



CRF antagonists for  
anxiety/depression  
and IBS



# Indiplon and beyond

2006 annual report



Indiplon for insomnia




GnRH antagonists  
for women's health



**neurocrine**  
BIOSCIENCES







Working as a team, Neurocrine's R&D and clinical development groups possess the skills and experience to identify, select and optimize new compounds, to screen for therapeutic development, and to advance these compounds efficiently through clinical trials. Their success is the core of Neurocrine's product pipeline and is fueling our ability to bring multiple novel therapies to market.

# our product pipeline

Product	Indication	Preclinical	Phase I	Phase 2	Phase 3	Registration
<i>indiplon</i> (capsules and tablets)	Insomnia					
GnRH Antagonist	Endometriosis					
GnRH Antagonist	BPH					
CRF <sub>1</sub> Antagonist	Anxiety/Depression					
CRF <sub>1</sub> Antagonist	Irritable Bowel Syndrome (IBS)					
CRF <sub>1</sub> Antagonist (back-up)	Anxiety/Depression					
CRF <sub>2</sub> Peptide Agonist (Urocortin 2)	Cardiovascular					
sNRI	Neuropathic Pain					
Glucose Dependent Insulin Secretagogues	Type II Diabetes					
GnRH Antagonist	Endometriosis, Benign Prostatic Hyperplasia					
Adenosine <sub>2A</sub> Receptor Antagonist	Parkinson's Disease					
Ion Channel Blocker	Chronic Pain					



# president's message

This past year was a very challenging one for Neurocrine employees and shareholders. The regulatory setback for *indiplon* approval on May 15, 2006 resulted in our need to reduce our work force by approximately one half including our 200-person sales force. This was a difficult decision but it was necessary to preserve cash and refocus our efforts to put *indiplon* back on an approval path which is what we have done. We are grateful to our former employees for their dedication to our success and to the contributions they made during their tenure. These actions resulted in an annual savings of over \$50 million, which is sufficient to resubmit our *indiplon* capsule NDA to the FDA and to prepare for commercialization in anticipation of product approval by year end 2007. In addition, we have streamlined our R&D organization to maintain "critical mass" to achieve our objectives of filling our product pipeline with at least one new clinical candidate per year to create shareholder value in addition to *indiplon*.

Our resources and efforts are divided equally between investments in *indiplon* development and commercialization, our gonadotropin-releasing hormone (GnRH) program for endometriosis, and all other R&D and pipeline activities. We feel it is imperative to not just fund our *indiplon* efforts but to invest in our future by developing our pipeline for new Neurocrine product opportunities, or as a source of future revenues through corporate collaborations, all of which are under way. We are fortunate that our corticotropin-releasing factor (CRF) program for anxiety, depression and irritable bowel syndrome (IBS) is not only making excellent progress but is being fully funded by our partner GlaxoSmithKline (GSK).

## *Indiplon*

Since May 16, 2006 we have had multiple meetings and communications with the FDA to confirm the requirements for our *indiplon* capsule NDA complete response and our *indiplon* MR tablet clinical work and NDA. For *indiplon* capsules we have completed the requested reanalysis of several of our clinical trials and have re-aggregated certain data as requested. We believe that this work supports our original clinical trial results. In addition, we have reviewed these findings with biostatisticians, sleep experts and FDA consultants, all of whom agree that these results support a resubmission of our NDA. For this reason we are working on our application and are on track to file before the end of the second quarter which should lead to a six-month or year-end action date by the FDA. Assuming a favorable review we are planning for a year-end approval and product launch in the first half of 2008. We are currently beginning partnering discussions with a goal of having a commercial partner on board in time for a 2008 launch.



Our pre-launch and medical education efforts are under way for *indiplon* capsules. Our market research results and interactions with key opinion leaders in the field of sleep support our belief that a sleep aid promoting rapid sleep onset, duration of treatment, and the ability to use the product in the middle of the night to maintain an adequate night's sleep, offers a unique advantage in the market and can be differentiated from all other currently available insomnia treatments. Throughout the balance of the year we will develop our brand identity, conduct educational programs, and present data at key congresses focusing on sleep disorders to prepare for commercialization.

In addition to the efforts supporting the approval and launch of *indiplon* capsules, we are conducting several studies with *indiplon* to select the optimal product to address "traditional sleep maintenance." The FDA has provided guidance that a separate *indiplon* MR tablet dose would be needed for the elderly and that additional efficacy and long-term safety data with a MR tablet formulation would be needed for adults. Neurocrine should be in a position to file a sNDA or complete response for the NDA once these studies are completed.

## R&D Pipeline

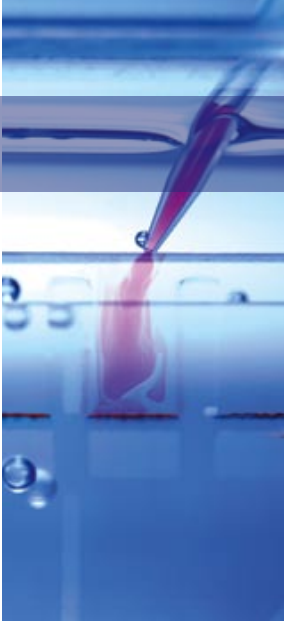
While we experienced setbacks with *indiplon* in 2006, we made excellent progress in advancing our pipeline and in particular our GnRH and CRF programs. Let me begin with GnRH.

## GnRH

Our GnRH antagonist program represents a novel potential treatment option for women who suffer from a debilitating condition known as endometriosis. There are estimated to be six million women in the U.S. who suffer from this condition and treatment options are limited. Our compound, known as NBI-56418, was discovered and developed by Neurocrine scientists. Over the past few years this compound has successfully advanced through preclinical and early clinical development. In 2006 we completed two three-month Phase II clinical trials in patients with moderate to severe endometriosis symptoms and

# R&D Pipeline

Neurocrine's research group continues to identify new therapeutic approaches to treat neurological and endocrine diseases and disorders. Our goal is to identify one new drug candidate every year. The Company is currently advancing 6 potential drug candidates through clinical development.



