standards of the Public Company Accounting Oversight Board (United States), the effectiveness of Neurocrine Biosciences, Inc.'s internal control over financial reporting as of December 31, 2006, based on the criteria established in Internal Control-Integrated Framework issued by the Committee of Sponsoring Organizations of the Treadway Commission and our report dated February 2, 2007, expressed an unqualified opinion thereon.

As discussed in Note #1 to the consolidated financial statements, Neurocrine Biosciences, Inc. changed its method of accounting for Share-Based Payments in accordance with Statement of Financial Accounting Standards No. 123 (revised 2004) on January 1, 2006.

/s/ ERNST & YOUNG LLP

San Diego, California  
February 2, 2007

**Table of Contents****NEUROCRINE BIOSCIENCES, INC.****Consolidated Balance Sheets**

	<b>December 31,</b>	
	<b>2006</b>	<b>2005</b>
	<b>(In thousands, except for par value and share totals)</b>	
<b>ASSETS</b>		
Current assets:		
Cash and cash equivalents	\$ 80,981	\$ 49,948
Short-term investments, available-for-sale	101,623	223,120
Receivables under collaborative agreements	7,191	858
Other current assets	3,863	5,384
Total current assets	193,658	279,310
Property and equipment, net	91,378	99,307
Restricted cash	5,250	5,775
Prepaid royalty	94,000	94,000
Other non-current assets	5,391	4,731
Total assets	\$ 389,677	\$ 483,123
<b>LIABILITIES AND STOCKHOLDERS EQUITY</b>		
Current liabilities:		
Accounts payable	\$ 3,213	\$ 3,447
Accrued liabilities	12,414	17,895
Deferred revenues		6,537
Current portion of long-term debt	4,489	5,814
Total current liabilities	20,116	33,693
Long-term debt	49,152	53,590
Other liabilities	5,693	5,736
Total liabilities	74,961	93,019
Commitments and contingencies		
Stockholders' equity:		
Preferred stock, \$0.001 par value; 5,000,000 shares authorized; no shares issued and outstanding		
Common stock, \$0.001 par value; 110,000,000 shares authorized; issued and outstanding shares were 37,905,988 at December 31, 2006 and 37,132,478 at December 31, 2005	38	37
Additional paid-in capital	721,930	691,717
Accumulated other comprehensive income (loss)	99	(1,504)
Accumulated deficit	(407,351)	(300,146)



Edgar Filing: NEUROCRINE BIOSCIENCES INC - Form 10-K

Total stockholders' equity	314,716	390,104
Total liabilities and stockholders' equity	\$ 389,677	\$ 483,123

See accompanying notes.

F-3

---

**Table of Contents****NEUROCRINE BIOSCIENCES, INC.****Consolidated Statements of Operations**

	<b>Year Ended December 31,</b>		
	<b>2006</b>	<b>2005</b>	<b>2004</b>
	<b>(In thousands, except loss per share data)</b>		
Revenues:			
Sponsored research and development	\$ 6,716	\$ 9,187	\$ 27,156
Milestones and license fees	16,038	92,702	57,612
Sales force allowance	16,480	22,000	
Grant income			408
Total revenues	39,234	123,889	85,176
Operating expenses:			
Research and development	97,678	106,628	115,066
Sales, general and administrative	54,873	42,333	22,444
Total operating expenses	152,551	148,961	137,510
Loss from operations	(113,317)	(25,072)	(52,334)
Other income and (expense):			
Interest income	9,834	7,039	8,601
Interest expense	(3,722)	(4,158)	(1,961)
Total other income	6,112	2,881	6,640
Loss before taxes	(107,205)	(22,191)	(45,694)
Income taxes			79
Net loss	\$ (107,205)	\$ (22,191)	\$ (45,773)
Net loss per common share:			
Basic and diluted	\$ (2.84)	\$ (0.60)	\$ (1.26)
Shares used in the calculation of net loss per common share:			
Basic and diluted	37,722	36,763	36,201

See accompanying notes.

Table of Contents**NEUROCRINE BIOSCIENCES, INC.****Consolidated Statements of Stockholders Equity**

	Common Stock		Additional Paid-in Capital	Deferred Compensation	Notes Receivable from Stockholders	Accumulated Other Comprehensive Income (loss)	Accumulated Deficit	Total Stockholders Equity
	Shares	Amount						
	(In thousands)							
BALANCE AT DECEMBER 31, 2003	35,312	\$ 35	\$ 622,526	\$ (784)	\$ (139)	\$ 1,664	\$ (232,182)	\$ 391,120
Net loss							(45,773)	(45,773)
Unrealized loss on short-term investments						(3,572)		(3,572)
Comprehensive loss								(49,345)
Issuance of common stock for option exercises	268	1	4,763					4,764
Tax benefit of stock options			236					236
Issuance of common stock pursuant to the Employee Stock Purchase Plan	47		1,999					1,999
Issuance of common stock, related to royalty stream purchase	803	1	44,999					45,000
Reversal of offering expenses			50					50
Amortization of deferred compensation, net			61	472				533
Buyout of minority interest in Science Park Center, LLC			(600)					(600)
Issuance of common stock for exercise of warrants	103							
Stockholder note forgiveness					70			70
BALANCE AT DECEMBER 31, 2004	36,533	37	674,034	(312)	(69)	(1,908)	(277,955)	393,827
Net loss							(22,191)	(22,191)
Unrealized loss on short-term investments						404		404
Comprehensive loss								(21,787)
	529		14,457					14,457

Issuance of common stock for option exercises								
Issuance of common stock pursuant to the Employee Stock Purchase Plan	70		2,514					2,514
Amortization of deferred compensation, net			98	312				410
Vesting acceleration of unvested options (Note 6)			614					614
Stockholder note forgiveness						69		69
<b>BALANCE AT DECEMBER 31, 2005</b>	<b>37,132</b>	<b>37</b>	<b>691,717</b>			<b>(1,504)</b>	<b>(300,146)</b>	<b>390,104</b>
Net loss							(107,205)	(107,205)
Unrealized gain on short-term investments						1,603		1,603
Comprehensive loss								(105,602)
Share-based compensation			14,365					14,365
Issuance of common stock for exercise of warrants	147		44					44
Issuance of common stock for option exercises	579	1	15,368					15,369
Issuance of common stock pursuant to the Employee Stock Purchase Plan	48		436					436
<b>BALANCE AT DECEMBER 31, 2006</b>	<b>37,906</b>	<b>\$ 38</b>	<b>\$ 721,930</b>	<b>\$</b>	<b>\$</b>	<b>\$ 99</b>	<b>\$ (407,351)</b>	<b>\$ 314,716</b>

See accompanying notes.

