



**SECURITIES AND EXCHANGE COMMISSION**

**Washington, D.C. 20549**

**FORM 10-K**

**FOR ANNUAL AND TRANSITION REPORTS  
PURSUANT TO SECTIONS 13 OR 15(d) OF THE  
SECURITIES EXCHANGE ACT OF 1934**

(Mark One)

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

For the fiscal year ended December 31, 2002

OR

TRANSITION REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934

For the transition period from \_\_\_\_\_ to \_\_\_\_\_

Commission file number: 0-28150

**NEUROCRINE BIOSCIENCES, INC.**

(Exact name of registrant as specified in its charter)

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

**33-0525145**  
(I.R.S. Employer  
Identification Number)

**10555 Science Center Drive, San Diego, CA**  
(Address of principal executive office)

**92121**  
(Zip Code)

Registrant's telephone number, including area code: **(858) 658-7600**

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

Title of Each Class

Name of Each Exchange on Which Registered

**None**

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

Common Stock, \$0.001 par value

(Title of Class)

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

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

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Indicate by check mark whether the registrant is an accelerated filer (as defined in Exchange Act Rule 12b-2). Yes  No

The aggregate market value of the voting stock held by non-affiliates of the Registrant as of June 30, 2003 totaled approximately \$832,923,000 based on the closing stock price as reported by the Nasdaq National Market.

As of February 21, 2003, there were 30,719,501 shares of the Registrant's Common Stock, \$0.001 par value per share, outstanding.

**DOCUMENTS INCORPORATED BY REFERENCE**

**Document Description**

**10-K Part**

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Portions of the Registrant's notice of annual meeting of stockholders and proxy statement to be filed pursuant to Regulation 14A within 120 days after Registrant's fiscal year end of December 31, 2002 are incorporated by reference into Part III of this report

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III, ITEMS 10, 11, 12, 13

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**PART I****FORWARD-LOOKING STATEMENTS**

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

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

The cautionary statements made in this report are intended to be applicable to all related forward-looking statements wherever they may appear in this report. We urge you not to place undue reliance on these forward-looking statements, which speak only as of the date of this report.

**ITEM 1. BUSINESS**

We develop and intend to commercialize drugs for the treatment of neurologic and endocrine system-related diseases and disorders. Our product candidates address some of the largest pharmaceutical markets in the world including insomnia, anxiety, depression, malignant brain tumors and peripheral cancers, diabetes mellitus, multiple sclerosis, irritable bowel syndrome, eating disorders, pain, prostate cancer, obesity and certain female health disorders. We currently have 16 programs in various stages of research and development, including seven programs in clinical development. Our lead clinical development program is indiplon our drug for the treatment of insomnia currently being evaluated in Phase III clinical trials.

While we independently develop the majority of our product candidates, we have entered into collaborations for seven of our 16 programs. We currently have active product development collaborations with Pfizer, Inc. (Pfizer), GlaxoSmithKline (GSK), Wyeth and Taisho Pharmaceutical Co., Ltd. (Taisho).

**Our Product Pipeline**

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

<b>Program</b>	<b>Compound</b>	<b>Targeted Indication</b>	<b>Status</b>	<b>Commercial Rights</b>
<b>Products under clinical development:</b>				
GABA-A Agonist	indiplon	Insomnia	Phase III	Pfizer/Neurocrine
Altered Peptide Ligand	NBI-5788	Multiple Sclerosis	Phase II	Neurocrine
Altered Peptide Ligand	NBI-6024	Type 1 Diabetes	Phase II	Taisho/Neurocrine
GnRH Antagonist	NBI-42902	Endometriosis, Fibroids Prostate Cancer	Phase I	Neurocrine
CRF R <sub>1</sub> Antagonist	NBI-34041	Anxiety, Depression, Gastrointestinal	Development	GlaxoSmithKline/Neurocrine

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Program	Compound	Targeted Indication	Status	Commercial Rights
IL-4 Fusion Toxin	NBI-3001	Malignant Glioma	Phase II	Neurocrine
IL-4 Fusion Toxin	NBI-3001	Solid Tumors	Phase I	Neurocrine
<b>Research:</b>				
CRF R <sub>1</sub> Antagonist		Anxiety, Depression, Gastrointestinal Disorders	Research	GlaxoSmithKline/Neurocrine
CRF R <sub>2</sub> Antagonist		Psychiatric Disorders, Eating Disorders	Research	GlaxoSmithKline/Neurocrine
GnRH Antagonist		Endometriosis, Fibroids, Prostate Cancer	Research	Neurocrine
CRF R <sub>2</sub> Agonist		Obesity	Research	Eli Lilly/Neurocrine
Melanocortin Receptor Agonist/Antagonist		Obesity, Cachexia	Research	Neurocrine
Melanin Concentrating Hormone Antagonist		Depression, Obesity, Anxiety	Research	Neurocrine
Excitatory Amino Acid Transporters		Neurodegenerative Diseases/Schizophrenia	Research	Wyeth/Neurocrine
CCR7		Autoimmunity	Research	Neurocrine
Fractalkine		Pain	Research	Neurocrine

“Phase III” indicates that we or our collaborators are conducting confirmatory clinical trials to determine safety and efficacy as primary support for regulatory approval to market a product for a specific disease or condition.

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

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

“Development” indicates lead compound(s) have been selected and are undergoing GLP toxicology studies to prepare for Phase I clinical trials.

“Research” indicates identification and evaluation of compound(s) in laboratory and pre-clinical models.

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

### **Products under Clinical Development**

#### *indiplon*

Insomnia is a prevalent neurological disorder in the United States, with approximately 79 million adults reporting trouble sleeping a few nights per week or more. Mattson Jack (epidemiological database used to determine the prevalence of a disease or disorder) states that 24 million adults indicated that they experience chronic insomnia, having trouble sleeping every night or almost every night. Despite this widespread prevalence, insomnia remains a disorder without a satisfactory therapeutic option, in that there is currently no therapy which induces and maintains sleep throughout the night without next-day residual effects.

Researchers have found that insomnia can be treated by drugs that interact with the site of action of a natural brain chemical involved in promoting and maintaining sleep. This chemical is called gamma amino-butyric acid (GABA), and the site of action is called the GABA-A receptor. During the 1980s, drugs that non-selectively target the GABA-A receptor, known as benzodiazepines, were used as sedatives to treat insomnia. This class of drugs produce several undesirable side effects, including negative interactions with other central nervous system depressants, such as alcohol, the development of tolerance upon repeat dosing, and rebound insomnia (recurrence of insomnia) following discontinuation of dosing. Additional side effects, due to the long half life (duration of action of

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a compound) associated with this class of drugs, include next-day residual sedation effects, and impairment of coordination and memory. Memory impairment, which can include amnesia for events occurring prior to and after drug administration, is of particular concern in the elderly who comprise approximately 20% of the total insomnia population according to Mattson Jack.

During the late 1980s, a class of drugs targeting a specific site on the GABA-A receptor, known as non-benzodiazepines, was developed. The non-benzodiazepines are believed to act more selectively on a GABA-A receptor subtype than the benzodiazepines and thus are believed to result in reduced incidence of side effects. The most popular of the non-benzodiazepines are marketed in the U.S. as Ambien® and Sonata®. Ambien® is the current market leader, with approximately \$1.3 billion in worldwide sales in 2002, according Sanofi-Synthelabo, with sales growing in excess of 20% per year. Additionally, in early 2003, Sepracor filed a New Drug Application (NDA) for Estorra™ (esopiclone), another non-benzodiazepine.

Of the patients reporting insomnia, over 75% of the patients state that they have experienced some sort of insomnia for at least a period of a year, with over 30% stating that the condition has persisted for at least five years. The indications of insomnia range from difficulty falling asleep, to difficulty staying asleep, to trouble going back to sleep after awakening in the middle of the night.

Our drug candidate for the treatment of insomnia, indiplon (formerly known as NBI-34060), a non-benzodiazepine GABA-A receptor agonist, acts via the same mechanism as the currently marketed non-benzodiazepine therapeutics. However, preclinical studies suggest that indiplon is more potent than the currently marketed non-benzodiazepines, including Ambien® and Sonata®. We believe that this improved profile will reduce the side effects characteristic of the currently marketed products. In our Phase II and III clinical studies, indiplon demonstrated no significant effects of next-day residual sedation at clinically relevant doses.

We are developing two formulations of indiplon, an immediate release formulation and a modified release formulation, to address the different needs of the insomnia patient population. To develop these two different formulations we have capitalized on an important feature of indiplon, its rapid absorption, and its short half-life in the body. Based on our clinical studies, we have determined that the concentration of indiplon in the bloodstream reaches levels high enough to induce sedation approximately 15 minutes after the patient takes the tablet. Indiplon is then rapidly metabolized and eliminated. This results in rapid sleep onset followed by rapid elimination of the drug from the body, reducing the risk of next-day residual sedation effects.