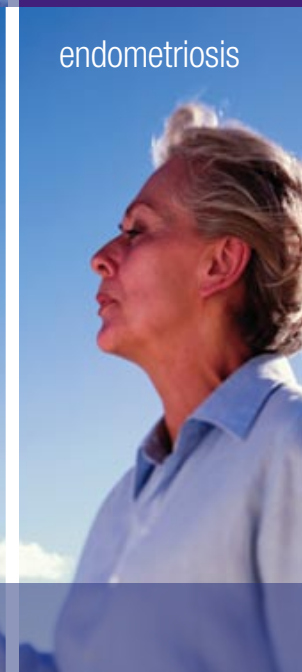
# Advanced Clinical Development

Strong clinical data supported the advancement of several of our product candidates through development in 2006. Neurocrine completed two "proof of concept" Phase II clinical trials, and initiated a Phase IIb study, for NBI-56418 for the treatment of endometriosis. Together with our partner, GlaxoSmithKline (GSK), we have two CRF compounds in development, the most advanced of which has entered Phase II clinical trials in two indications: social anxiety disorder and irritable bowel syndrome.



## GnRH

endometriosis



## CRF

social anxiety disorder & irritable bowel syndrome

# Registration



## indiplon

insomnia

demonstrated that this compound lowers estrogen to levels associated with a reduction in pain. This was achieved without apparent bone-loss risk, menopausal symptoms or other side effects which plague existing therapies. We are pleased with these results and have advanced the compound into a six-month Phase IIb clinical trial to confirm and extend these findings. This trial is enrolling on schedule. The treatment phase is expected to complete by the first quarter of 2008. In conjunction with data from the other Phase II studies, we will enter into discussion with the FDA to plan for Phase III trials. In parallel to the clinical development activities, we have initiated partnering discussions in various territories throughout the world to help fund and advance this compound towards commercialization.

## CRF

Our CRF program represents a novel approach for the treatment of mood disorders such as anxiety and depression as well as irritable bowel syndrome (IBS). Neurocrine is the leader in CRF discovery research and our collaboration with GSK has moved two compounds into clinical trials. The first of these compounds successfully completed an extensive Phase I safety evaluation last year and is now being evaluated in four Phase II clinical trials in patients with social anxiety disorder or IBS. Our partner, GSK, fully funds this effort and we expect data from these trials beginning in late 2007 and extending into mid 2008. If successful, this approach will represent the first truly impactful treatment option for patients with these disorders in over 20 years. In addition GSK has advanced a second collaboration compound into extensive Phase I safety evaluations and expects to complete these trials in 2007 at which time the compound should be ready for Phase II safety and efficacy evaluation in patients. Neurocrine received \$8 million in milestone payments in 2006 and stands to receive significant additional milestones, royalties and co-promotion rights in the future, dependent upon continued success.

## Early Stage Programs

Behind our three advanced clinical programs Neurocrine is fortunate to have multiple early stage programs to feed our pipeline. Our Urocortin 2 program for the treatment of congestive heart failure (CHF) has completed a Phase I safety evaluation as well as a preliminary Phase II efficacy evaluation. There are approximately one million hospitalized CHF patients in the U.S. each year which represents an enormous cost to the health care system. It is hoped that Urocortin 2 can stabilize their deteriorating condition, safely relieve symptoms and significantly reduce hospitalization costs. Our Phase II trial results in stable CHF patients met our objectives by showing improvements in cardiac output without excessive increases in heart rate or abnormalities in renal function. We are completing the required preclinical work necessary to extend treatment duration (i.e., longer infusions) and are evaluating whether we will move into expanded Phase II clinical development on our own or with a partner.

Also from our internal research efforts we have moved a compound targeted to reduce neuropathic pain into Phase I safety evaluations and expect results by mid year which will allow for a go/no go decision on additional development.

Our A2A program for Parkinson's disease is in preclinical development and could represent our next clinical program. We were honored to receive a research grant from the Michael J. Fox Foundation to help support this work and we hope to nominate our development candidate by year end.

In summary, our R&D efforts have been productive and continue to fuel our pipeline necessary to create long-term shareholder value.

## Financial Perspective

From a financial perspective Neurocrine remains strong, ending the year with over \$180 million. We continue to prudently manage our cash and expect to consume approximately \$80 million in cash in 2007. We have plans to extract equity from our facility by way of a sale leaseback or secondary financing to replenish our cash position for the year. We have no plans to sell stock until such time as our share price is at a more attractive level and are hopeful that an *indiplon* capsule approval at year end will provide this momentum.

## Personnel

This past year brought a number of changes to our employment base. Having downsized to approximately 265 employees we have focused our efforts on retention, motivation and communication. These efforts are paying off. Morale is high and all employees have a renewed commitment to make Neurocrine a success.

During the year Kevin Gorman, Ph.D., our former SVP of Business Development, was promoted to Chief Operating Officer and now oversees R&D, Clinical, Regulatory, Marketing and Business Development. Dimitri Grigoriadis, Ph.D., was promoted to VP of Research and has led our effort to streamline and restructure Research. Haig Bozigian, Ph.D., has been promoted to SVP of Development and has assumed responsibility for all non-clinical development activities including preclinical toxicology, pharmacokinetics, chemical and pharmaceutical development. Chris O'Brien, M.D., was promoted to Chief Medical Officer and continues to be responsible for all clinical research programs. In addition, Tim Coughlin, formerly VP and Controller, was promoted to Chief Financial Officer. My congratulations go out to these individuals for their leadership and for the positive impact that they are having on our organization.