**Table of Contents****NEUROCRINE BIOSCIENCES, INC.****Consolidated Statements of Cash Flows**

	<b>Years Ended December 31,</b>		
	<b>2006</b>	<b>2005</b>	<b>2004</b>
	<b>(In thousands)</b>		
<b>CASH FLOW FROM OPERATING ACTIVITIES</b>			
Net loss	\$ (107,205)	\$ (22,191)	\$ (45,773)
Adjustments to reconcile net loss to net cash used in operating activities:			
Depreciation and amortization	10,566	10,094	7,081
Loss on sale/abandonment of assets	473		136
Deferred revenues	(6,537)	(23,137)	(38,233)
Deferred expenses			1,000
Loan forgiveness on notes receivable	50	119	200
Non-cash compensation expense	14,365	1,025	533
Change in operating assets and liabilities:			
Accounts receivable and other current assets	(4,812)	6,444	5,955
Other non-current assets	(476)	(636)	(982)
Other non-current liabilities	(43)	1,383	1,244
Accounts payable and accrued liabilities	(5,715)	(3,895)	(31,149)
Net cash used in operating activities	(99,334)	(30,794)	(99,988)
<b>CASH FLOW FROM INVESTING ACTIVITIES</b>			
Purchases of short-term investments	(64,044)	(382,829)	(543,722)
Sales/maturities of short-term investments	186,910	399,971	645,049
Deposits and restricted cash	525	(525)	20,289
Purchase of prepaid royalty stream			(50,000)
Purchases of property and equipment, net	(3,110)	(7,235)	(53,147)
Net cash provided by investing activities	120,281	9,382	18,469
<b>CASH FLOW FROM FINANCING ACTIVITIES</b>			
Issuance of common stock	15,849	16,970	6,763
Proceeds received from debt			94,570
Principal payments on debt	(5,763)	(6,722)	(64,877)
Tax benefit from exercise of stock options			236
Payments received on notes receivable from employees		85	
Net cash provided by financing activities	10,086	10,333	36,692
Net increase (decrease) in cash and cash equivalents	31,033	(11,079)	(44,827)
Cash and cash equivalents at beginning of the year	49,948	61,027	105,854
Cash and cash equivalents at end of the year	\$ 80,981	\$ 49,948	\$ 61,027

**SUPPLEMENTAL DISCLOSURES**

Edgar Filing: NEUROCRINE BIOSCIENCES INC - Form 10-K

Supplemental disclosures of cash flow information:

Interest paid	\$	3,694	\$	4,454	\$	1,331
Taxes paid	\$		\$		\$	
Stock issued for prepaid royalty	\$		\$		\$	45,000

See accompanying notes.

F-6

---

**Table of Contents**

**NEUROCRINE BIOSCIENCES, INC.**

**NOTES TO THE CONSOLIDATED FINANCIAL STATEMENTS**

**December 31, 2006**

**NOTE 1. ORGANIZATION AND SUMMARY OF SIGNIFICANT ACCOUNTING POLICIES**

**Business Activities.** Neurocrine Biosciences, Inc. (the Company or Neurocrine) incorporated in California in 1992 and reincorporated in Delaware in 1996. The Company discovers, develops and intends to commercialize drugs for the treatment of neurological and endocrine-related diseases and disorders. The Company's product candidates address some of the largest pharmaceutical markets in the world, including insomnia, anxiety, depression, various female and male health disorders, diabetes and other neurological and endocrine related diseases and disorders.

In May 1997, the Company along with two unrelated parties formed Science Park Center LLC (Science Park) in order to construct an office and laboratory facility which was subsequently leased by the Company. Science Park is a California limited liability company, of which the Company, prior to April 2003, owned only a nominal minority interest. The Company became the majority owner of Science Park effective April 1, 2003, and acquired the remaining interest in Science Park during 2004.

Other subsidiaries of the Company include Neurocrine Continental, Inc. (formerly Neurocrine Commercial Operations, Inc.) a Delaware corporation and wholly owned subsidiary of the Company, which was established to support the sales operations beginning in 2005; Neurocrine International LLC, a Delaware limited liability company in which the Company holds a 99% ownership interest and Science Park holds a 1% interest, and Neurocrine HQ Inc., a Delaware corporation and wholly owned subsidiary of the Company, both of which are primarily inactive.

**Principles of consolidation.** The consolidated financial statements include the accounts of Neurocrine as well as its wholly owned subsidiaries. We do not have any significant interests in any variable interest entities. All intercompany transactions and balances have been eliminated in consolidation.

**Use of Estimates.** The preparation of financial statements in conformity with accounting principles generally accepted in the United States requires management to make estimates and assumptions that affect the amounts reported in the financial statements and the accompanying notes. Actual results could differ from those estimates.

**Cash Equivalents.** The Company considers all highly liquid investments with a maturity of three months or less when purchased to be cash equivalents.

**Short-Term Investments Available-for-Sale.** In accordance with SFAS No. 115, Accounting for Certain Debt and Equity Securities, short-term investments are classified as available-for-sale. Available-for-sale securities are carried at fair value, with the unrealized gains and losses reported in other comprehensive income (loss). The amortized cost of debt securities in this category is adjusted for amortization of premiums and accretion of discounts to maturity. Such amortization is included in interest income. Realized gains and losses and declines in value judged to be other-than-temporary, if any, on available-for-sale securities are included in other income or expense. The cost of securities sold is based on the specific identification method. Interest and dividends on securities classified as available-for-sale are included in interest income.

**Concentration of Credit Risk.** Financial instruments that potentially subject the Company to concentrations of credit risk consist primarily of cash, cash equivalents and short-term investments. The Company has established guidelines to limit its exposure to credit expense by placing investments with high credit quality financial institutions, diversifying its investment portfolio and placing investments with maturities that maintain safety and liquidity.

***Collaboration Agreements.*** During the years ended December 31, 2006, 2005 and 2004, collaborative research and development agreements accounted for substantially all of the Company's revenue.

F-7

---



**Table of Contents**

**NEUROCRINE BIOSCIENCES, INC.**

**NOTES TO THE CONSOLIDATED FINANCIAL STATEMENTS (Continued)**

***Property and Equipment.*** Property and equipment are stated at cost and depreciated over the estimated useful lives of the assets using the straight-line method. Building costs are depreciated over an average estimated useful life of 25 years and equipment is over three to seven years.

***Industry Segment and Geographic Information.*** The Company operates in a single industry segment the discovery and development of therapeutics for the treatment of neurological and endocrine related diseases and disorders. The Company had no foreign operations for the years ended December 31, 2006, 2005 and 2004.

***Other Non-Current Assets.*** Includes \$5.1 million and \$4.2 million, respectively, of mutual fund investments related to the Company's nonqualified deferred compensation plan for certain employees as of December 31, 2006 and 2005, respectively. Net unrealized gains related to these mutual funds were approximately \$712,000 and \$478,000 as of December 31, 2006 and December 31, 2005, respectively. Additionally, the Company has recorded a liability for these deferred compensation investments in other liabilities.

The participants in the deferred compensation plan may select from a variety of investment options and have the ability to make investment changes on a daily basis. A participant may elect to receive all or a portion of his or her deferred compensation on a fixed payment date of his or her choosing and may delay that fixed date, subject to plan limitations. The Board of Directors may, at its sole discretion, suspend or terminate the plan.

Other non-current assets also includes \$315,000 and \$483,000 of notes receivable from employees as of December 31, 2006 and 2005, respectively. The notes are secured by real property.

***Impairment of Long-Lived Assets.*** In accordance with SFAS No. 144, Accounting for the Impairment or Disposal of Long-Lived Assets, if indicators of impairment exist, the Company assesses the recoverability of the affected long-lived assets by determining whether the carrying value of such assets can be recovered through undiscounted future operating cash flows. If the carrying amount is not recoverable, the Company measures the amount of any impairment by comparing the carrying value of the asset to the present value of the expected future cash flows associated with the use of the asset.