We believe that both formulations of indiplon will address the above mentioned forms of insomnia - difficulty falling asleep; difficulty staying asleep; and middle of the night awakenings, with difficulty getting back to sleep. The immediate release formulation can be used by people who have trouble falling asleep or those who wake up unexpectedly in the middle of the night and can't get back to sleep. The modified release formulation (which will provide two doses of drug, a bedtime dose and a middle of the night dose), will both rapidly induce sleep and maintain sleep through the night. If successful, this would represent the first non-benzodiazepine GABA-A receptor agonist approved by the United States Food and Drug Administration (FDA) for maintaining, rather than simply inducing, sleep.

During 2002, we completed our first Phase III clinical trial which included 593 subjects with transient insomnia. The results of this trial demonstrated that indiplon was safe, well tolerated, and effective in achieving rapid sleep induction without next-day residual effects. Our entire Phase III program will consist of eight studies with approximately 4,000 subjects. We have also completed 27 Phase I and Phase II clinical trials of indiplon for efficacy and safety involving approximately 1,400 subjects.

In our Phase II clinical studies, indiplon was also shown to be safe and effective in helping subjects with both chronic and transient insomnia to fall asleep rapidly without adverse side effects as compared to a placebo. Results of a single dose Phase II clinical trial in 35 healthy volunteers comparing an immediate release formulation of indiplon, 10 mg Ambien® and 7.5 mg zopiclone (a sedative available in Europe and under development in the U.S.) relative to placebo during middle of the night dosing demonstrated that indiplon does not lead to next-day residual sedation effects, while both Ambien® and zopiclone exhibited statistically significant measures of next-day adverse side effects of residual sedation when compared with placebo. Our gender and age studies to date have indicated that indiplon works with no major differences between male and female subjects and young adult and elderly subjects. In two studies of transient insomnia involving an aggregate of 559 patients, the median time to fall asleep, the primary clinical goal, was reduced by 40% to 59% compared to a placebo. In a study of chronic insomnia, subjects receiving



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indiplon compared to a placebo showed a statistically significant decrease in time to sleep onset and increase in sleep duration as well as quality of sleep at every dose.

We face the risk that the side effects and efficacy profile of indiplon seen in our Phase I, II, and III trials may not be confirmed in additional clinical trials or that the results of future trials may not warrant further trials.

### *Altered Peptide Ligand*

The American Autoimmune Related Diseases Association estimates that approximately 50 million people in the United States suffer from autoimmune diseases such as multiple sclerosis, rheumatoid arthritis, Type 1 diabetes, systemic lupus erythematosus and thyroiditis. Scientists believe that the body's immune system causes these diseases. The immune system protects an individual from disease agents, such as viruses, by recognizing and destroying those foreign substances using specialized blood cells, called lymphocytes. Occasionally, however, certain lymphocytes arise that inappropriately recognize the body's own tissues as an invader and begin to attack normal healthy tissue, resulting in an autoimmune disease like Type 1 diabetes. While the mechanism through which the lymphocyte initiates the autoimmune disease is still unknown, the development of drugs that specifically suppress the action of self-reactive lymphocytes or restore the function of regulatory cells may prove advantageous for the prevention, cure or treatment of an autoimmune disease.

One type of lymphocyte involved in the immune response to self or foreign substances is the T cell. T cells detect antigens, which are foreign substances, such as viruses or bacteria, and destroy them. Experiments conducted by our scientists determined that specific amino acid residues within a peptide sequence of an antigen are required for T cell recognition and subsequent cellular activation. Scientists can specifically alter the structure of such a peptide fragment so that it will not properly activate the T cell. This altered peptide ligand can thus prevent the T cell from destroying its target, or in the case of an autoimmune reaction, prevent the T cell from destroying the healthy tissue.

*Multiple Sclerosis.* Multiple sclerosis is a chronic autoimmune disease characterized by recurrent attacks of neurologic dysfunction due to damage in the central nervous system. The classic clinical features of multiple sclerosis include impaired vision and weakness or paralysis of one or more limbs. Patients develop a slow, steady deterioration of neurologic function over an average duration of approximately 30 years. According to the National Multiple Sclerosis Society, there are approximately 400,000 cases of multiple sclerosis in the United States. Currently available treatments for multiple sclerosis offer only limited efficacy. Doctors often prescribe steroids to reduce the severity of acute flare-ups and speed recovery. Experimental therapy with other immune-suppressive agents has shown limited success. Nevertheless, worldwide sales of multiple sclerosis therapies reached \$2.9 billion in 2002.

Our co-founder and Chief Scientific Advisor, Dr. Lawrence Steinman, identified one of the dominant destructive T cell types in the brains of patients who had died of multiple sclerosis. Dr. Steinman further identified one of the dominant antigens on the normal cell targeted by the autoreactive T cells, a peptide from a brain protein known as myelin basic protein. We designed a novel altered peptide ligand based on myelin basic protein that would target the autoreactive T cells that cause neurological damage in multiple sclerosis. Together with Novartis Pharmaceuticals Corporation, our former collaborative partner for this program, we filed an investigational new drug (IND) application with the FDA and received approval in 1996 to commence clinical trials. We subsequently completed Phase I clinical trials and two Phase II clinical trials of our altered peptide ligand for the treatment of multiple sclerosis, NBI-5788.

One of the Phase II trials was a multi-center, placebo-controlled, randomized, parallel design study in which patients received one of three doses of NBI-5788, and the other Phase II trial was an open label, unblinded, non-placebo-controlled study in eight patients conducted in collaboration with the National Institutes of Health (NIH). While allergic reactions were seen in approximately 10% of patients in these trials, suggesting that optimal dosing may be at lower levels than those selected for the trials, of the patients completing the placebo controlled study, the total volume of enhancing lesions was reduced in the lowest dose group compared to the placebo control. Moreover, in this study 57% of the patients in the lowest dose group experienced reductions in the volume of new enhancing lesions compared to 25% in the placebo group. In the open label study, a higher incidence of new brain lesions was found in two patients who received the highest dose and the one patient who received the low dose. As a result, the trial was stopped.

We plan to initiate a confirmatory Phase II safety and efficacy trial in 2003 to determine the optimal dose and frequency of administration. Our aim for future trials will be to further establish the benefit of altered peptide ligand therapy in patients with multiple sclerosis. We face the risks that we may not initiate or complete additional

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clinical trials or that results of any such studies may not warrant additional clinical development of potential products related to NBI-5788.

*Type 1 Diabetes.* Utilizing our experience in the development of altered peptide ligands for multiple sclerosis, we have extended this approach to Type 1 or insulin dependent diabetes mellitus, which is a metabolic disease in which the body does not produce enough insulin. Like multiple sclerosis, in Type 1 diabetes the immune system erroneously targets healthy tissue, in this case the pancreatic cells responsible for the production of insulin. According to the International Diabetes Federation, Type 1 diabetes is one of the most prevalent chronic childhood conditions worldwide, afflicting approximately 2.3 million patients in 2002. Diabetics often suffer from a number of complications of the disease including heart disease, circulatory problems, kidney failure, neurologic disorders and blindness. Current therapy for Type 1 diabetes consists of daily insulin injections to regulate blood glucose levels. This therapy does not cure nor does it prevent the disease.

We believe that an altered peptide ligand specific for autoimmune T cells involved in diabetes may stop the destruction of the insulin-secreting cells in early onset Type 1 diabetic patients, thus allowing them to delay or avoid chronic insulin therapy. In pre-clinical studies, this altered peptide ligand, NBI-6024, was capable of eliciting a protective immune response and reducing the incidence of diabetes. In addition, experiments using immune cells derived from the blood of Type 1 diabetes patients indicate that patients' immune cells recognize NBI-6024. This suggests that NBI-6024 may have the potential to intervene in the disease process in humans. We have completed four Phase I/IIa safety and dose escalating clinical trials in approximately 120 diabetic patients. Data from these trials indicates that NBI-6024 is safe and well tolerated. A Phase IIB clinical trial was initiated consisting of a randomized, double blind, placebo-controlled, multi-center, multi-national study in adolescent and adult patients with new onset Type 1 diabetes. This study will involve approximately 20 medical sites in Canada, Europe and South America and approximately 200 patients. We are also in discussions with the National Institutes of Health Type 1 Diabetes Research Group to initiate a second Phase IIB trial, which may begin in 2003 pending requested funding and agreement on study specifications from NIH.

In 2000, we entered into agreements with Taisho providing them with worldwide rights to NBI-6024. Pursuant to the collaboration agreement, we received licensing and option fees, payments for certain development milestones, and reimbursement of a significant portion of worldwide development expenses. In September 2002, the collaboration agreement with Taisho was restructured to provide that worldwide rights, excluding Japan, revert to us. The restructuring agreement provides that under certain circumstances, if we enter into a business arrangement with specified third parties, then Taisho will be entitled to receive a percentage of certain consideration received by us. Generally, if we do not enter into a business discussion with one of the specified third parties on or before a specified date, the restructured agreement will expire, and at that time the rights to Japan will revert to us.

We face the risks that we may not initiate or complete additional clinical trials or that results of any such studies may not warrant additional clinical development of NBI-6024.