In conclusion, 2006 was a very challenging year, yet a year of important accomplishments. I believe we are well poised and financed to deliver on our promise to soon become a fully integrated research, development and commercial biopharmaceutical company. My appreciation goes out to our shareholders who have stood by us and to our collaborators and employees for your trust, support and dedication.



Gary A. Lyons  
Chief Executive Officer, President and Director

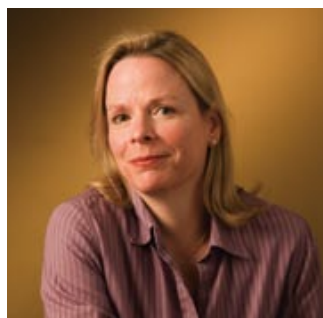


Kevin C. Gorman, Ph.D.  
Executive Vice President,  
Chief Operating Officer



Timothy P. Coughlin, CPA  
Vice President,  
Chief Financial Officer

Richard J. Ranieri  
Senior Vice President,  
Human Resources



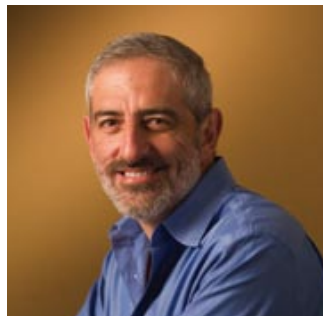
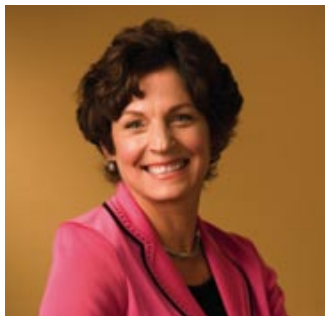
Margaret E. Valeur-Jensen, Ph.D., JD  
Executive Vice President,  
General Counsel and  
Corporate Secretary

Haig Bozigian, Ph.D.  
Senior Vice President  
of Pharmaceutical and  
Preclinical Development



Christopher F. O'Brien, M.D.  
Senior Vice President of  
Clinical Development,  
Chief Medical Officer

Carol A. Baum, MBA  
Vice President,  
Marketing



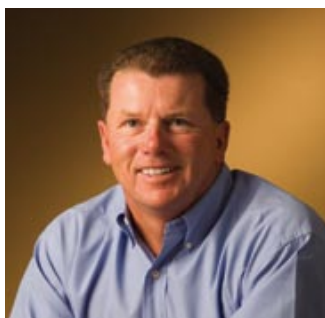
Dimitri E. Grigoriadis, Ph.D.  
Vice President of Research

Barbara M. Finn  
Vice President,  
Regulatory Affairs  
& Quality Assurance



Alan C. Foster, Ph.D.  
Neurocrine Fellow

Hernand W. Wilson  
Vice President,  
Information Technology



## Our Management Team

# Indiplon – A Potential New Treatment Option for Insomnia

Insomnia is a central nervous system disorder that results in an inability to sleep or to remain asleep throughout the night. Approximately 86 million adults in the United States report trouble sleeping a few nights per week or more, with an additional 26 million experiencing chronic insomnia, which is trouble sleeping every night or almost every night.<sup>1</sup>

These statistics are cause for concern because the effects of sleep deprivation can influence quality of life, and in some cases, compromise the safety and normal functioning of the patient in the workplace. In addition, frequent sleep problems in people who 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.<sup>2</sup>

*Indiplon* is a unique non-narcotic, non-benzodiazepine agent that acts on a specific site of the GABA receptor. Its potency, high affinity and selectivity for the  $\alpha_1$  GABA-A receptor subtype differentiates it from currently marketed non-benzodiazepine sleep agents. This unique selectivity profile together with an optimized duration of action underlies the excellent efficacy and safety demonstrated by *indiplon* in multiple clinical studies of insomnia patients.

Neurocrine plans to resubmit the New Drug Application (NDA) for *indiplon* immediate-release capsules to the U.S. Food and Drug Administration (FDA) by the end of the second quarter of 2007. The decision to resubmit the NDA in this time frame is based on reviewing this data with independent statistical, regulatory and clinical consultants. We have also had interactions with the FDA regarding additional analyses of data previously submitted on *indiplon* capsules. Neurocrine believes that *indiplon* will provide physicians with a novel option in treating insomnia, one that will enable patients to fall asleep quickly, or return to sleep after nighttime awakenings.

<sup>1</sup>Mattson Jack (2006)

<sup>2</sup>National Sleep Foundation (2003)







“Several new medications have recently become available for the clinical treatment of insomnia patients. However, there remains a need for an effective, short-acting agent suited for the flexible dosing necessary to optimally treat many patients.”

**Andrew D. Krystal, MD, MS**  
Director, Insomnia and Sleep Research Program;  
Associate Professor with Tenure  
Department of Psychiatry and Behavioral Sciences,  
Duke University School of Medicine

# insomnia indiplon



*“Indiplon is the result of an extensive development program that promises a safe and effective treatment for insomnia. Data regarding middle-of-the-night use of indiplon indicate that this medication can be used to promote sleep even after bedtime, allowing physicians to personalize treatment based on their patients’ complaints. This allows us to explore treatment models for insomnia that were never before possible.”*

Gary Zammit, Ph.D.  
President and CEO, Clinilabs, Inc.  
Clinical Associate Professor of Psychology  
(in Psychiatry) Columbia University  
College of Physicians and Surgeons;  
Director, Sleep Disorders Institute of  
St. Luke's/Roosevelt Hospital Center





# The Growing Impact of Endometriosis

There are estimated to be approximately six million women in the United States who are impacted by chronic endometriosis.<sup>1</sup> The disease is believed to account for a significant proportion of female infertility and greater than 90% of the reported cases of chronic pelvic pain. The cause of endometriosis is unknown, but the condition occurs when endometrial tissue implants outside of the uterus. Endometrial lesions are most often found in the pelvic cavity where in addition to pain, they can cause cysts, scar tissue and adhesions.