The Company carries as a long-lived asset on its balance sheet a prepaid royalty arising from its acquisition in February 2004 of Wyeth's financial interest in the Company's lead drug candidate, indiplon for insomnia. The Company's current and historical operating and cash flow losses and the action letters on indiplon from the Food and Drug Administration (FDA) are indicators of impairment for the prepaid royalty. However, the Company believes the future cash flows to be realized from the prepaid royalty will exceed the asset's carrying value. The Company intends to pursue approvals of indiplon for both sleep onset and maintenance and to seek a commercialization partner. Accordingly, the Company has not recognized any impairment losses through December 31, 2006. However, events both within and outside of the Company's control, such as competition from other insomnia therapeutic agents, disease prevalence, further FDA actions related to indiplon, the Company's ability to partner indiplon, insomnia market dynamics and general market conditions may have an impact on the Company's ability to recover the carrying value of this asset in the future.

***Fair Value of Financial Instruments.*** Financial instruments, including cash and cash equivalents, accounts receivable, accounts payable, and accrued liabilities, are carried at cost, which management believes approximates fair value because of the short-term maturity of these instruments.

**Revenue Recognition.** Revenues under collaborative research agreements are recognized as research costs and are incurred over the period specified in the related agreement or as the services are performed. These agreements are on a best-efforts basis and do not require scientific achievement as a performance obligation and provide for payment to be made when costs are incurred or the services are performed. All fees received from the Company's collaborative partners are nonrefundable. Upfront, nonrefundable payments for license fees and advance payments for sponsored research revenues received in excess of amounts earned are classified as deferred revenue and recognized as income over the contract or development period. Estimating the duration of the development period includes continual assessment of development stages and regulatory requirements. Milestone

**Table of Contents**

**NEUROCRINE BIOSCIENCES, INC.**

**NOTES TO THE CONSOLIDATED FINANCIAL STATEMENTS (Continued)**

payments are recognized as revenue upon achievement of pre-defined scientific events, which requires substantive effort, and for which achievement of the milestone was not readily assured at the inception of the agreement.

License fees are received in exchange for a grant to use the Company's proprietary technologies on an as-is basis for the term of the collaborative agreement. Milestones are received for specific scientific achievements determined at the beginning of the collaboration. These achievements are substantive and are based on the success of scientific efforts.

**Comprehensive Income.** Comprehensive income is calculated in accordance with SFAS No. 130, Comprehensive Income. SFAS No. 130 requires the disclosure of all components of comprehensive income, including net income and changes in equity during a period from transactions and other events and circumstances generated from non-owner sources. The Company's other comprehensive income/loss consisted of unrealized gains and losses on short-term investments and is reported in the statements of stockholders' equity.

**Research and Development Expenses.** Research and development (R&D) expenses include related salaries, contractor fees, clinical trial costs, facilities costs, administrative expenses and allocations of corporate costs. All such costs are charged to R&D expense as incurred. These expenses result from the Company's independent R&D efforts as well as efforts associated with collaborations and in-licensing arrangements. In addition, the Company funds R&D at other companies and research institutions under agreements, which are generally cancelable. The Company reviews and accrues clinical trial expenses based on work performed, which relies on estimates of total costs incurred based on patient enrollment, completion of patient studies and other events. The Company follows this method since reasonably dependable estimates of the costs applicable to various stages of a research agreement or clinical trial can be made. Accrued clinical costs are subject to revisions as trials progress to completion. Revisions are charged to expense in the period in which the facts that give rise to the revision become known.

**Restructuring.** During the third quarter of 2006, the Company eliminated its entire sales force and also reduced its research and development and general and administrative staff in San Diego by approximately 100 employees. Pursuant to SFAS No. 146, Accounting for Costs Associated with Exit or Disposal Activities, the Company recorded a charge of approximately \$9.5 million in the third quarter of 2006 related to this reduction in workforce, of which \$2.8 million is included in research and development expense and \$6.7 million is included in sales, general and administrative expense. Substantially all costs were paid out in cash during 2006. The Company completed the employee termination activities and no further expenses related to this reduction in workforce are anticipated.

**Share-Based Compensation.** Prior to January 1, 2006, the Company accounted for share-based compensation under the recognition and measurement principles of Accounting Principles Board Opinion No. 25, Accounting for Stock Issued to Employees (APB 25). Therefore, the Company measured compensation expense for its share-based compensation using the intrinsic value method, that is, as the excess, if any, of the fair market value of the Company's stock at the grant date over the amount required to be paid to acquire the stock, and provided the disclosures required by SFAS 123, Accounting for Stock-Based Compensation (SFAS 123) and SFAS 148, Accounting for Stock-Based Compensation-Transition and Disclosure (SFAS 148).

Effective January 1, 2006, the Company began recording compensation expense associated with stock options and other equity-based compensation in accordance with SFAS 123R, using the modified prospective transition method and therefore has not restated results for prior periods. Under the modified prospective transition method, share-based compensation expense for 2006 includes 1) compensation expense for all share-based awards granted on or after January 1, 2006 as determined based on the grant-date fair value estimated in accordance with the provisions of

SFAS 123R and 2) compensation expense for share-based compensation awards granted prior to, but not yet vested as of January 1, 2006, based on the grant date fair value estimated in accordance with the original provisions of SFAS 123. The Company recognizes compensation expense on a straight-line basis over the requisite service period of the award, which is generally four years; however, certain provisions in the Company's equity compensation plans provide for shorter vesting periods under certain circumstances.

Table of Contents**NEUROCRINE BIOSCIENCES, INC.****NOTES TO THE CONSOLIDATED FINANCIAL STATEMENTS (Continued)**

**Net Loss Per Share.** The Company computes net loss per share in accordance with SFAS No. 128, Earnings Per Share. Under the provisions of SFAS No. 128, basic net income (loss) per share is computed by dividing the net income (loss) for the period by the weighted average number of common shares outstanding during the period. Diluted net income (loss) per share is computed by dividing the net income (loss) for the period by the weighted average number of common and common equivalent shares outstanding during the period. Potentially dilutive securities comprised of incremental common shares issuable upon the exercise of stock options and warrants, were excluded from historical diluted loss per share because of their anti-dilutive effect. Dilutive common stock equivalents would include the dilutive effects of common stock options and warrants for common stock. Potentially dilutive securities totaled 1.0 million, 1.5 million and 2.0 million for the years ended December 31, 2006, 2005 and 2004, respectively, and were excluded from the diluted earnings per share because of their anti-dilutive effect.