### *GnRH Antagonist*

Gonadotropin-releasing hormone, or GnRH, is a brain peptide that stimulates the secretion of the pituitary hormones that are responsible for sex steroid production and normal reproductive function. Researchers have found that chronic administration of GnRH agonists reversibly shuts down this transmitter pathway and is clinically useful in treating hormone-dependent diseases such as prostate cancer, endometriosis and uterine fibroids. Other companies have developed several peptide drugs on this principle, such as Lupron® and Zoladex®, and according to market analyst reports by Med Ad News, the annual worldwide sales in 2001 for these drugs were approximately \$2.5 billion. However, since these drugs are peptides, they must be injected rather than taken orally. In addition, these types of agonists take up to several weeks to exert their effect, a factor not seen with direct gonadotropin-releasing hormone antagonists, and until these drugs exert their effects, they have shown a tendency to exacerbate the condition. We believe that there is a large potential market for an orally delivered gonadotropin-releasing hormone antagonist.

Our GnRH clinical efforts are focused on providing new treatments for prostate cancer, endometriosis and uterine fibroids. According to Mattson Jack, there are more than 5.7 million women in the U.S. are clinically recognized as having chronic endometriosis. Of those afflicted, approximately 200,000 patients are treated in a hospital setting, and approximately 250,000 are treated in an outpatient setting, according to a 1998 National Patient Profile audit. We believe that the availability of an oral treatment lacking the side effect profile of the currently

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available peptide agonists may be an alternative to surgery and encourage a higher treatment rate. Additionally, approximately 2.8 million women are symptomatic for uterine fibroids, according to TDR Data. We also believe our drug will have utility on the treatment of prostate cancer, of which there are expected to be approximately 221,000 new cases in 2003 in the U.S., according to the American Cancer Society.

We selected a lead clinical candidate in early 2001 and initiated our Phase I clinical program in November 2001. The results of the first Phase I trial demonstrated that GnRH reduced gonadotropin production (a surrogate for efficacy). In late 2002, we initiated another study which is a one week multiple dose study. We have also selected a second development candidate which will move into clinical trials during 2003. We face the risk that clinical studies may show different results than our pre-clinical studies or that clinical trials may show that our GnRH antagonist product candidates are not safe or effective.

### *Corticotropin-Releasing Factor*

According to the Mattson Jack, in 2002 over 45 million people in the United States had symptoms of depression. The National Institute of Mental Health has also indicated that over 16% of the United States population has an anxiety disorder. Top-selling anti-depressant and anti-anxiety therapeutics sold in excess of \$12 billion worldwide in 2001, according to market analyst reports from Med Ad News. However, there remain significant unmet medical needs. The leading drug class, known as the selective serotonin reuptake inhibitors, is not effective or intolerable in one-third of patients. These drugs frequently require as long as three weeks to take effect, and have significant adverse side effects such as sexual dysfunction. Therefore, a rapid acting anti-depressant with fewer side effects would represent a major advance in the treatment of depression.

Researchers have identified what they believe to be the central mediator of the body's stress responses or stress-induced disorders. This mediator is a brain chemical known as corticotropin-releasing factor, or CRF. CRF is overproduced in clinically depressed patients and individuals with anxiety disorders. Current research indicates that clinically depressed patients and patients with anxiety experience dysfunction of the hypothalamic-pituitary-adrenal axis, which is the system that manages the body's overall response to stress. When the body detects a threat to physical or psychological well-being, the region of the brain called the hypothalamus amplifies production of CRF, which induces the physical effects that are associated with stress which can lead to depression or anxiety.

The novelty and specificity of the CRF mechanism of action and the prospect of improving upon selective serotonin reuptake inhibitor therapy is a topic of interest throughout the psychiatric community and pharmaceutical industry, representing a market opportunity both to better serve patients and expand overall treatment for this life threatening disease.

We have a strategic position in the CRF field through our intellectual property portfolio and relationship with experts in the neuropsychiatric field. Wylie W. Vale, Ph.D., our co-founder and Chief Scientific Advisor, is considered a leader in this field of research. We have further characterized the CRF receptor system and have identified additional members of the CRF receptor family. We have patent rights on two receptor subtypes called CRF R<sub>1</sub> and CRF R<sub>2</sub>, and we have pending patent applications on small molecule organic compounds modulating the CRF receptors.

*Depression.* Depression is one of a group of neuropsychiatric disorders that is characterized by extreme feelings of elation and despair, loss of body weight, decreased aggressiveness and sexual behavior, and loss of sleep. Researchers believe that depression results from a combination of environmental factors, including stress, as well as an individual's biochemical vulnerability, which is genetically predetermined. Researchers believe that the biochemical basis of depression involves elevated secretion of CRF and abnormally low levels of other neurotransmitters in the brain such as serotonin. The most frequently prescribed antidepressant therapies are selective serotonin reuptake inhibitors such as Zoloft®, Paxil®, Celexa® and Prozac® which act to increase the levels of serotonin and several other chemicals in the brain. However, because these drugs affect a wide range of neurotransmitters, they have been associated with a number of adverse side effects. While newer, more selective drugs offer some safety improvement, side effects remain problematic. In addition, one of the biggest limitations of most existing antidepressant therapies is their slow onset of action.

The first clinical trial to offer evidence of proof of concept of CRF antagonists in addressing depression was a Phase IIa open label trial conducted with our NBI-30775 product candidate in 1999 pursuant to our two collaborations with Janssen Pharmaceutica N.V. (Janssen), in the field of CRF antagonists. Results from this trial

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indicated that NBI-30775 was safe and well tolerated and demonstrated anti-depressant activity as measured by a widely-accepted depression scale known as the Hamilton Depression Scores. In this trial, NBI-30775 was administered to 20 patients with major depressive disorders. Results from the trial, as reported in the Journal of Psychiatric Research, showed that treatment response, as defined by more than a 50% reduction in Hamilton Depression Scores, occurred in 50% of the patients in the low dose group and 80% of the patients in the higher dose group. While development of NBI-30775 was discontinued for safety reasons by our collaborator, Janssen we were encouraged by these results, which we believe support the hypothesized mechanism of action. In March 2002, Janssen notified us that it had elected to terminate the 1995 and 1999 agreements with us. As a result, exclusive rights to these first generation CRF antagonist compounds have reverted to us.

In 1998, we initiated a proprietary CRF R<sub>1</sub> antagonist program independent of Janssen. This program led to the discovery of a novel class of second generation CRF R<sub>1</sub> antagonist compounds of a chemical class distinct from the class of compounds that were subject to the Janssen collaboration. Clinical development of our second generation CRF R<sub>1</sub> antagonists began in December 2000 when we initiated a Phase I clinical program with NBI-34041, our current lead candidate. Our first study was a Phase I, randomized, double blind, placebo controlled single dose clinical trial of NBI-34041. The trial was conducted in normal volunteers and was designed to evaluate the safety, tolerability, pharmacokinetics and pharmacodynamics over a range of six escalating doses. The study results indicated no safety issues which would preclude advancement of the candidate to the next phase of clinical evaluation.

In July 2001, we announced our second CRF antagonist collaboration, a worldwide collaboration with GlaxoSmithKline, or GSK, to develop and commercialize CRF antagonists for psychiatric, neurological and gastrointestinal diseases. Under the terms of this agreement, Neurocrine and GSK will conduct a collaborative research program for up to five years and collaborate in the development of NBI-34041, as well as novel back-up candidates and second generation compounds identified through the collaborative research. In the second quarter of 2001, we initiated a Phase I sequential dose escalation study with three doses of NBI-34041 which has been completed. Data from this study indicates that NBI-34041 was safe and well tolerated at all doses tested with an adverse event profile no different than that of the placebo. As part of the collaboration agreement with GlaxoSmithKline, we continue to perform research and discovery in CRF. During 2003, we expect back up CRF compounds and follow on compounds to move into Phase I clinical development and preclinical studies.

In March 2002, the joint steering committee made a decision not to advance NBI-34041 into later stage clinical trials. Recent results from preclinical studies of NBI-34041 and its backup product candidate, NBI-35583, indicate that NBI-35583 has a superior product profile and greater safety margin compared to NBI-34041. The joint steering committee recommended moving NBI-35583 into advanced pre-clinical studies to support Phase I clinical development later this year. In addition, two additional back-up compounds were selected from the research pipeline.

We face the risk that CRF R<sub>1</sub> antagonist compounds may not be effective and safe therapeutics for the treatment of depression or any other conditions. In addition, we or GSK may decide not to initiate Phase I clinical testing on NBI-35583 or progress to later clinical trials in a timely manner, if at all.