When treating endometriosis, the choice between surgery and other medical treatments depends on the woman's symptoms, age, and fertility wishes. Many women refuse hysterectomy in order to retain their ability to have a child. Current hormonal treatments such as injectable GnRH agonists are associated with a range of potentially unacceptable side effects, including bone loss and hot flashes. Consequently, prescribing physicians often reserve these medical interventions for patients with severe endometriosis. For the majority of endometriosis patients suffering from moderate or mild symptoms, the remaining treatment options including oral contraceptives and analgesics are only partially effective.

## GnRH – A New Approach Holds Promise

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. Scientists have found that chronic administration of peptide GnRH agonists reversibly shuts down this hormonal pathway and is clinically useful in treating a variety of hormone-dependent diseases such as endometriosis and uterine fibroids in women's health, and in men's health, prostate cancer and benign prostatic hyperplasia (BPH).

Neurocrine researchers have developed a potential new treatment for endometriosis that we believe will improve pain relief, while limiting the occurrence of unacceptable side effects seen with current hormone therapies. NBI-56418 is an orally active, nonpeptide GnRH antagonist that has a rapid onset of estradiol<sup>2</sup> suppression and pain reduction, and does not produce the hormonal flare seen with injectable GnRH agonists. By using NBI-56418, it may be possible to alter the level of hormone suppression by varying the dosage and thereby better regulating the circulating levels of estradiol. This could also eliminate the need for the active management of bone loss that is experienced with current injectable hormone therapies for endometriosis.

<sup>1</sup> Mattson Jack (2006)

<sup>2</sup> Estradiol is one of three major naturally occurring estrogens in women.





## Jana's Story: Living with Endometriosis



"Endometriosis is something that none of us plan for. We were married at 23 and tried to get pregnant at 26. When you get married, you are happy and you expect to have kids. This is the circle of life. Then the unexpected happened. I was diagnosed with endometriosis and we realized that it would be more difficult to start a family.

"The pain was difficult to bear. I continued to try to get pregnant, but the pain was getting progressively worse. I had 5 laparoscopic surgeries within 12 years to reduce the scar tissue. The scar tissue kept building up fast and had to be removed again and again. The worst part was the debilitating effect of the pain, so severe that I had to stay in bed 3 days out of every month. I was taking strong pain medication and also experienced bad hot flashes.

"My husband, Eric, was concerned about the extreme pain I had to endure. He was very supportive. Eric was there every step of the way but he said that he didn't want to see me in this much pain. Pregnancy often provides relief from the pain of endometriosis, but I was not able to get pregnant. To relieve the pain, I had a hysterectomy at 38 years old. It was rough going through menopause at an early age which also brought on other problems such as hot flashes, weight gain, insomnia and mood swings."

# Making Strides in our GnRH Program

Neurocrine has made progress in demonstrating preliminary efficacy and safety results with our oral GnRH antagonist (NBI-56418) in 2006, completing two Phase II “proof of concept” clinical trials and initiating a Phase IIb clinical study in patients with endometriosis. The results of the two Phase II trials were encouraging and suggest that NBI-56418 achieves sufficient estradiol suppression for pain reduction while potentially avoiding reduction in bone mineral density and the other undesirable metabolic consequences of current GnRH agonist therapies.

The Composite Pelvic Sign and Symptoms Score (CPSSS) and Visual Analog Scale (VAS) are industry-standard and validated measures for evaluating pain reduction in endometriosis patients and were used to assess efficacy in the Phase II studies of NBI-56418. In addition to the standard clinical and laboratory assessments of safety, a biomarker for bone resorption (n-telopeptide) was also measured to assess potential detrimental impact on bone mineral density.

Treatment in the first Phase II trial was completed in April 2006. This trial followed a parallel-group design in which 76 subjects were randomized into one of three treatment groups: placebo, 75 mg of NBI-56418 or 150 mg of NBI-56418. This six-month trial included a 3-month double-blind, placebo controlled post-treatment, followed by a post treatment 3-month period to assess safety.

Our clinical results showed that this oral GnRH antagonist reduced pain scores measured by both CPSSS and VAS. In fact, pain reduction was reported within the first few weeks of treatment by some patients and benefits were sustained for up to 12 weeks after discontinuation in many patients. In contrast to GnRH agonists, there was no increase in hot flashes reported by the NBI-56418 treated groups as compared with placebo. Menstrual cycles and ovulation were normal in the 3-month follow-up period off treatment, while values of plasma n-telopeptide remained within the normal range.

The 3-month treatment plan of the second Phase II clinical trial of NBI-56418 was completed in December 2006. This trial was designed to evaluate dose response, specifically the effects of twice daily dosing. It enrolled 68 subjects randomized into one of three treatment groups: placebo, 50 mg of NBI-56418 twice daily or 100 mg of NBI-56418 once daily. The results of the treatment phase of this trial were consistent with the first Phase II study, with NBI-56418 demonstrating dose-related reductions in estradiol without evidence of increased risk of bone loss. The reduction in pain as measured by CPSSS and VAS was significant and dose-dependent. The extent of estradiol suppression and lack of undesirable metabolic consequences, such as bone loss or hot flashes, suggest that even higher doses may be acceptable with the potential for even greater symptom reduction.