**Proforma Financial Information.** For stock options granted prior to the adoption of SFAS 123R, the following table illustrates the pro forma effect on net income and earnings per common share as if the Company had applied the fair value recognition provisions of SFAS 123 in determining stock-based compensation (in thousands, except loss per share data):

	<b>Years Ended December 31,</b>	
	<b>2005</b>	<b>2004</b>
Net loss, as reported	\$ (22,191)	\$ (45,773)
Stock option expense	(38,472)	(24,368)
Pro forma net loss	\$ (60,663)	\$ (70,141)
Loss per share:		
Basic and diluted as reported	\$ (0.60)	\$ (1.26)
Basic and diluted proforma	\$ (1.65)	\$ (1.94)

**Impact of Recently Issued Accounting Standards.** In July 2006, the FASB issued FASB Interpretation No. 48, Accounting for Uncertainty in Income Taxes, an interpretation of FASB Statement No. 109 (FIN 48). FIN 48 clarifies the accounting for uncertainty in income taxes by prescribing the recognition threshold a tax position is required to meet before being recognized in the financial statements. It also provides guidance on derecognition, classification, interest and penalties, accounting in interim periods, disclosure, and transition. FIN 48 is effective for fiscal years beginning after December 15, 2006 and is required to be adopted by the Company in 2007. The Company does not expect the adoption of FIN 48 to have a material impact on its consolidated results of operations and financial condition.

In September 2006, the FASB issued SFAS No. 157, Fair Value Measurements (SFAS 157). SFAS 157 provides guidance for using fair value to measure assets and liabilities. It also responds to investors' requests for expanded information about the extent to which companies measure assets and liabilities at fair value, the information used to

measure fair value, and the effect of fair value measurements on earnings. SFAS 157 applies whenever other standards required (or permit) assets or liabilities to be measured at fair value, and does not expand the use of fair value in any new circumstances. SFAS 157 is effective for financial statements issued for fiscal years beginning after November 15, 2007. The Company is currently evaluating the effect that the adoption of SFAS 157 will have on its consolidated results of operations and financial condition and is not yet in a position to determine such effects.

In September 2006, the Securities and Exchange Commission issued Staff Accounting Bulletin No. 108, *Considering the Effects of Prior Year Misstatements when Quantifying Misstatements in Current Year Financial Statements* (SAB 108). SAB 108 provides guidance on the consideration of the effects of prior year misstatements in quantifying current year misstatements for the purpose of a materiality assessment. SAB 108 establishes an approach that requires quantification of financial statement errors based on the effects of each of the company's

**Table of Contents****NEUROCRINE BIOSCIENCES, INC.****NOTES TO THE CONSOLIDATED FINANCIAL STATEMENTS (Continued)**

balance sheet and statement of operations and the related financial statement disclosures. Early application of the guidance in SAB 108 is encouraged in any report for an interim period of the first fiscal year ending after November 15, 2006, and will be adopted by the Company in the first quarter of fiscal 2007. The Company does not expect the adoption of SAB 108 to have a material impact on its consolidated results of operations and financial condition.

**NOTE 2. SHORT-TERM INVESTMENTS**

Cash, cash equivalents, and short-term investments totaled \$182.6 million and \$273.1 million as of December 31, 2006 and 2005, respectively. The following is a summary of short-term investments classified as available-for-sale securities (in thousands):

	<b>Amortized Cost</b>	<b>Gross Unrealized Gains</b>	<b>Gross Unrealized Losses</b>	<b>Estimated Fair Value</b>
<b>December 31, 2006</b>				
U.S. Government securities	\$ 44,454	\$	\$ (281)	\$ 44,173
Corporate debt securities	56,032		(332)	55,700
Other debt securities	1,750			1,750
Total investments	\$ 102,236	\$	\$ (613)	\$ 101,623
<b>December 31, 2005</b>				
U.S. Government securities	\$ 72,446	\$	\$ (1,150)	\$ 71,296
Corporate debt securities	141,725	1	(732)	140,994
Short-term municipals	4,489			4,489
Other debt securities	6,442		(101)	6,341
Total investments	\$ 225,102	\$ 1	\$ (1,983)	\$ 223,120

The amortized cost and estimated fair value of debt securities by contractual maturity at December 31, 2006 are shown below (in thousands):

	<b>Amortized Cost</b>	<b>Estimated Fair Value</b>
Due in 12 months or less	\$ 67,370	\$ 66,978
Due between 12 months and 14 months	34,866	34,645
	\$ 102,236	\$ 101,623

The following table presents certain information related to sales of available-for-sale securities (in thousands):

	<b>Years Ended December 31,</b>		
	<b>2006</b>	<b>2005</b>	<b>2004</b>
Proceeds from sales	\$ 186,910	\$ 399,971	\$ 645,049
Gross realized gains on sales	\$	\$	\$ 1,110
Gross realized losses on sales	\$	\$ (975)	\$ (139)

F-11

---



**Table of Contents****NEUROCRINE BIOSCIENCES, INC.****NOTES TO THE CONSOLIDATED FINANCIAL STATEMENTS (Continued)****NOTE 3. PROPERTY AND EQUIPMENT**

Property and equipment at December 31, 2006 and 2005 consist of the following (in thousands):

	<b>2006</b>	<b>2005</b>
Land	\$ 25,370	\$ 25,370
Buildings	56,884	56,765
Furniture and fixtures	3,187	3,166
Equipment	43,414	41,376
	128,855	126,677
Less accumulated depreciation	(37,477)	(27,370)
Property and equipment, net	\$ 91,378	\$ 99,307

For the years ended December 31, 2006, 2005 and 2004, depreciation expense was \$10.6 million, \$10.1 million and \$7.1 million, respectively. During 2006, the Company realized a loss of approximately \$473,000 related to disposal of sales force related equipment.

**NOTE 4. ACCRUED LIABILITIES**

Accrued liabilities at December 31, 2006 and 2005 consist of the following (in thousands):

	<b>2006</b>	<b>2005</b>
Accrued employee benefits	\$ 5,391	\$ 6,362
Accrued development costs	3,438	6,599
Other accrued liabilities	3,585	4,934
	\$ 12,414	\$ 17,895

**NOTE 5. COMMITMENTS AND CONTINGENCIES**

**Debt.** In October 2004, the Company repaid the outstanding amount under a construction loan which was replaced with a \$49.5 million loan secured by a first mortgage on the Company's corporate facility. The mortgage bears interest at a rate of 6.48% per annum, and principal is being amortized over a period of thirty years, with a balloon principal payment of \$42.0 million due on the tenth anniversary of the loan. Monthly principal and interest payments total \$312,000. At December 31, 2006, \$48.3 million was outstanding under this loan agreement. Additionally, the Company is required by the lender to maintain a \$5.0 million letter of credit with a local bank as security for the loan.

This letter of credit is further secured by a mandatory deposit of \$5.2 million with the bank providing the letter of credit. This deposit is recorded in restricted cash in the consolidated balance sheet at December 31, 2006.

The Company has also entered into equipment financing arrangements with lenders to finance equipment purchases, which expire on various dates through the year 2008 and bear interest at rates between 6.3% and 7.3%. The debt obligations are repayable in monthly installments. Amounts outstanding under these loans at December 31, 2006 and 2005 totaled \$5.3 million and \$10.6 million respectively.

**Rent Expense.** Rent expense was \$1.2 million, \$1.0 million and \$2.7 million for the years ended December 31, 2006, 2005 and 2004, respectively.