*Anxiety.* Anxiety is among the most commonly observed group of central nervous system disorders, which includes phobias or irrational fears, panic attacks, obsessive-compulsive disorders and other fear and tension syndromes. Of the pharmaceutical agents that other companies currently market for the treatment of anxiety disorders, benzodiazepines, such as Valium<sup>®</sup> and Xanax<sup>®</sup>, and the anxiolytic BuSpar<sup>®</sup> and their generic equivalents are the most frequently prescribed. Several side effects, however, limit the utility of these anti-anxiety drugs. Most problematic among these are drowsiness, the inability to stand up, amnesia, drug dependency and withdrawal reactions following the termination of therapy. In view of significant evidence implicating CRF in anxiety-related disorders, we are developing small molecule CRF R<sub>1</sub> receptor antagonists as anti-anxiety agents that block the effects of overproduction of CRF. We believe that these compounds utilize a novel mechanism of action that may offer the advantage of being more selective, thereby providing increased efficacy with reduced side effects as compared to benzodiazepines.

As a co-examined variable in the NBI-30775 open label Phase IIa clinical trial for depression described above, the anti-anxiety effects of the CRF R<sub>1</sub> receptor antagonist NBI-30775 showed a reduction in Hamilton Anxiety Scores from baseline in both treatment groups at all times after dosing. In addition, in pre-clinical studies used to evaluate anti-anxiety drugs, our scientists have demonstrated with statistical significance that clinical compound

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candidates from our independent CRF R<sub>1</sub> antagonist program are effective following oral administration. We did not observe any evidence of clinically relevant side effects. These results are encouraging because they suggest that compounds blocking the CRF R<sub>1</sub> receptor may be effective in treating anxiety-related disorders. Despite these early results, further clinical studies may fail to demonstrate that CRF R<sub>1</sub> antagonists are safe or effective in addressing anxiety.

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

Irritable bowel syndrome is a gastrointestinal inflammatory disease that affects approximately 110 million people worldwide. Irritable bowel syndrome can be a lifelong, intermittent disease, involving chronic or recurrent abdominal pain and frequent diarrhea or constipation, or both. Some patients with irritable bowel syndrome report the onset of symptoms of the disease following a major life stress event, such as death in the family, which suggests that the causes of irritable bowel syndrome may be related to stress. In addition, most irritable bowel syndrome sufferers also experience anxiety and depression.

Clinical studies may fail to demonstrate that the CRF R<sub>1</sub> antagonists are safe or effective in addressing irritable bowel syndrome.

### *IL-4 Fusion Toxin*

Interleukin 4, or IL-4, is a natural chemical that modulates cell growth. Proteins that bind to IL-4, known as IL-4 receptors, are highly concentrated on the cells of malignant brain tumors as well as many other cancers, including some types of kidney and lung cancer. Targeted toxins are a novel form of anticancer therapy under investigation in a variety of clinical settings. Targeted toxin therapeutics carry a toxin to a target site on the cancer cell and subsequently kills the cancer cell. Many scientists believe that targeted toxins have several potential advantages over conventional chemotherapy in that they are more selective and effective in the treatment of chemotherapy-resistant cancer cells.

In 1998, we exclusively licensed from the NIH, a targeted toxin compound, IL-4 fusion toxin, which we call NBI-3001. A collaboration between the FDA and the National Cancer Institute designed the IL-4 fusion toxin. It is a combination protein in which IL-4 is attached to *Pseudomonas* exotoxin, a toxin that can kill cells. The IL-4 portion of the fusion toxin preferentially binds to human cancer cells because the cancer cells express elevated levels of receptors for IL-4 on their surface, while IL-4 receptor expression is absent or undetectable in normal tissue. Once the IL-4 portion of the IL-4 fusion toxin targets the toxin to the cancer cells, the toxin portion of the molecule preferentially kills the cancer cells.

*Malignant Glioma.* Malignant brain tumors are an extremely aggressive form of cancer. Despite current therapeutic options such as surgery, radiation and chemotherapy, the two year survival rate for malignant glioma, the most common form of malignant brain cancer, is only 10 percent. These tumors arise within the brain and generally remain confined to the brain. The clinical course of malignant glioma is characterized by relentless loss of vital neurological functions and death within approximately 12 months.

In 1999, we initiated a Phase I/II trial of NBI-3001 in patients with malignant glioma in which the primary endpoints were to determine safety and the maximum tolerated dose. This trial found NBI-3001 to be safe and to have an acceptable degree of tolerability in this patient population. While approximately one-third of the patients exhibited side effects during or immediately following therapy, these effects were consistent with marked tumor cell death and the subsequent inflammatory response to this tumor cell death, as well as the six month median survival data showing trends towards efficacy.

During 2002, we also completed a Phase II study designed to explore an improved delivery regimen and to determine a safe and optimal dose for Phase III trials. The study enrolled 32 patients with recurrent malignant glioma where NBI-3001 was infused intratumorally at high, medium, and low dose levels over 5 days, followed 3 weeks later by tumor resection. At the low dose of 90 mcg, the drug was well tolerated and was associated with a low

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incidence (10%) of drug-related serious adverse events within the first 2 weeks of infusion. Median survival for this dose group was greater than six months with the majority of patients still alive at the time follow up data were last analyzed. Additionally, MRI scans showed approximately 25% of the patients reached stable or partial regression of disease. These results indicate a safe and well-tolerated dose has been determined and that the compound is now ready to enter advanced efficacy trials using survival as the endpoint.

In October 1999, the FDA granted us fast track designation for NBI-3001. Fast track designation allows us to accelerate our clinical program for NBI-3001 and expedite receipt of regulatory approvals. In April 2000, we were awarded orphan drug designation for NBI-3001 for astrocytic glioma. Under FDA rules, drug developers may obtain orphan drug designation for drugs that treat a disease or condition that affects fewer than 200,000 people in the United States per year. Orphan drug designation provides us with seven years of marketing exclusivity following approval, tax incentives and access to grant funding. We face the risk that we will not successfully complete clinical testing or progress to later clinical trials in a timely manner, or at all.

*Solid Tumor Cancers.* In conjunction with our clinical trials of IL-4 fusion toxin in malignant glioma, we entered into a collaborative research and development agreement with the FDA to investigate the safety and efficacy of IL-4 fusion toxin in laboratory models of different cancers and by different routes of administration. Research teams from the FDA and NIH have published results with IL-4 fusion toxin demonstrating a high level of binding and destruction of specific types of cancers. We have conducted pre-clinical research to support the application of NBI-3001 to peripheral solid tumors and have shown that IL-4 fusion toxin can be safely administered intravenously in pre-clinical models. We filed an IND application with the FDA in July 2001 and initiated a Phase I clinical trial in November 2001 to first investigate the safety and efficacy of NBI-3001 against kidney (renal cell carcinoma) and non-small-cell lung cancers. These two cancers have a combined expected incidence in 2003 of approximately 170,000 people in the United States according to the American Cancer Society. While the study is still ongoing, preliminary results indicate this study has met the primary objectives of defining a dose-limiting toxicity and the maximum tolerated dose.

We face the risks that the effectiveness of NBI-3001 seen in our laboratory models, or the safety profile of NBI-3001 seen in our pre-clinical models, may not be confirmed in clinical trials or that the results of future clinical trials may not warrant further development in any of these settings or that the trial results may not support initiating clinical trials in cancers other than malignant glioma.

## **Research**

Our research focus is on addressing diseases and disorders of the central nervous system and endocrine system, which includes stress related disorders and neurodegenerative diseases, as well as eating disorders and autoimmune diseases. Central nervous system drug therapies represent one of the largest sectors of the worldwide drug market, accounting for over \$55 billion in worldwide drug sales in 2002, second only to cardiovascular drugs. Additionally, central nervous system drug therapies experienced a growth rate of approximately 10% during 2002.

### *CRF R<sub>1</sub> Antagonist*

As mentioned previously, the CRF R<sub>1</sub> antagonist has been identified by researchers to be the central mediator of the body's stress responses or stress related disorders. Since researchers believe that CRF is the primary mediator of stress, they have suggested that CRF R<sub>1</sub> antagonists may provide a treatment for irritable bowel syndrome. Researchers have demonstrated the CRF R<sub>1</sub> antagonists demonstrate dose dependent effect with in vivo preclinical models of irritable bowel syndrome. Together with GlaxoSmithKline, we are evaluating our proprietary CRF R<sub>1</sub> antagonists for treatment of stress, anxiety, depression, and irritable bowel syndrome. We face the risks that pre-clinical studies may not warrant initiating clinical testing of these candidates or that initial clinical data may not support continuation of the program and additional clinical trials.

### *CRF R<sub>2</sub> Antagonist*

Our scientists were the first to isolate a second CRF receptor, called CRF R<sub>2</sub>. We believe the distribution of CRF R<sub>2</sub> in the brain suggests that CRF R<sub>2</sub> could play a role in some forms of anxiety and some eating disorders. Our researchers have demonstrated that administration of a CRF R<sub>2</sub> antagonist reduces measures of anxiety in studies of obsessive compulsive disorder and conditioned fear. We are also working with GlaxoSmithKline in evaluating our proprietary CRF R<sub>2</sub> antagonist for treatment of a variety of psychiatric and eating disorders. We have screened our small molecule

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library and conducted exploratory chemistry to identify a new series of compounds to undergo further study. We face the risks that our work in this area will not lead to clinical candidates or that clinical trials will not find our candidates to be safe and effective.