Based on the combined data of these two Phase II clinical trials of NBI-56418, Neurocrine is actively enrolling patients in an expanded 6-month Phase IIb study which will include 240 patients with endometriosis. The objective of this trial is to assess the impact of NBI-56418 on bone mineral density, as well as on pain symptoms. The results of this 6-month trial, together with data from the previous two Phase II studies, will be the basis for securing agreement to a registration plan for NBI-56418 with the FDA.





“We are very blessed to have a beautiful child in our lives, my 15 year old foster son. I have a wonderful life, a wonderful marriage, and if something gets in the way of the plans of life, it is not worth the pain. After my surgery, I am now pain free.”

Jana Cahill  
Wife and Mother



# CRF — Better Regulating the Stress Response

Not only is stress mentally and emotionally draining, it can take a physical toll on your body. The key hormone in the regulation of the stress response is a brain chemical called corticotropin-releasing factor (CRF). This hormone is overproduced in patients with major depression and is thought to underlie the manifestation of anxiety-related disorders, including social anxiety and inflammatory bowel syndrome (IBS).

These two indications impact millions of people worldwide. In 2006, over 19 million Americans suffered from a debilitating anxiety disorder.<sup>1</sup> For its part, IBS affects approximately 30 million people in the United States,<sup>2</sup> accounting for over \$25 billion in direct and indirect costs each year.<sup>3</sup>

The receptors for CRF are found in specific brain regions that are responsible for the regulation of mood. CRF receptor antagonists offer a novel mechanism of action with the advantage of being more selective, potentially increasing efficacy and having a more rapid onset of action while reducing the number of side effects. Neurocrine has characterized the CRF receptor system, identified additional members of this protein family and holds a unique strategic position in the CRF field through a robust intellectual property portfolio and close relationships with leading experts in the neuropsychiatric field.

Through Neurocrine's collaboration with GlaxoSmithKline (GSK) we have identified multiple unique high

affinity and selective antagonists for the CRF receptor. GSK recently initiated Phase II "proof of concept" clinical trials with a lead Corticotropin Releasing Factor (CRF<sub>1</sub>) receptor antagonist compound for two indications, social anxiety disorder (SocAD) and 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<sub>1</sub> receptor 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.

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.

In the first quarter of 2006, GSK advanced an additional lead CRF<sub>1</sub> receptor antagonist into a Phase I single dose study for the same indications. This compound is currently in a Phase I multi-dose study.

<sup>1</sup> National Institute of Mental Health

<sup>2</sup> Mattson Jack (2006)

<sup>3</sup> International Foundation for Functional Gastrointestinal Disorders







The key hormone in the regulation of the stress response is a brain chemical called corticotropin-releasing factor (CRF).

Neurocrine's Research Group is focused on developing novel small molecule therapeutics that address diseases and disorders of the central nervous system and endocrine system, which includes stress-related disorders, certain neuro-degenerative diseases and neuropathic pain. Central nervous system and endocrinology drug therapies are two of the largest therapeutic categories, accounting for over \$60 billion in worldwide drug sales in 2005.<sup>1</sup>



## 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. 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. Neurocrine is evaluating Urocortin 2 in preclinical and clinical trials for CHF.

## sNRI

There are approximately eight million chronic neuropathic pain sufferers in the United States alone.<sup>2</sup>

## A2A Antagonists

Parkinson's disease afflicts over one million people in the United States.<sup>3</sup> Our A2A receptor antagonists are showing promise in preclinical trials where they appear to help restore function in models of Parkinson's disease.

## GnRH

Following the success of NBI-56418 currently in Phase II clinical trials in endometriosis, Neurocrine's research group is investigating the potential of certain GnRH antagonists in treating other hormone dependent diseases.







# new product candidates



## Glucose Dependent Insulin Secretagogues

Type II diabetes affects more than 19 million Americans.<sup>4</sup> Neurocrine is optimizing several glucose dependent insulin secretagogues with the goal of identifying a novel oral therapy for glucose control in diabetes.



## Ion Channel Blockers

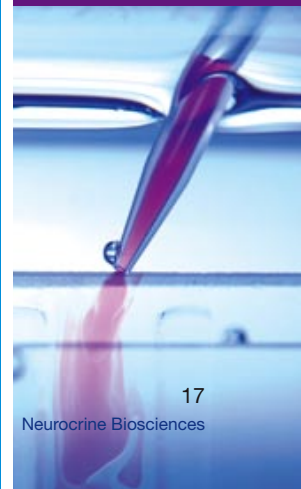
Ion channels play a significant role in transmitting pain signals to the central nervous system. Neurocrine is identifying compounds that block certain ion channels as candidates to take into preclinical development.

<sup>1</sup> Medical Advertising News

<sup>2</sup> National Institute of Arthritis and Musculoskeletal and Skin Diseases

<sup>3</sup> National Parkinson Foundation

<sup>4</sup> Mattson Jack 2006



## Research Continues to Fuel Our Pipeline

Neurocrine's research team brings experience and scientific savvy to the identification of small molecules with the potential to become breakthrough therapies. Employing a proprietary approach to drug design, this team is succeeding in delivering strong drug candidates into clinical development.

### Urocortin 2 for CHF Continues Preclinical Evaluation

Initial results of a Phase II study in patients with stable CHF indicate that urocortin 2 is generally well tolerated and that the predicted hemodynamic effects on systolic and diastolic blood pressure, heart rate, cardiac work and, most importantly, cardiac output occur over the entire 4-hour infusion. This Phase II study in stable CHF patients, was designed to assess various hemodynamic endpoints, safety and PK/PD over the 4-hour infusion treatment period. Cardiac output increased with minimal increases in heart rate. No abnormalities of renal function, electrocardiograms or biomarkers of cardiac injury were observed.