**Licensing and Research Agreements.** The Company has entered into licensing agreements with various universities and research organizations, which are generally cancelable at the option of the Company with terms ranging from 0-180 days written notice. Under the terms of these agreements, the Company has received licenses to research tools, know-how and technology claimed, in certain patents or patent applications. The Company is

**Table of Contents****NEUROCRINE BIOSCIENCES, INC.****NOTES TO THE CONSOLIDATED FINANCIAL STATEMENTS (Continued)**

required to pay fees, milestones and/or royalties on future sales of products employing the technology or falling under claims of a patent, and some of the agreements require minimum royalty payments. Some of the agreements also require the Company to pay expenses arising from the prosecution and maintenance of the patents covering the licensed technology. The Company continually reassesses the value of the license agreements and cancels them when research efforts are discontinued on these programs. If all licensed and research candidates are successfully developed, the Company may be required to pay milestone payments of approximately \$33.5 million over the lives of these agreements, in addition to royalties on sales of the affected products at rates ranging up to 6%. Due to the uncertainties of the development process, the timing and probability of the milestone and royalty payments cannot be accurately estimated.

**Related Party Transactions.** The Company has entered into agreements with a vendor to provide research support. An officer of this vendor also serves as a director of the Company. During 2005 and 2004, the Company paid approximately \$950,000 and \$950,000, respectively, to the vendor for these research support services. Several of the Company's officers have entered into agreements for estate tax planning. All of these officers have agreed to indemnify the Company for any payroll withholding taxes and related costs and expenses that may result from these estate tax planning initiatives.

**Clinical Development Agreements.** The Company has entered into agreements with various vendors for the pre-clinical and clinical development of its product candidates, which are generally cancelable at the option of the Company for convenience or performance, with terms ranging from 0-180 days written notice. Under the terms of these agreements, the vendors provide a variety of services including conducting pre-clinical development research, manufacturing clinical compounds, enrolling patients, recruiting patients, monitoring studies, data analysis and regulatory filing assistance. Payments under these agreements typically include fees for services and reimbursement of expenses. Some agreements also may include incentive bonuses for time-sensitive activities. The timing of payments due under these agreements were estimated based on current schedules of clinical studies in progress.

Payment schedules for commitments and contractual obligations at December 31, 2006 are as follows (in thousands):

<b>Fiscal Year</b>	<b>Mortgage Debt</b>	<b>Equipment Debt</b>	<b>Operating Leases</b>	<b>Licenses and Research Agreements</b>	<b>Clinical Development Agreements</b>
2007	\$ 635	\$ 3,854	\$ 201	\$ 1,098	\$ 11,375
2008	678	1,486	133	95	3,888
2009	723		36	75	299
2010	771			75	
2011	823			75	
Thereafter	44,671			75	
<b>Total minimum payments</b>	<b>\$ 48,301</b>	<b>\$ 5,340</b>	<b>\$ 370</b>	<b>\$ 1,493</b>	<b>\$ 15,562</b>

**NOTE 6. SHARE-BASED COMPENSATION**

***Share-Based Compensation Plans.*** The Company grants stock options, restricted stock units and stock bonuses (collectively, share-based compensation) to its employees and directors under the 2003 Incentive Stock Plan, as amended (the 2003 Plan) and grants stock options to certain employees pursuant to Employment Commencement Nonstatutory Stock Options. Until June 30, 2006, eligible employees could also purchase shares of the Company's common stock at 85% of the fair market value on the last day of each six-month offering period under the Company's Amended and Restated Employee Stock Purchase Plan. The benefits provided under these Plans are share-based compensation subject to the provisions of SFAS 123R.

F-13

---

Table of Contents**NEUROCRINE BIOSCIENCES, INC.****NOTES TO THE CONSOLIDATED FINANCIAL STATEMENTS (Continued)**

Since 1992, the Company has authorized a total of 13.7 million shares of common stock for issuance pursuant to its 1992 Plan, 1996 Director Option Plan, 1997 Northwest Neurologic, Inc. Restated Incentive Stock Plan, 2001 Plan, several Employment Commencement Nonstatutory Stock Option Agreements and the 2003 Plan (collectively, the Option Plans). The Option Plans provide for the grant of stock options, restricted stock, restricted stock units, and stock bonuses to officers, directors, employees, and consultants of the Company. Currently, all new grants of stock options are made from the 2003 Plan or through Employment Commencement Nonstatutory Stock Option Agreements. As of December 31, 2006, of the 13.7 million shares reserved for issuance under the Option Plans, 1.5 million of these shares were originally reserved for issuance pursuant to the terms of the Company's 1992 Plan, 1996 Director Stock Option Plan and 2001 Plan and would currently be available for issuance but for the Company's determination in 2003 not to make further grants under these plans; 5.7 million were issued upon exercise of stock options previously granted or pursuant to restricted stock or stock bonus awards; 5.2 million were subject to outstanding options and restricted stock units; and 1.3 million remained available for future grant under the 2003 Plan. Share awards made under the 2003 Plan that are later cancelled due to forfeiture or expiration return to the pool available for future grants.

The Company issues new shares upon the exercise of stock options, the issuance of stock bonus awards and vesting of restricted stock units.

As a result of the adoption of SFAS 123R, the Company's net loss for the year ended December 31, 2006 includes \$14.6 million of compensation expense related to the Company's share-based compensation awards. The compensation expense related to the Company's share-based compensation arrangements is recorded as components of sales, general and administrative expense and research and development expense (\$8.3 million and \$6.3 million, respectively for the year ended December 31, 2006). SFAS 123R requires that cash flows resulting from tax deductions in excess of the cumulative compensation cost recognized for options exercised (excess tax benefits) be classified as cash inflows provided by financing activities and cash outflows used in operating activities. Due to the Company's net loss position, no tax benefits have been recognized in the cash flow statement.

In November 2005, the FASB issued Staff Position (FSP) No. FAS 123(R)-3, *Transition Election Related to Accounting for Tax Effects of Share-Based Payment Awards* (FSP 123R-3). Neurocrine has elected to adopt the alternative transition method provided in the FSP 123R-3 for calculating the tax effects of stock-based compensation pursuant to SFAS 123R. The alternative transition method includes simplified methods to establish the beginning balance of the APIC pool related to the tax effects of employee stock-based compensation, and to determine the subsequent impact on the APIC pool and Consolidated Statements of Cash Flows of the tax effects of employee stock-based compensation awards that are outstanding upon adoption of SFAS 123R.

***Vesting Provisions of Share-Based Compensation.*** Stock options granted under the Option Plans primarily have terms of up to ten years from the date of grant, and generally vest over a three to four-year period. Stock bonuses granted under the Option Plans generally have vesting periods ranging from two to four years. Restricted stock units granted under the Option Plans have vesting periods of three years. The expense recognized under SFAS 123R is generally recognized ratably over the vesting period. However, certain retirement provisions in the Option Plans provide that employees who are age 55 or older and have five or more years of service with the Company will be entitled to accelerated vesting of all of the unvested share-based compensation awards upon retirement from the Company. In these cases, share-based compensation expense may be recognized over a shorter period of time, and in some cases the entire share-based compensation expense may be recognized upon grant of the share-based

compensation award. Effective January 1, 2006, the maximum contractual term for all options granted from the 2003 Plan was reduced to seven years.