### *GnRH Antagonists*

As previously mentioned, GnRH may be useful in treating certain hormone dependent diseases. Our discovery work in GnRH has allowed us to select a backup compound to move into pre-clinical studies during 2003. This compound is expected to complete GLP pre-clinical studies in mid-2003 and if successful, will advance to Phase I testing. We continue to search for innovative formulations of GnRH that may lead to additional candidates for clinical trials. We face the risks that our work in this area will not lead to clinical candidates or that clinical trials will not find our candidates to be safe and effective.

### *CRF R<sub>2</sub> Agonist*

CRF R<sub>2</sub> agonists may also represent a therapeutic strategy for diseases and disorders of the central nervous system. Preliminary data indicates that CRF may act as central regulators of both appetite and metabolism and may play a role in neurodegenerative diseases. In 1996, we initiated a three-year research collaboration with Eli Lilly to screen and optimize CRF R<sub>2</sub> agonists. In October 1999, the funded research portion of the program was completed as scheduled and Eli Lilly has retained control of the program and exclusive rights to the compounds. We face the risks that Eli Lilly may not initiate further research and that, if they do, the research may not identify suitable candidate compounds for development in a timely manner, or at all.

### *Melanocortin Receptor Agonist/Antagonist*

Melanocortin receptors are proteins on the surface of cells which help regulate some body functions such as eating and skin color. Researchers discovered that one of the melanocortin receptor subtypes, subtype 4, plays an important role in the mechanism regulating appetite and body weight. The subtype 4 receptor is activated by melanocyte stimulating hormone. When melanocyte stimulating hormone is injected into the brain, it reduces food intake and body weight. Responses have included the apparent increase in basal metabolic rate and lowering of serum insulin levels. We believe that an orally active subtype 4 agonist may produce the same effects and, thus, may provide a novel approach to the treatment of obesity. Conversely, the endogenous peptide antagonist of the central melanocortin subtype 4 receptor, has been shown to have the reverse effect, increasing food intake over a sustained period of time after a single brain injection and this observation has prompted significant interest in diseases such as cancer and AIDS related cachexia. For these reasons, we are also studying melanocortin subtype 4 receptor antagonists and have discovered novel, potent and selective compounds that are now being evaluated in relevant animal models. Additionally, researchers have recently suggested that melanocortin receptor subtype 4 agonists may also have a role in sexual dysfunction, and studies are underway to explore this further. We have screened our small molecule library and identified highly potent, selective orally active melanocortin subtype 4 receptor antagonist compounds. However, these compounds may fail to progress beyond the research phase, and we face the risk that our melanocortin research will not lead to product candidates.

### *Melanin Concentrating Hormone Antagonist*

Recent studies suggest that melanin concentrating hormone (MCH) plays a role in the regulation of eating behavior. Based on these findings, we believe that blocking the effect of MCH with a small molecule antagonist may represent a novel approach to the treatment of obesity. Additional indications include anxiety and depression. Through our research efforts, we have identified and screened small-molecule, orally-active compounds which will block the activity of MCH at its receptor. We believe that these compounds may provide a novel therapeutic strategy for treating obesity and related disorders. We face the risk that our research in this area will not lead to product candidates.

### *Excitatory Amino Acid Transporters*

Some of the most successful central nervous system drugs, including selective serotonin reuptake inhibitors such as Prozac<sup>®</sup>, selectively target transporters of neurotransmitters in the brain. Similarly, we are targeting a set of proteins, called excitatory amino acid transporters, generally located in the brain, which transport glutamate in and out of cells, to selectively control the levels of this neurotransmitter. Drugs which alter the activity of these

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transporters are expected to produce a therapeutic benefit in disorders where glutamate levels are abnormal such as head trauma, schizophrenia, Lou Gehrig's Disease and other neurodegenerative and psychiatric disorders.

We collaborate with Wyeth to investigate controlling the glutamate transporter function as a novel strategy for the treatment of neurodegenerative and psychiatric disorders which included basic research to understand the function and regulation of the transporters, along with the identification and characterization of chemical and biological leads. We face the risks that we may be unable to demonstrate that these excitatory amino acid transporters are therapeutic targets or that we may fail to identify any product candidates for pre-clinical or subsequent clinical development.

The excitatory amino acid transporter research has also been expanded to focus on retinal cell death associated with damage from low blood flow. In 2000, the NIH awarded us a research grant to fund our work to identify novel compounds for the alleviation of neuronal cell death in response to a wide range of conditions including diabetic induced nerve damage, glaucoma and other circulatory conditions of the eye. This work is independent of our collaboration with Wyeth.

### *CCR7 Antagonist*

Chemokine receptors are necessary for developing immune responses to viruses or bacterial infections. However, in some cases an inappropriate immune response to the body's own tissues is created, resulting in autoimmune and inflammatory diseases. The chemokine receptor CCR7 has been shown in mice experiments to play a role in creating these inappropriate autoimmune responses. We have an ongoing research effort in this area and have identified small molecule, orally-active compounds which will facilitate blockage of the CCR7 receptor. These compounds may provide a novel therapeutic strategy for treating rheumatoid arthritis, diabetes, or multiple sclerosis and other autoimmunity diseases. We face the risk that our research in this area will not lead to product candidates.

### *Fractalkine*

Fractalkine is a unique member of the chemokine family, which is highly expressed by neurons in the brain. Recent evidence suggests that blockade of CX3CR1, the receptor for fractalkine, may be beneficial for prevention of chronic pain. We have initiated a research effort to identify small-molecule, orally-active compounds as fractalkine receptor antagonists. We believe that these compounds may provide a novel therapeutic strategy for treating pain and related disorders. We face the risk that our research in this area will not lead to product candidates.

## **Our Discovery Technology**

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

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

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

The power of MCD however, lies not in its application to a single receptor as a drug target but in the database of compounds that are characterized and isolated for the next target from the same class of receptors. Our



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current focus is on the most attractive receptor class in the pharmaceutical industry, G-protein-coupled receptors. MCD is not a static process, but one that becomes more powerful, more predictive, and more efficient with each subsequent use. It is an artificial intelligence system applied to drug design.

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

*High-Throughput Screening.* We have assembled a chemical library of diverse, low molecular weight organic molecules for lead compound identification and we have implemented robotics screening capabilities linked to our library of compounds that facilitate the rapid identification of new drug candidates for multiple drug targets. In addition, we have designed a 175,000-compound library focused on some of our molecular targets. We believe that our utilization of high-throughput screening and medicinal and peptide chemistry will enable us to rapidly identify and optimize lead molecules.

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

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

*Gene Sequencing.* We apply integrated automated DNA sequencing and gene identification technology in our drug discovery program, enabling us to perform extended gene analysis in a rapid, high-throughput format with independent linkage into a sequence identification database. We have optimized gene sequencing instrumentation for differential display, a technique that may facilitate the rapid identification of novel genes.

## **Our Business Strategy**

Our goal is to become the leading therapeutic product-based biopharmaceutical company focused on neurologic and endocrine diseases and disorders. There are six key elements to our business strategy:

*Build a Large and Diversified Product Portfolio to Mitigate Overall Clinical and Technical Risk.* We believe that by building a large and diverse product pipeline, we can mitigate some of the risks associated with drug development. We currently have 16 programs in various stages of research and development, with seven projects in clinical development and nine research projects to supply clinical compounds for the future. We take a portfolio approach to managing our pipeline that balances the size of the market opportunities with clear and defined clinical and regulatory paths to approval. We do this to ensure that we focus our internal development resources on innovative therapies with high probabilities of technical and commercial success.

*Identify Novel Drug Targets for the Development of Innovative Therapies to Address Large Unmet Market Opportunities.* We seek to identify and validate novel drug targets for internal development or collaboration. For example, the novel drug candidates we have identified to regulate CRF, which is believed to be the central mediator of the body's stress response, may represent the first new breakthrough for anxiety and depression in over 20 years. Gonadotropin-releasing factor antagonists, compounds designed to reduce the secretions of sex steroids, may represent the first novel non-injectible means of treatment of prostate cancer and endometriosis. Additionally, Melanocortin and MCH modulators are compounds which affect proteins in the brain believed to be involved in many activities of the body. The creativity and productivity of our discovery research group will continue to be a critical component for our continued success. Our team of approximately 125 biologists and chemists has a goal of delivering three innovative clinical compounds over the next five years to fuel our research and development pipeline.

*Establish Corporate Collaborations with Global Pharmaceutical Companies to Assist in the Development of Our Products and Mitigate Financial Risk While Retaining Significant Commercial Upside.* We leverage the development, regulatory and commercialization expertise of our corporate collaborators to accelerate the development of our potential products while typically retaining co-promotional rights, and at times commercial

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rights, in North America. We intend to further leverage our resources by continuing to enter into strategic alliances to enhance our internal development and commercialization capabilities. We currently have strategic alliances with:

- Pfizer, for indiplon for the treatment of insomnia;
- GlaxoSmithKline, for second generation corticotropin-releasing factor receptor antagonists to treat anxiety and depression and irritable bowel syndrome;
- Wyeth, for compounds to treat neurodegenerative and psychiatric diseases;
- Taisho, for compounds to treat Type 1 diabetes, in which the body does not produce enough insulin; and
- Eli Lilly, for treatments of central nervous system disorders, including obesity.