Based on this data, it had been our intent to initiate additional Phase II studies in late 2006 with longer duration infusions of up to 72 hours. However, additional preclinical investigations are necessary to support longer exposures prior to proceeding. We believe that this preclinical data will be available in mid-2007.

### sNRI

Neurocrine identified a new compound, called a selective norepinephrine reuptake inhibitor (sNRI) to take into development for the treatment of neuropathic pain and psychiatric disorders. Our lead candidate has been efficacious in multiple preclinical models of neuropathic pain, including those for persistent pain and hyperalgesia. Based on its selective pharmacologic effect as a norepinephrine reuptake inhibitor, this drug could also offer potential clinical utility in a variety of other therapeutic areas including psychiatry, gastroenterology and urology. In the first quarter of 2007, Neurocrine initiated Phase I clinical trials of our lead sNRI candidate to assess safety and tolerability.

### A2A

A2A receptor antagonists have been shown to be effective at relieving symptoms in preclinical 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 an area of the brain called the basal ganglia that also express dopamine

D2 receptors. Parkinsonian symptoms result from impairment in the function of these neurons resulting from the dopamine depletion that occurs as neuronal degeneration progresses. Antagonism of A2A receptors appears to help restore normal function, and several lines of evidence also suggest that A2A antagonism can help protect against neuronal degeneration.

In January 2007, we were pleased to receive a 2-year grant from The Michael J. Fox Foundation to study the potential neuroprotective effects of adenosine A2A receptor antagonists in models of Parkinson's disease. We anticipate selecting a compound from our A2A program to bring into R&D for further study under this grant.

### GnRH

Our discovery work continues to focus on GnRH clinical candidates that show benefit in models of endometriosis and benign prostatic hyperplasia. Because GnRH antagonists may be useful in treating other hormone dependent diseases, we are also investigating GnRH compounds that show promise in these indications.

### Glucose Dependent Insulin Secretagogues

Type II diabetes is growing to epidemic proportions worldwide. The disease is characterized by reduced ability to secrete and respond to insulin. Drugs that can enhance the secretion of insulin in response to rising blood glucose levels could 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.

### Ion Channel Blockers

Capitalizing on our small molecule expertise in the area of neurology and pain management, 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 believe that a compound that blocks this channel could provide relief from chronic pain.



## 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.

	2006	2005	2004	2003	2002
(in thousands, except for loss per share data)					
<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	<u><u>\$ (107,205)</u></u>	<u><u>\$ (22,191)</u></u>	<u><u>\$ (45,773)</u></u>	<u><u>\$ (30,256)</u></u>	<u><u>\$ (94,536)</u></u>
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
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

## 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 our Annual Report on Form 10-K for 2006 filed with the Securities and Exchange Commission.*

#### 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 *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



## Management's Discussion and Analysis

### of Financial Condition and Results of Operations

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 (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 (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 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

## Management's Discussion and Analysis

### of Financial Condition and Results of Operations

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 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

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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:

Year Ended December 31, (in thousands)	2006	2005	2004
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	<u>\$ 39,234</u>	<u>\$ 123,889</u>	<u>\$ 85,176</u>

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.

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.



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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 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 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

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\$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 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



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us in the worldwide development and commercialization of *indip-  
lon*. 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 cancel-  
able 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 milestone payments, plus  
sales royalties, in the event that all scientific research under these  
agreements is successful. Some of our clinical development agree-  
ments contain incentives for time-sensitive activities.

Contractual Obligations	Total	Less than 1 year	1-3 years	3-5 years	More than 5 years
(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 develop- ment agreements	15,562	11,375	4,187	—	—
Total contractual obligations	<u>\$71,066</u>	<u>\$17,163</u>	<u>\$7,413</u>	<u>\$1,744</u>	<u>\$44,746</u>

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 num-  
ber 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 spend-  
ing. 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 candi-  
dates 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-clini-  
cal 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 clini-  
cal trials for certain product candidates or for certain indications  
in order to focus our resources on more promising product candi-  
dates 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 therapeu-  
tic 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 clini-  
cal trials may not be predictive of 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.

## Management's Discussion and Analysis

### of Financial Condition and Results of Operations

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 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



## Management's Discussion and Analysis

### of Financial Condition and Results of Operations

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.

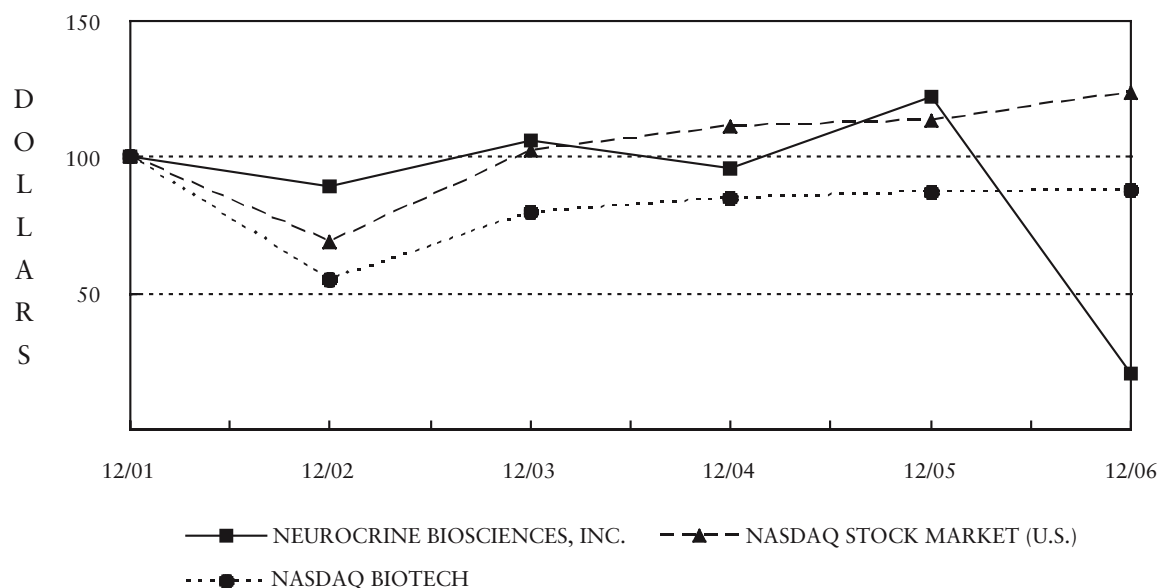
In September 2006, the FASB issued SFAS No. 157, "Fair Value Measurements" (SFAS 157). SFAS 157 provides guidance for using fair value to measure assets and liabilities. It also responds to investors' requests for expanded information about the extent to which companies measure assets and liabilities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