On November 7, 2005, the Company accelerated vesting of all unvested stock options to purchase shares of common stock that were held by then-current employees and had an exercise price per share equal to or greater than \$50.00. Stock options to purchase approximately 472,000 shares of common stock were subject to this acceleration. The exercise prices and number of shares subject to the accelerated stock options were unchanged. The expense resulting from the acceleration was included in the pro forma results of operations for the fourth quarter of 2005

**Table of Contents****NEUROCRINE BIOSCIENCES, INC.****NOTES TO THE CONSOLIDATED FINANCIAL STATEMENTS (Continued)**

which were disclosed in the notes to the Company's consolidated financial statements for the year ended December 31, 2005 pursuant to SFAS 123. The acceleration of these stock options was undertaken to eliminate the future compensation expense of approximately \$10.5 million that the Company would have otherwise recognized under SFAS 123R in its future consolidated statements of operations.

**Stock Options.** The exercise price of all options granted during the years ended December 31, 2006, 2005 and 2004 was equal to the market value on the date of grant and, accordingly, no share-based compensation expense for such options is reflected in net income for the years ended December 31, 2005 and 2004 in accordance with APB 25. The estimated fair value of each option award granted was determined on the date of grant using the Black-Scholes option valuation model with the following weighted-average assumptions for option grants during the years ended December 31, 2006, 2005 and 2004:

	<b>Years Ended December 31,</b>		
	<b>2006</b>	<b>2005</b>	<b>2004</b>
Risk-free interest rate	4.6%	4.2%	3.6%
Expected volatility of common stock	62%	34%	40%
Dividend yield	0.0%	0.0%	0.0%
Expected option term	4.3 years	5.8 years	5.0 years

The risk-free interest rate assumption is based upon observed interest rates appropriate for the expected term of the Company's employee stock options. The expected volatility is based on the historical volatility of the Company's stock. The Company has not paid any dividends on common stock since its inception and does not anticipate paying dividends on its common stock in the foreseeable future. Except for options issued in the Tender Offer, the computation of the expected option term is based on a weighted-average calculation combining the average life of options that have already been exercised or cancelled with the estimated life of all unexercised options. Per Staff Accounting Bulletin 107, the Company used the simplified method to compute the expected option term for all options granted in the Tender Offer. The simplified method was used because the contractual life of the amended or exchanged options varied from approximately three to seven years due to the terms of the Tender Offer. The decrease in the expected option term from 2005 to 2006 is due to the decrease in the maximum term of the options granted after January 1, 2006 from ten years to seven years.

Share-based compensation expense recognized in the Consolidated Statement of Operations for the year ended December 31, 2006 is based on awards ultimately expected to vest, net of estimated forfeitures. SFAS 123R 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 for awards with monthly vesting terms were estimated to be 0% in 2006 based on historical experience. The effect of pre-vesting forfeitures for awards with monthly vesting terms has historically been negligible on the Company's recorded expense. Pre-vesting forfeitures for awards with annual vesting terms were estimated at 10% in 2006 based on historical employee turnover experience. The effect of the restructuring has been excluded from the historical review of employee turnover because it was a one-time event and also included minimal pre-vesting forfeitures. In the Company's pro forma information required under SFAS 123 for the periods prior to fiscal 2006, the Company accounted for forfeitures as they occurred. The Company's determination of fair value is affected by the Company's stock price as well as a number of assumptions that require judgment. The

weighted-average fair values of options granted during the years ended December 31, 2006, 2005 and 2004, estimated as of the grant date using the Black-Scholes option valuation model, was \$9.73, \$17.22 and \$21.25, respectively.

***Tender Offer.*** On September 26, 2006, the Company completed a Tender Offer (Offer) to holders of outstanding options to purchase its common stock under the 2003 Plan, 1992 Incentive Stock Plan (the 1992 Plan) and 2001 Stock Option Plan, as amended (the 2001 Plan). The Offer was for holders of options under the 2003 Plan to cancel their options in exchange for a lesser number of new options (at a two-for-one exchange ratio) to purchase shares of the Company's common stock issued under the 2003 Plan and for holders of options under the 1992 Plan



**Table of Contents****NEUROCRINE BIOSCIENCES, INC.****NOTES TO THE CONSOLIDATED FINANCIAL STATEMENTS (Continued)**

and 2001 Plan to cancel one-half of their options and amend their remaining options to purchase shares of the Company's common stock. The Offer was open to eligible employees and active consultants of the Company who held options with an exercise price of \$20.00 or higher per share as of September 25, 2006. Certain executives and members of the Board of Directors were not eligible to participate in the Offer. Approximately 2.0 million options were exchanged or amended resulting in approximately 1.0 million new or amended option grants and approximately 1.0 million cancelled option grants at the completion of the Offer. New or amended options under the Offer vest annually over a period of three years and have a weighted average exercise price of \$10.90. Share based compensation expense related to the Offer totaled approximately \$8.7 million and will be amortized over 3 years.

A summary of the status of the Company's stock option plans as of December 31, 2006 and of changes in options outstanding under the plans during the year ended December 31, 2006 is as follows (in thousands, except for weighted average exercise price and weighted average remaining contractual term data):

	<b>2006</b>		<b>2005</b>		<b>2004</b>	
	<b>Options</b>	<b>Weighted Average Exercise Price</b>	<b>Options</b>	<b>Weighted Average Exercise Price</b>	<b>Options</b>	<b>Weighted Average Exercise Price</b>
Outstanding at January 1	6,544	\$ 38.32	5,987	\$ 36.40	5,220	\$ 32.25
Granted/amended	1,609	16.87	1,321	43.14	1,138	52.66
Exercised	(578)	26.62	(560)	27.19	(269)	20.55
Canceled	(3,311)	42.36	(204)	45.38	(102)	47.44
Outstanding at December 31	4,264	\$ 28.49	6,544	\$ 38.32	5,987	\$ 36.40

<b>Range of Exercise Prices</b>	<b>Options Outstanding</b>			<b>Options Exercisable</b>		
	<b>Outstanding as of 12/31/06</b>	<b>Weighted Average Remaining Contractual Term (In Years)</b>	<b>Weighted Average Exercise Price</b>	<b>Exercisable as of 12/31/06</b>	<b>Weighted Average Exercise Price</b>	
\$ 1.51 to \$10.89	517	2.7	\$ 6.82	445	\$ 6.31	
\$10.90 to \$13.92	1,255	5.6	10.90	169	10.93	
\$13.93 to \$34.82	596	3.3	26.35	587	26.46	
\$34.83 to \$41.78	780	5.4	37.24	693	36.84	
\$41.79 to \$55.71	597	6.5	48.83	516	49.53	
\$55.72 to \$62.68	519	5.8	58.51	426	57.98	

\$ 1.51 to \$62.68	4,264	5.0	\$	28.49	2,836	\$	33.84
--------------------	-------	-----	----	-------	-------	----	-------

For the year ended December 31, 2006, share-based compensation expense related to stock options was \$13.5 million. As of December 31, 2006 and 2005, the fair value of unamortized compensation cost related to unvested stock option awards was approximately \$12.6 million and \$32.5 million, respectively. Unamortized compensation cost as of December 31, 2006 is expected to be recognized over a remaining weighted-average vesting period of 2.7 years. As of December 31, 2006, options exercisable have a weighted-average remaining contractual term of 5.1 years. The total intrinsic value, which is the difference between the exercise price and sale price of the Company's common stock on the date of sale, of stock option exercises during the years ended December 31, 2006, 2005, and 2004 was \$18.1 million, \$13.2 million and \$9.2 million, respectively. As of December 31, 2006 the total intrinsic value, which is the difference between the exercise price and closing price of the Company's common stock as of December 31, 2006 and 2005, of options outstanding and exercisable was \$1.9 million and \$1.8 million, respectively. Cash received from stock option exercises for the years ended

Table of Contents**NEUROCRINE BIOSCIENCES, INC.****NOTES TO THE CONSOLIDATED FINANCIAL STATEMENTS (Continued)**

December 31, 2006, 2005 and 2004 was \$15.4 million, \$14.5 million and \$5.4 million, respectively. For the year ended December 31, 2006, the weighted average fair value of options exercised was \$14.75.