*Acquire Rights to Complementary Drug Candidates.* We plan to continue to selectively acquire rights to products in various stages of development to take advantage of our drug development capabilities. For example, in May 1998, we licensed from the NIH an IL-4 fusion toxin which is currently in Phase II clinical trials for recurrent malignant glioma, as well as kidney, non-small cell lung cancer. In May 1998, we acquired Northwest NeuroLogic, Inc. and thereby considerably expanded our research pipeline. Through this acquisition, we acquired the technology and intellectual property rights surrounding excitatory amino acid transporters, a portion of which is now in collaboration with Wyeth. We also acquired from Northwest NeuroLogic intellectual property relating to melanocortin technology and other technologies that we are developing. In June 1998, we licensed exclusive worldwide commercial rights for indiplon, our compound for the treatment of insomnia, from DOV Pharmaceutical, Inc. (DOV) and have since moved this compound into advanced clinical development.

*Supplement Our Internal Research Capabilities by Collaborating with Leading Platform Technology Companies.* We believe we can complement our multidisciplinary research process by selectively accessing new technologies from platform technology companies. Through creative collaborations with technology leaders, we believe we can accelerate and expand our internal discovery efforts. We have entered into a number of alliances with other platform technology companies to enhance our drug discovery and development capabilities. The most recent of these is our alliance with MediChem Life Sciences to crystallize the CRF<sub>1</sub> receptor to aid in design of a new class of CRF blockers.

*Outsource Capital Intensive and Non-Strategic Activities.* We intend to focus our resources on research and development activities by outsourcing our requirements for clinical drug supply and certain pre-clinical studies and clinical monitoring activities. We believe the availability of skilled contract manufacturers and contractors will allow us to cost-effectively meet these needs and thereby allow us to concentrate our full attention and resources on our core discovery and development programs to generate additional product opportunities.

## **Our Strategic Alliances**

One of our business strategies is to utilize strategic alliances to enhance our development and commercialization capabilities. To date, we have formed the following alliances:

**Pfizer.** In December 2002, we announced 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 we will collaborate in the completion of the indiplon Phase III clinical program. We will be responsible for \$15 million in development costs, and all other external collaboration costs will be borne by Pfizer. Following the filing of a New Drug Application (NDA) with the FDA regarding indiplon, Pfizer will support the creation of a 200 person Neurocrine sales force. Our sales force will detail Pfizer's antidepressant drug Zoloft® to psychiatrists in the United States. Upon approval of the indiplon NDA, our sales force will also co-promote indiplon to psychiatrists and sleep specialists in the United States. During the first quarter of 2003, we received an upfront payment of \$100 million and will also be eligible to receive up to \$300 million in additional pre-commercialization milestone payments as indiplon moves toward commercialization. Further, upon commercialization of indiplon, we will be entitled to a percentage of worldwide sales of indiplon for the longer of 10 years or the life of the indiplon patent rights as well as co-promotion payments on sales of Zoloft® and indiplon in the United States. In addition, Pfizer has committed to loan us up to \$175 million, at commercial terms, pursuant to a secured short-term credit facility, subject to U.S. launch of indiplon and various other conditions. Pfizer may terminate the collaboration at its discretion upon 180-days written notice to us. In such event, we would be entitled to certain payments for ongoing clinical development and related activities and all indiplon product rights would revert to us. We have obtained rights to indiplon pursuant to a 1998 sublicense

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and Development Agreement with DOV and we are responsible for specified milestone payments and royalties on net sales to DOV under the license agreement.

**GlaxoSmithKline.** In July 2001, we announced a worldwide collaboration with GSK to develop and commercialize CRF antagonists for psychiatric, neurological and gastrointestinal diseases. Under the terms of this agreement, Neurocrine and GSK will conduct a collaborative research program for up to five years and collaborate in the development of our current lead compounds, as well as novel back-up candidates and second generation compounds identified through the collaborative research. In addition, Neurocrine 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 us. In such event, we may be entitled to certain payments and all product rights would revert to us. As of December 31, 2002, we have recorded revenues of \$2.2 million in license fees, \$15.8 million in milestone payments, \$8.2 million in sponsored research and development and \$694,000 in reimbursement of development costs. In addition, at December 31, 2002 we have \$2.3 million of deferred license fees that will be amortized over the remaining life of the agreement. GSK also sponsors a portion of our research efforts related to CRF (as discussed previously) through annual payments, of which \$3.1 million is deferred and will be amortized over the remaining sponsored research period.

**Taisho.** In December 1999, we entered into an agreement with Taisho, providing to them an exclusive option to obtain European, Asian and North American development and commercialization rights for our altered peptide ligand product, NBI-6024, for Type 1 diabetes in exchange for a \$2.0 million option fee. In July 2000, Taisho exercised its option as to Europe and Asia, and in December 2000, Taisho exercised its option as to North America. In September 2002, the collaboration agreement with Taisho was further restructured to provide that worldwide rights, excluding Japan, revert to us. The restructuring agreement further provides that under certain circumstances, if we enter into a business arrangement with specified third parties, then Taisho will be entitled to receive a percentage of certain consideration received by us. Generally, if we do not enter into a business discussion with one of the specified third parties on or before a specified date, the restructured agreement will expire, and at that time the rights to Japan will revert to us. As of December 31, 2002, we have recorded revenues of \$4.9 million in license fees, \$9.5 million in milestone payments \$5.6 million in sponsored research and \$10.5 million in reimbursement of development costs. In addition, we have \$1.1 million remaining of deferred license fees that will be recognized as revenue in 2003.

**Wyeth.** Effective January 1999, we entered into a collaboration and license agreement with Wyeth relating to the research, development and commercialization of compounds that control excitatory amino acid transporters for the treatment of neurodegenerative and psychiatric diseases. We have granted Wyeth exclusive and non-exclusive rights to our excitatory amino acid transporters technology as well as exclusive rights to any products developed during the collaboration. These licenses are for the term of the patents licensed. We will receive royalties on product sales for the terms of the patents covering the collaboration products, subject to adjustments for royalties payable to other parties and for competition. We will also receive royalties for products that are not the subject of issued patents. Under certain conditions, we have the option to co-promote collaboration products in Canada and the United States. Wyeth may terminate the agreement if they decide that the research is not successful, if they decide to stop the program or if we are acquired by another company. The agreement may also be terminated by either party for the other party's failure to meet its obligations under the agreement or bankruptcy. The three-year sponsored research portion of the Wyeth agreement was completed on schedule in December 2001 and was subsequently extended on a smaller scale through December 2002.

As of December 31, 2002, we recognized a total of \$13.9 million under the Wyeth agreement consisting of \$10.5 million in sponsored research and \$3.4 million in milestone payments.

**Eli Lilly and Company.** In October 1996, we entered into a research and license agreement with Eli Lilly to collaborate in the discovery, development and commercialization of CRF binding protein ligand inhibitors for the treatment of central nervous system disorders including obesity and dementias, such as Alzheimer's disease, and CRF R<sub>2</sub> agonists for central nervous system diseases and disorders. Under the agreement we are entitled to milestone payments for certain development and regulatory accomplishments. We will have the option to receive co-promotion rights and share profits from commercial sales of select products that result from the collaboration in the U.S. or receive royalties on U.S. product sales. We will receive royalties on product sales for the rest of the world.

In October 1999, the funded portion of the research program concluded as scheduled and, to our knowledge, Eli Lilly is not planning any specific future development efforts, and we do not expect to receive any additional

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payments under this agreement. During the funded portion of the research program we received payments totaling \$17.2 million.

**Janssen Pharmaceutica, N.V.** In January 1995, we entered into the first of two research and development agreements with Janssen to collaborate in the discovery, development and commercialization of small molecule CRF R<sub>1</sub> antagonists for the treatment of anxiety, depression and substance abuse. Under the January 1995 agreement, Janssen funded three years of research at Neurocrine and received exclusive licenses to all CRF R<sub>1</sub> antagonist compounds developed during the term of the funded research or during the year thereafter. The terms of the licenses are for the term of the patents licensed under the agreement. The collaborative research portion of the first Janssen agreement was completed as scheduled in 1997. In September 1999, together with Janssen, we entered into an amended agreement to expand the collaborative research and development efforts to identify additional small molecule CRF antagonists for the treatment of psychiatric disorders. In connection with the amended Janssen agreement, we received an initial payment and two years of additional research funding for our scientists working in collaboration with Janssen. This additional research was completed in February 2001.