### Stock Performance Graph

The following graph indicates the Company's total stockholder return for the five-year period ended December 31, 2006, as compared to the total return for the NASDAQ® Stock Market—U.S. Index and the NASDAQ® Biotechnology Index, assuming a common starting point of \$100.\*

Please note that the graph is a five-year historical representation and, as such, is not indicative of future performance.



\*\$100 invested on 12/31/01 in stock or index – including reinvestment of dividends at fiscal years ending December 31.

## Consolidated Balance Sheets

December 31,	2006	2005
(in thousands, except for par value and share totals)		
<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	<u>\$ 389,677</u>	<u>\$ 483,123</u>
<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)
Total stockholders' equity	314,716	390,104
Total liabilities and stockholders' equity	<u>\$ 389,677</u>	<u>\$ 483,123</u>

See accompanying notes.



## Consolidated Statements of Operations

Years Ended December 31,	2006	2005	2004
(in thousands, except loss per share data)			
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	<u>39,234</u>	<u>123,889</u>	<u>85,176</u>
Operating expenses:			
Research and development	97,678	106,628	115,066
Sales, general and administrative	54,873	42,333	22,444
Total operating expenses	<u>152,551</u>	<u>148,961</u>	<u>137,510</u>
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	<u>6,112</u>	<u>2,881</u>	<u>6,640</u>
Loss before taxes	(107,205)	(22,191)	(45,694)
Income taxes	<u>—</u>	<u>—</u>	<u>79</u>
Net loss	<u><u>\$(107,205)</u></u>	<u><u>\$(22,191)</u></u>	<u><u>\$(45,773)</u></u>
Net loss per common share:			
Basic and diluted	<u><u>\$ (2.84)</u></u>	<u><u>\$ (0.60)</u></u>	<u><u>\$ (1.26)</u></u>
Shares used in the calculation of net loss per common share:			
Basic and diluted	<u><u>37,722</u></u>	<u><u>36,763</u></u>	<u><u>36,201</u></u>

See accompanying notes.

## Consolidated Statements of Stockholders' Equity

	Common Stock		Additional	Deferred	Notes	Accumulated	Accumulated	Total
	Shares	Amount	Paid-in	Compensation	Receivable	Other Com-	Deficit	Stockholders'
			Capital		from	prehensive		Equity
					Stockholders	Income (loss)		
(in thousands)								
<b>Balance at December 31, 2003</b>	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
<b>Balance at December 31, 2004</b>	36,533	37	674,034	(312)	(69)	(1,908)	(277,955)	393,827
Net loss	—	—	—	—	—	—	(22,191)	(22,191)
Unrealized gain on short-term investments	—	—	—	—	—	404	—	404
Comprehensive loss	—	—	—	—	—	—	—	(21,787)
Issuance of common stock for option exercises	529	—	14,457	—	—	—	—	14,457
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>	37,132	37	691,717	—	—	(1,504)	(300,146)	390,104
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>	37,906	\$38	\$721,930	\$ —	\$ —	\$ 99	\$(407,351)	\$314,716

See accompanying notes.

## Consolidated Statements of Cash Flows

Years Ended December 31,	2006	2005	2004
(in thousands)			
<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
<b>Supplemental Disclosures</b>			
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.



# 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.

**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.

## Notes to the Consolidated Financial Statements

December 31, 2006

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 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

## Notes to the Consolidated Financial Statements

December 31, 2006

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.

**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 proforma 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):

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

**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



## Notes to the Consolidated Financial Statements

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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 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):

	Amortized Cost	Gross Unrealized Gains	Gross Unrealized Losses	Estimated Fair Value
<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	<u>\$102,236</u>	<u>\$ —</u>	<u>\$ (613)</u>	<u>\$101,623</u>
<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	<u>\$225,102</u>	<u>\$ 1</u>	<u>\$ (1,983)</u>	<u>\$223,120</u>

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

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

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

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

### NOTE 3. PROPERTY AND EQUIPMENT

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

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

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):

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

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## 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 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):

Fiscal Year	Mortgage Debt	Equipment Debt	Operating Leases	Licenses & Research Agreements	Clinical Development Agreements
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	—
Total minimum payments	<u>\$48,301</u>	<u>\$ 5,340</u>	<u>\$ 370</u>	<u>\$ 1,493</u>	<u>\$ 15,562</u>

## 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

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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.

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 exer-

cised (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 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



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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:

Years Ended December 31,	2006	2005	2004
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 proforma 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 Incentive Stock Plan (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 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):

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	2006		2005		2004	
	Options (in thousands)	Weighted Average Exercise Price	Options (in thousands)	Weighted Average Exercise Price	Options (in thousands)	Weighted Average Exercise Price
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

Options Outstanding			Options Exercisable		
Range of Exercise Prices	Outstanding as of 12/31/06	Weighted Average Remaining Contractual Life (In Years)	Weighted Average Exercise Price	Exercisable as of 12/31/06	Weighted Average Exercise Price
\$ 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 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

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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.