**Restricted Stock Units.** Beginning in January 2006, certain employees are eligible to receive restricted stock units under the 2003 Plan. In accordance with SFAS 123R, the fair value of restricted stock units is estimated based on the closing sale price of the Company's common stock on the Nasdaq Global Select Market on the date of issuance. The total number of restricted stock awards expected to vest is adjusted by estimated forfeiture rates, which has been estimated at 0% based on historical experience of stock bonus awards. As of December 31, 2006, there is approximately \$8.8 million of unamortized compensation cost related to restricted stock units, which is expected to be recognized over a remaining weighted-average vesting period of 2.7 years. The restricted stock units, at the election of eligible employees, may be subject to deferred delivery arrangement. If restricted stock units are deferred, they are recorded as other long-term liabilities in the consolidated balance sheet and expense is adjusted based on the closing market price of the Company's stock each period. For the year ended December 31, 2006, share-based compensation expense related to restricted stock units was \$1.1 million.

A summary of the status of the Company's restricted stock units as of December 31, 2006 and of changes in restricted stock units outstanding under the plan during the year ended December 31, 2006 is as follows (in thousands, except for weighted average grant date fair value per unit):

	Number of Units	Weighted Average Grant Date Fair Value per Unit
Restricted stock units outstanding at December 31, 2005		\$
Restricted stock units granted	914	\$ 13.07
Restricted stock units cancelled	(18)	\$ 10.90
Restricted stock units outstanding at December 31, 2006	896	\$ 13.11
Restricted stock units vested at December 31, 2006	12	\$ 60.95

**Stock Bonus Awards.** The Company granted approximately 39,000 shares of its common stock pursuant to stock bonus awards between 2003 and 2005 from the 2003 Plan. Based upon the Company's closing stock price as of December 31, 2006, there was approximately \$52,000 of unamortized compensation cost related to these stock bonus awards on that date, representing approximately 4,900 shares of common stock, which is expected to be recognized over a remaining weighted-average vesting period of approximately 1.3 years. The common stock related to these awards has been recorded in the Company's deferred compensation plan and is recorded as other long-term liabilities in the consolidated balance sheet. Once in the deferred compensation plan, the related liability and expense for these stock bonus awards is adjusted to reflect the market value of the Company's stock for each reporting period.

**Employee Stock Purchase Plan.** The Company had reserved 725,000 shares of common stock for issuance under the 1996 Employee Stock Purchase Plan, as amended (the Purchase Plan). The Purchase Plan had a six-month contribution period with purchase dates of June 30 and December 31 each year. Effective January 1, 2006, the

Purchase Plan was amended such that the purchase price of common stock would be at 85% of the fair market value per share of common stock on the date on which the shares are purchased. As of June 30, 2006, 640,000 shares had been issued pursuant to the Purchase Plan. The Company recognized approximately \$77,000 in share-based compensation expense related to the purchase on June 30, 2006.

Effective July 1, 2006, the Company terminated the Purchase Plan. The termination was a result of a review of the Purchase Plan's effectiveness in providing long-term share ownership to the Company's employees. In addition, the Purchase Plan had an insufficient amount of shares available to allow full participation by employees.

**Warrants.** The Company has outstanding warrants to purchase 3,940 shares of common stock at \$52.05 that expire in December 2012.

Table of Contents**NEUROCRINE BIOSCIENCES, INC.****NOTES TO THE CONSOLIDATED FINANCIAL STATEMENTS (Continued)**

The following shares of common stock are reserved for future issuance at December 31, 2006 (in thousands):

Share based compensation plans	6,490
Warrants	4
Total	6,494

**NOTE 7. SIGNIFICANT COLLABORATIVE RESEARCH AND DEVELOPMENT AGREEMENTS**

*Pfizer.* In December 2002, the Company entered into an exclusive worldwide collaboration with Pfizer, Inc. (Pfizer) to complete the clinical development of, and to commercialize, indiplon for the treatment of insomnia. Under the terms of the agreement, Pfizer and Neurocrine collaborated in the completion of the indiplon Phase III clinical program. During 2005 and 2004, the Company was responsible for \$5.5 million and \$7.5 million, respectively, in development costs, and all other external collaboration costs were borne by Pfizer. During 2005, Pfizer supported the creation and operation of a 200-person Neurocrine sales force to detail Pfizer's antidepressant drug Zoloft® to psychiatrists in the United States. During 2003, the Company received an upfront license fee of \$100 million under the collaboration.

For the years ended December 31, 2006, 2005 and 2004, the Company recognized revenue of \$6.6 million, \$8.7 million and \$21.7 million, respectively, from the reimbursement of clinical development expenses under the Pfizer agreement. The Company also amortized into revenue \$6.5 million, \$20.7 million and \$34.8 million of the upfront license fee for the years ended December 31, 2006, 2005 and 2004, respectively. During 2005, the Company received a \$70.0 million milestone payment from Pfizer related to the FDA's accepting for review the NDA filings for the indiplon capsules and tablets. During 2004, the Company received \$20.5 million from Pfizer for certain clinical development milestones related to successful completion of Phase III studies for long-term administration and sleep maintenance of indiplon. The Company also recognized \$16.5 million and \$22.0 million from Pfizer during 2006 and 2005, respectively, as a sales force allowance for the building and operation of the Company's 200-person sales force.

On June 22, 2006 the Company and Pfizer agreed to terminate the collaboration and license agreements to develop and co-promote indiplon effective December 19, 2006. As a result, the Company reacquired all worldwide rights for indiplon capsules and tablets and is responsible for any further costs associated with development, registration, marketing and commercialization of indiplon.

The Company obtained rights to indiplon pursuant to a 1998 Sublicense and Development Agreement with DOV Pharmaceutical, Inc. (DOV) and is responsible for specified milestone payments and royalties to DOV on net sales under the license agreement. Wyeth licensed the indiplon technology to DOV in 1998 in exchange for milestone payments and royalties on future sales of indiplon. On February 26, 2004, the Company entered into several agreements with Wyeth and DOV pursuant to which the Company acquired Wyeth's financial interest in indiplon for approximately \$95.0 million, consisting of \$50.0 million in cash and \$45.0 million of the Company's common stock. The agreements among the Company, Wyeth and DOV provide that the Company will make milestone and royalty payments to DOV net of amounts that DOV would have been obligated to pay to Wyeth such that the Company will

retain all milestone, royalty and other payments on indiplon commercialization that would have otherwise been payable to Wyeth, effectively decreasing the Company's royalty obligation on sales of indiplon from six percent to three and one-half percent. This transaction was recorded as a prepaid royalty and will be amortized over the commercialization period of indiplon, based primarily upon total estimated indiplon sales. Additionally, the Company is responsible for specified milestone payments up to \$3.5 million to DOV Pharmaceutical under the license agreement, of which \$2.0 million was paid during 2004 and the balance will be payable upon commercialization of indiplon.