In March 2002, Janssen notified us that it elected to terminate both the 1995 and 1999 agreements. As a result, exclusive rights to all of the first generation CRF R<sub>1</sub> antagonist compounds developed thereunder reverted to us. We do not expect any additional payments of any kind under the Janssen agreement and no revenue was recognized under this agreement during 2002. During the funding portion of the agreement we received payments totaling \$21.1 million

**Risks Related to Our Strategic Alliances.** We face the risks that we or any of the above collaborators may not be successful in research and drug discovery, that any pre-clinical and clinical drug candidates arising from the collaborations may not generate commercial product candidates that have viable clinical, regulatory and intellectual property profiles or that any commercial products arising from any of these collaborations may not enjoy market acceptance. Therefore, we may never receive any milestone payments or royalty income under any of our collaboration agreements.

### **Intellectual Property**

We seek to protect our lead compounds, compound libraries, expressed proteins, synthetic organic processes, formulations, assays, cloned targets, screening technology and other technologies by filing, or by causing to be filed on our behalf, patent applications in the United States and abroad. We have 25 issued U.S. patents, approximately 50 pending U.S. patent applications and approximately another 150 issued and pending foreign patents and applications. We have licensed, from institutions such as The Salk Institute, Stanford University, Oregon Health Sciences University, DOV Pharmaceutical and others the rights to an additional 30 issued U.S. patents, 20 pending U.S. patent applications, and 50 issued and pending foreign filings. We face the risk that one or more of the above patent applications may be denied. We also face the risk that our issued patents may be challenged or circumvented or may otherwise not provide protection for any commercially viable products we develop.

The technologies we use in our research, as well as the drug targets we select, may unintentionally infringe the patents or violate the proprietary rights of third parties. If this occurs, we may be required to obtain licenses to patents or proprietary rights of others in order to continue with the commercialization of our products. We are aware of a patent application controlled by another company, which if granted in its broadest scope and held to be valid, could impact the commercialization of our modified release insomnia formulation unless we obtain a license, which may not be available to us. We are also aware of pending and issued patent claims to melanin concentrating hormone ligand and receptor, and certain uses of melanocortin subtype 4 agonists. We are conducting research in all of those areas and may ultimately need to license those patents in order to proceed. In addition, we are aware of two U.S. patents relating to IL-4 proteins that are controlled by other entities which, if construed very broadly, and if valid as so construed, could prevent us from commercializing our IL-4 fusion toxin products in the United States unless we obtain a license, which may not be available to us on commercially reasonable terms, or at all. We do not believe that our research and development activities as currently conducted infringe any valid issued patents.

Indiplon, our leading gamma amino-butyric acid agonist compound for the treatment of insomnia, is covered in an issued U.S. patent, which we licensed from DOV Pharmaceutical. The term of the U.S. patent is due to expire in 2020. Additional U.S. patents covering synthesis, formulations and forms of indiplon were issued in 2002 and do not expire until 2020. Indiplon is not currently covered by any foreign patents of which we are aware. We intend to seek additional protection of this compound through nine U.S. and foreign patent applications directed to the synthesis,

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formulations and various forms of indiplon, which could extend certain patent protection to the year 2020. We face the risk that these patents may not issue, or may subsequently be challenged successfully. In addition to the granted and potential patent protection, the United States, the European Union and Japan all provide data protection for new medicinal compounds. If this protection is available, no competitor may use the original applicant's data as the basis of a generic marketing application during the period of data protection. This period of exclusivity is five years in the United States, six years in Japan and six to ten years in the European Union, measured from the date of FDA, or corresponding foreign, approval.

### **In-Licensed Technology**

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

- In December 2002, we entered into a collaboration and license agreement with Biosite Incorporated relating to high affinity antibodies
- In December 2002, we licensed library development software from Deltagen Research Laboratories, Inc.
- In December 2002, we licensed knock-out mice to certain target genes from Deltagen, Inc.
- In May 2002, we licensed a SK-MEL-37 cell line from the Sloan-Kettering Institute for Cancer Research.
- In June 2001, we licensed nonexclusive rights to the BON cell line from the University of Texas Medical Branch.
- In May 2001, we licensed nonexclusive rights to a murine CCR7 expressing cell line from Public Health Service.
- In March 2001, we licensed nonexclusive rights to a saoS-2 cell line from The Sloan-Kettering Institute for Cancer Research.
- In March 2001, we licensed a HERG cell line from Wisconsin Alumni Research Foundation.
- In October 2000, we licensed nonexclusive rights to several GT1-cell lines from The Salk Institute.
- In August 2000, we licensed nonexclusive rights to CRF R<sub>1</sub> deficient mice from the Research Development Foundation.
- In July 2000, we licensed exclusive rights to melanocortin subtype 3 receptor knock-out mice from Oregon Health Sciences University.
- In August 1999, we licensed nonexclusive rights to the human gonadotropin-releasing hormone receptor from Mount Sinai School of Medicine.
- In January 1999, we licensed exclusive worldwide rights to patents relating to excitatory amino acid transporters and melanocortin 1-5 from Oregon Health Sciences University.
- In December 1998, we licensed nonexclusive rights to technology covering melanocortin subtype 4 from the University of Michigan.
- In June 1998, we licensed exclusive worldwide rights to our sedative compound, indiplon, from DOV Pharmaceutical, Inc.
- In May 1998, we licensed exclusive worldwide rights to patents covering NBI-3001, our IL-4 fusion toxin, from the National Institutes of Health and inventors Ira Pastan and David Fitzgerald.

### **Manufacturing**

We currently rely on contract manufacturers, and will continue to rely on contract manufacturers for at least the next few years, to produce sufficient quantities of our product candidates for use in our pre-clinical and anticipated clinical trials. We have established an internal pharmaceutical development group to develop manufacturing methods for our products, to optimize manufacturing processes, and to select and transfer these manufacturing technologies to our suppliers. We continue to contract with multiple manufacturers to ensure adequate product supply and to mitigate risk.

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

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If we are unable to establish and maintain relationships with third parties for manufacturing sufficient quantities of our product candidates and their components that meet our planned time and cost parameters, it could delay the development and timing of our clinical trials.

### **Marketing and Sales**

We currently have no sales or distribution capabilities. In order to commercialize any of our product candidates, we must either internally develop sales and distribution capabilities or make arrangements with third parties to perform these services. Additionally, we currently have no experience in marketing or selling pharmaceutical products. We are currently initiating marketing activities for indiplon by hiring staff with experience in pharmaceutical sales, marketing and distribution.

As part of our collaboration agreement with Pfizer, we will receive funding from Pfizer for a 200 person United States sales force. This funding will commence upon our filing of a NDA for indiplon and the sales force will immediately focus on detailing Pfizer's antidepressant drug Zoloft® to psychiatrists. Upon government approval of the indiplon NDA, the sales force will also co-promote indiplon to psychiatrists and sleep specialists. Pfizer will manage all aspects of distribution for both Zoloft® and indiplon.

Additionally, under our collaboration agreements with GlaxoSmithKline, Wyeth, and Eli Lilly, we may have the opportunity to co-promote some of our other products in the United States. To market any of our other products directly, we must develop a sales force with technical expertise and with supporting distributions capabilities, none of which we currently have.

### **Government Regulation**

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

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

Phase I	Clinical trials are conducted with a small number of subjects to determine the early safety profile, maximum tolerated dose and pharmacokinetics of the product in human volunteers.
Phase II	Clinical trials are conducted with groups of patients afflicted with a specific disease in order to determine preliminary efficacy, optimal dosages and expanded evidence of safety.
Phase III	Large-scale, multi-center, comparative trials are conducted with patients afflicted with a target disease in order to provide enough data to demonstrate with substantial evidence the efficacy and safety required by the FDA.

The FDA closely monitors the progress of each of the three phases of clinical trials that are conducted in the United States and may, at its discretion, reevaluate, alter, suspend or terminate the testing based upon the data accumulated to that point and the FDA's assessment of the risk/benefit ratio to the patient. To date we have also conducted some of our clinical trials in Europe and South Africa.

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Once Phase III trials are completed, drug developers submit the results of pre-clinical studies and clinical trials to the FDA in the form of a new drug application, or a biologics licensing application for approval to commence commercial sales. In response, the FDA may grant marketing approval, request additional information or deny the application if the FDA determines that the application does not meet regulatory approval criteria. FDA approvals may not be granted on a timely basis, or at all. Furthermore, the FDA may prevent a drug developer from marketing a product under a label for its desired indications, which may impair commercialization of the product. Similar regulatory procedures must also be complied within countries outside the United States.

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

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

### *Orphan Drug Designation*

The FDA may grant orphan drug designation to drugs intended to treat a “rare disease or condition,” which is generally a disease or condition that affects fewer than 200,000 individuals in the United States. Orphan drug designation must be requested before submitting a new drug application. After the FDA grants orphan drug designation, the generic identity of the therapeutic agent and its potential orphan use are disclosed publicly by the FDA. Orphan drug designation does not convey any advantage in, or shorten the duration of, the regulatory review and approval process. If a product that has orphan drug designation subsequently receives FDA approval for the indication for which it has orphan drug designation, the product is entitled to orphan exclusivity, which means the FDA may not approve any other applications to market the same drug for the same indication, except in very limited circumstances, for seven years. Our IL-4 fusion toxin product candidate has received orphan drug designation from the FDA for astrocytic glioma.