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	<u>6,494</u>

### 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



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

	2006	2005
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
Total deferred tax assets	232,300	183,400
Deferred tax liabilities:		
Investment in LLC	11,300	10,000
Intangibles	7,200	4,600
Fixed assets	3,200	3,700
Total deferred tax liabilities	21,700	18,300
Net deferred tax asset	210,600	165,100
Valuation allowance	(210,600)	(165,100)
Net deferred tax assets	\$ —	\$ —

## Notes to the Consolidated Financial Statements

December 31, 2006

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):

	2006	2005	2004
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
	<u>\$ —</u>	<u>\$ —</u>	<u>\$ 79</u>

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.

### NOTE 10. SELECTED QUARTERLY FINANCIAL DATA (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):

	Quarters Ended				Year Ended
	Mar 31	Jun 30	Sep 30	Dec 31	Dec 31
<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

## Report of Independent Registered Public Accounting Firm on Financial Statements

The Board of Directors and Stockholders  
Neurocrine Biosciences, Inc.

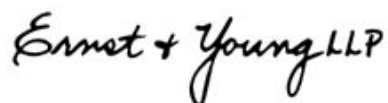
We have audited the accompanying consolidated balance sheets of Neurocrine Biosciences, Inc. as of December 31, 2006 and 2005, and the related consolidated statements of operations, stockholders' equity, and cash flows for each of the three years in the period ended December 31, 2006. These financial 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.

The signature of Ernst & Young LLP is written in a cursive, handwritten style in black ink.

San Diego, California  
February 2, 2007



## 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 the 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.

## 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.

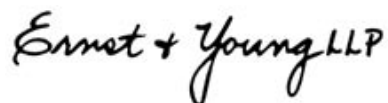
We conducted our audit in accordance with the standards of the Public Company Accounting Oversight Board (United States). Those standards require that we plan and perform the audit to obtain reasonable assurance about whether effective internal control over financial reporting was maintained in all material 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.

The signature of Ernst & Young LLP is written in a cursive, handwritten style.

San Diego, California  
February 2, 2007

# Corporate Information

## Corporate Management Committee

Gary A. Lyons  
*Chief Executive Officer, President and Director*

Kevin C. Gorman, Ph.D.  
*Executive Vice President,  
Chief Operating Officer*

Margaret E. Valeur-Jensen, Ph.D., JD  
*Executive Vice President, General Counsel and  
Corporate Secretary*

Richard J. Ranieri  
*Senior Vice President, Human Resources*

Timothy P. Coughlin, CPA  
*Vice President, Chief Financial Officer*

## Vice Presidents

Christopher F. O'Brien, M.D.  
*Senior Vice President of Clinical Development,  
Chief Medical Officer*

Haig Bozigian, Ph.D.  
*Senior Vice President of Pharmaceutical and  
Preclinical Development*

Dimitri E. Grigoriadis, Ph.D.  
*Vice President of Research*

Barbara M. Finn  
*Vice President, Regulatory Affairs  
& Quality Assurance*

Carol A. Baum, MBA  
*Vice President, Marketing*

Hernand W. Wilson  
*Vice President, Information Technology*

## Neurocrine Fellows

Alan C. Foster, Ph.D.  
Nicholas C. Ling, Ph.D., Emeritus

## Board of Directors

Joseph A. Mollica, Ph.D.  
*Chairman of the Board, Neurocrine Biosciences,  
Inc. and Chairman, Pharmacopeia Drug  
Discovery, Inc.*

Gary A. Lyons  
*Chief Executive Officer and President,  
Neurocrine Biosciences, Inc.*

Corinne H. Lyle  
*President, Global Operations,  
Edwards Lifesciences Corporation*

W. Thomas Mitchell  
*Former Chairman of the Board and  
Chief Executive Officer,  
Genencor International*

Richard F. Pops  
*Chairman of the Board,  
Alkermes, Inc.*

Stephen A. Sherwin, M.D.  
*Chairman and Chief Executive Officer,  
Cell Genesys, Inc.*

Wylie W. Vale, Ph.D.  
*Professor and Head, The Clayton Foundation,  
Laboratories for Peptide Biology, The Salk  
Institute*

## Corporate Headquarters

Neurocrine Biosciences, Inc.  
12790 El Camino Real  
San Diego, CA 92130  
Phone: (858) 617-7600  
Fax: (858) 617-7602  
[www.neurocrine.com](http://www.neurocrine.com)

## Auditors

Ernst & Young LLP

## Transfer Agent

American Stock Transfer

## SEC Form 10-K

A copy of the Company's annual report to the Securities and Exchange Commission on Form 10-K is available without charge, upon written request to: Investor Relations  
Neurocrine Biosciences, Inc.  
12790 El Camino Real  
San Diego, CA 92130  
Phone: (858) 617-7600  
Fax: (858) 617-7602  
[www.neurocrine.com](http://www.neurocrine.com)

## Market for Registrant's Common Equity and Related Stockholder Matters

The Company's common stock is traded on the Nasdaq Global Select Market System under the symbol "NBIX." The following table sets forth for the periods indicated the high and low sale price for the common stock as reported by the Nasdaq National Market. These prices do not include retail markups, markdowns or commissions.

	High	Low
Year ended December 31, 2005		
1st quarter	\$50.10	\$36.58
2nd quarter	44.09	33.86
3rd quarter	52.90	41.20
4th quarter	65.70	43.31
	High	Low
Year ended December 31, 2006		
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 shareholders of record of our common stock.

## Dividend Policy

The Company has not paid any cash dividends on its Common Stock since its inception and does not anticipate paying cash dividends on its Common Stock in the foreseeable future.