**GlaxoSmithKline.** In July 2001, the Company announced a worldwide collaboration with GlaxoSmithKline (GSK) to develop and commercialize CRF antagonists for psychiatric, neurological and gastrointestinal diseases.

**Table of Contents**

**NEUROCRINE BIOSCIENCES, INC.**

**NOTES TO THE CONSOLIDATED FINANCIAL STATEMENTS (Continued)**

Under the terms of this agreement, the Company and GSK will conduct a collaborative research program for up to five years and collaborate in the development of Neurocrine's current lead CRF compounds, as well as novel back-up candidates and second generation compounds identified through the collaborative research. In addition, the Company will be eligible to receive milestone payments as compounds progress through the research and development process, royalties on future product sales and co-promotion rights in the U.S. under some conditions. GSK may terminate the agreement at its discretion upon prior written notice to the Company. In such event, the Company may be entitled to certain payments and all product rights would revert to Neurocrine. For each of the years ended December 31, 2006, 2005 and 2004, the Company recognized \$9.1 million, \$2.5 million and \$7.8 million, respectively, in revenue under the GSK agreement. The sponsored research portion of this collaboration agreement ended in 2005. As of December 31, 2006, the Company has a \$7.0 million receivable from GSK related to milestones achieved for initiation of two Phase II proof of concept clinical trials for generalized social anxiety disorder and irritable bowel syndrome.

**NOTE 8. INCOME TAXES**

At December 31, 2006, the Company had Federal and California income tax net operating loss carry-forwards of approximately \$488.5 million and \$386.7 million, respectively. The Federal and California tax loss carry-forwards will begin to expire in 2010 and 2007, respectively, unless previously utilized. In addition, the Company has Federal and California research and development tax credit carry-forwards of \$22.1 million and \$15.6 million, respectively. The Federal research and development credit carry-forwards will begin to expire in 2007 unless previously utilized. The California research and development credit carry-forwards carry forward indefinitely. The Company also has Federal Alternative Minimum Tax credit carry-forwards of approximately \$256,000, which will carry-forward indefinitely. At December 31, 2006, approximately \$88.3 million of the net operating loss carry-forwards relate to stock option exercises, which will result in an increase to additional paid-in capital and a decrease in income taxes payable at the time when the tax loss carry-forwards are utilized.

Pursuant to Internal Revenue Code Sections 382 and 383, annual use of the Company's net operating loss and credit carry-forwards may be limited because of cumulative changes in ownership of more than 50%.

Significant components of the Company's deferred tax assets as of December 31, 2006 and 2005 relate primarily to its net operating loss and tax credit carry-forwards. A valuation allowance of \$210.6 million and \$165.1 million at December 31, 2006 and 2005, respectively, has been recognized to offset the net deferred tax

**Table of Contents****NEUROCRINE BIOSCIENCES, INC.****NOTES TO THE CONSOLIDATED FINANCIAL STATEMENTS (Continued)**

assets as realization of such assets is uncertain. Amounts are shown in thousands as of December 31, of the respective years (in thousands):

	<b>2006</b>	<b>2005</b>
Deferred tax assets:		
Net operating loss carry-forwards	\$ 186,300	\$ 144,200
Tax credit carry-forwards	32,300	26,600
Capitalized research and development	5,100	5,400
Deferred compensation	2,700	2,800
FAS 123R Expense	4,100	
Unrealized losses on investments	600	600
Deferred revenue		2,600
Other	1,200	1,200
<b>Total deferred tax assets</b>	<b>232,300</b>	<b>183,400</b>
Deferred tax liabilities:		
Investment in LLC	11,300	10,000
Intangibles	7,200	4,600
Fixed assets	3,200	3,700
<b>Total deferred tax liabilities</b>	<b>21,700</b>	<b>18,300</b>
<b>Net deferred tax asset</b>	<b>210,600</b>	<b>165,100</b>
Valuation allowance	(210,600)	(165,100)
<b>Net deferred tax assets</b>	<b>\$</b>	<b>\$</b>

The provision for income taxes on earnings subject to income taxes differs from the statutory Federal rate at December 31, 2006, 2005 and 2004, due to the following (in thousands):

	<b>2006</b>	<b>2005</b>	<b>2004</b>
Federal income taxes at 35%	\$ (37,522)	\$ (7,767)	\$ (16,020)
State income tax, net of Federal benefit	(6,170)	(1,077)	(4,151)
Tax effect on non-deductible expenses and credits	(1,854)	(112)	(2,676)
Increase in valuation allowance	45,546	8,956	22,926
	<b>\$</b>	<b>\$</b>	<b>\$ 79</b>



The provision for income taxes for the year ended December 31, 2004 was for current federal taxes.

**NOTE 9. RETIREMENT PLAN**

The Company has a 401(k) defined contribution savings plan (401(k) Plan). The 401(k) Plan is for the benefit of all qualifying employees and permits voluntary contributions by employees up to 60% of base salary limited by the IRS-imposed maximum. The Company matches 50% of employee contributions up to 6% of eligible compensation, with cliff vesting over four years. Employer contributions were \$1,152,000, \$1,069,000 and \$750,000 for the years ended December 31, 2006, 2005, and 2004, respectively.

F-20

---

Table of Contents**NEUROCRINE BIOSCIENCES, INC.****NOTES TO THE CONSOLIDATED FINANCIAL STATEMENTS (Continued)****NOTE 10. SELECTED QUARTERLY FINANCIAL DATE (UNAUDITED)**

The following is a summary of the quarterly results of operations for the years ended December 31, 2006 and 2005 (unaudited, in thousands, except for earnings (loss) per share data):

	<b>Mar 31</b>	<b>Quarters Ended</b>			<b>Year Ended</b>
		<b>Jun 30</b>	<b>Sep 30</b>	<b>Dec 31</b>	<b>Dec 31</b>
<b>2005</b>					
Revenues	\$ 11,864	\$ 33,169	\$ 64,745	\$ 14,111	\$ 123,889
Operating expenses	31,211	39,421	39,624	38,705	148,961
Net (loss) income	(18,830)	(5,604)	26,151	(23,908)	(22,191)
Net (loss) income per share:					
Basic	\$ (0.51)	\$ (0.15)	\$ 0.71	\$ (0.65)	\$ (0.60)
Diluted	\$ (0.51)	\$ (0.15)	\$ 0.68	\$ (0.65)	\$ (0.60)
Shares used in the calculation of net (loss) income per share:					
Basic	36,598	36,647	36,707	36,992	36,763
Diluted	36,598	36,647	38,406	36,992	36,763
<b>2006</b>					
Revenues	\$ 19,476	\$ 9,244	\$ 1,074	\$ 9,440	\$ 39,234
Operating expenses	47,070	38,508	41,270	25,703	152,551
Net loss	(25,901)	(27,449)	(39,143)	(14,712)	(107,205)
Net loss per share:					
Basic and diluted	\$ (0.69)	\$ (0.73)	\$ (1.03)	\$ (0.39)	\$ (2.84)
Shares used in the calculation of net loss per share:					
Basic and diluted	37,355	37,764	37,868	37,894	37,722