### *Approvals Outside the United States*

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

### *Fast Track Designation*

Congress enacted the Food and Drug Administration Modernization Act of 1997, in part, to ensure the timely availability of safe and effective drugs, biologics and medical devices by expediting the FDA review process for new products. The Food and Drug Administration Modernization Act establishes a statutory program for the approval of so-called fast track products. The new law defines a fast track product as a new drug or biologic intended for the treatment of a serious or life-threatening condition that demonstrates the potential to address unmet medical needs for such a condition. Under the new fast track program, the sponsor of a new drug or biologic may request the FDA to designate the drug or biologic as a fast track product at any time during clinical development of the product. Fast-track designation provides an expedited review of a product, which accelerates FDA approval.

We may seek fast track designation to secure expedited review of appropriate product candidates. We can never be sure that we will obtain fast track designation. We cannot predict the ultimate impact, if any, of the new fast track process on the timing or likelihood of FDA approval of any of our potential products. We received fast track designation for our IL-4 fusion toxin.

## **Competition**

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

- other drug development technologies;
- methods of preventing or reducing the incidence of disease, including vaccines; and
- new small molecule or other classes of therapeutic agents.

Developments by others may render our product candidates or technologies obsolete or noncompetitive. We are performing research on or developing products for the treatment of several disorders including insomnia, anxiety, depression, malignant brain tumors and peripheral cancers, diabetes mellitus, multiple sclerosis, irritable bowel syndrome, eating disorders, pain, prostate cancer, obesity and certain women's health disorders.

We are developing a gamma amino-butyric acid receptor agonist, indiplon, for the treatment of insomnia. Ambien<sup>®</sup> and Sonata<sup>®</sup> are already marketed for the treatment of insomnia by Sanofi-Synthelabo and King Pharmaceuticals, Inc., respectively. Additionally, Sepracor has filed a NDA for Estorra with the FDA for the treatment of insomnia.

Products that may compete with NBI-5788, our altered peptide ligand for multiple sclerosis, include Betaseron<sup>®</sup> and Avonex<sup>®</sup>, similar forms of beta-interferon marketed by Berlex BioSciences and Biogen, respectively, and Rebif<sup>®</sup> marketed by Ares Serono. Copaxone<sup>®</sup>, a peptide polymer marketed by Teva, has also been approved for the marketing in the United States and certain other countries for the treatment of multiple sclerosis.

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

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

Guilford Pharmaceuticals' Gliadel<sup>®</sup> is approved in the U.S. and Europe for use in a subset of brain cancers known as recurrent glioblastoma multiforme. Gliadel<sup>®</sup> is also under review by the FDA for treatment of primary glioblastoma. Gliadel<sup>®</sup> will potentially compete with our IL-4 fusion toxin product, NBI-3001, if our product is approved by the FDA. Temozolomide, marketed by Schering Plough, is approved in Europe for both recurrent malignant glioma and recurrent astrocytoma and in the U.S. for only recurrent astrocytoma. Temozolomide may also compete with our IL-4 fusion toxin product.

We are also pursuing development of NBI-3001 for the treatment of peripheral solid tumors, such as kidney cancer and non-small-cell lung cancer. Proleukin<sup>®</sup> is marketed by Chiron for the treatment of kidney cancer, and drug treatments for non-small-cell lung cancer include Taxotere<sup>®</sup>, marketed by Aventis, Taxol<sup>®</sup>, marketed by Bristol-Myers Squibb, Navelbine<sup>®</sup>, marketed by GSK, and Gemzar<sup>®</sup>, which is marketed by Eli Lilly.

There are a number of competitors to products in our research pipeline. Lupron Depot<sup>®</sup>, marketed by Takeda-Abbott Pharmaceuticals, Zoladex<sup>®</sup>, marketed by AstraZeneca, and Synarel<sup>®</sup>, marketed by Pharmacia, are gonadotropin-releasing hormone peptide agonists that have been approved for the treatment of prostate cancer, endometriosis, infertility, and central precocious puberty. These drugs may compete with any small molecule gonadotropin-releasing hormone antagonists we develop for these indications. Anti-obesity therapeutics currently available include Xenical<sup>®</sup> from Roche Laboratories and Meridia<sup>®</sup> from Abbott Laboratories. If one or more of these products or programs are successful, it may reduce or eliminate the market for our products.

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



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- capital resources;
- research and development resources, including personnel and technology;
- regulatory experience;
- pre-clinical study and clinical testing experience;
- manufacturing and marketing experience; and
- production facilities.

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

### **Employees**

As of December 31, 2002, we had 276 employees, consisting of 253 full-time and 23 part-time employees. Of the full-time employees, approximately 85 hold Ph.D., M.D. or equivalent degrees. None of our employees are represented by a collective bargaining arrangement, and we believe our relationship with our employees is good. Furthermore, recruiting and retaining qualified scientific personnel to perform research and development work in the future will also be critical to our success. We face the risk that we may not be able to attract and retain personnel on acceptable terms given the competition among biotechnology, pharmaceutical and health care companies, universities and non-profit research institutions for experienced scientists. In addition, we rely on members of our Scientific Advisory Board and a significant number of consultants to assist us in formulating our research and development strategies.

### **Insurance**

We maintain product liability insurance for our clinical trials. We intend to expand our insurance coverage to include the sale of commercial products if marketing approval is obtained for products in development. However, insurance coverage is becoming increasingly expensive, and no assurance can be given that we will be able to maintain insurance coverage at a reasonable cost or in sufficient amounts to protect us against losses due to liability. There can also be no assurance that we will be able to obtain commercially reasonable product liability insurance for any products approved for marketing.

### **Our Scientific Advisory Board**

We have assembled a Scientific Advisory Board that currently consists of 11 individuals. Members of our Scientific Advisory Board are leaders in the fields of neurobiology, immunology, endocrinology, psychiatry and medicinal chemistry. Our Scientific Advisory Board advises us in the selection, implementation and prioritization of our research programs.

Our Scientific Advisory Board presently consists of the following individuals:

*Susan G. Amara, Ph.D.*, a Senior Scientist and Professor at the Vollum Institute for Advanced Biomedical Research and an Investigator in the Howard Hughes Medical Institute, is an expert on the cellular and molecular biology of neurotransmitter transporters, excitatory amino acid transporter structure and regulation and signaling roles of neurotransmitter transporters.

*Dale Boger, Ph.D.*, joined the Scripps Institute in 1991 as the Richard and Alice Kramer Professor of Chemistry and in 1996 was also appointed as a member of Skaggs Institute for Chemical Biology. Dr. Boger is internationally recognized for his work in organic synthesis, heterocyclic chemistry, natural products total synthesis and biological evaluation, synthetic methodology development, medicinal and bioorganic chemistry and has made seminal contributions to the understanding of DNA-agent interactions of naturally occurring antitumor-antibiotics.

*Michael Brownstein, M.D., Ph.D.*, is Chief of the Laboratory of Genetics at the National Institute of Mental Health and National Human Research Institute. He is a recognized expert in molecular pharmacology as it applies to the field of neuroendocrinology, where he has defined many of the pharmaceutically important neurotransmitter receptors and transporter systems.

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*Roger D. Cone, Ph.D.*, a senior scientist at the Vollum Institute for Advanced Biomedical Research, is an international expert on the neuroendocrine system, with particular expertise on the melanocortin system and the hypothalamic control of energy homeostasis. Dr. Cone served as an editor of the Journal Endocrinology through December 2001.

*Florian Holsboer, M.D., Ph.D.*, is Director at the Max Planck Institute fur Psychiatrie. Dr. Holsboer is an international expert on the role of glucocorticoids and neuropeptides, particularly CRF, in neuropsychiatric disorders. He coordinates the efforts of several hundred scientists and clinicians at the Max Planck Institute, a major European neuropsychiatric institute.

*Michael E. Jung, Ph.D.*, is a Professor in the Department of Chemistry and Biochemistry at the University of California at Los Angeles. Dr. Jung is an internationally renowned expert on organic synthesis, development of new synthetic methods; study of electrocyclic reactions and their use in organic synthesis; and the design, synthesis, and testing of inhibitors of enzymatic reactions.

*Charles B. Nemeroff, M.D., Ph.D.*, is Chairman and Professor of the Department of Psychiatry and Behavioral Sciences at Emory University School of Medicine. Dr. Nemeroff is an internationally recognized expert on the effects of neuropeptides on behavior and their relevance in clinically important conditions such as depression, anxiety and schizophrenia, and has published over 400 articles on this subject.

*Thomas Roth, Ph.D.*, is the head of the Division of Sleep Disorder Research at the Henry Ford Hospital Research Institute. Dr. Roth is an internationally recognized expert in the field of sleep research. His areas of specialization are sleep homeostasis and neuropharmacology of sleep.

*Lawrence J. Steinman, M.D.*, is our Chief Scientific Advisor, Neuroimmunology and a member of our Founding Board of Scientific and Medical Advisors and our Board of Directors.

*Wylie W. Vale, Ph.D.*, is our Chief Scientific Advisor, Neuroendocrinology and a member of our Founding Board of Scientific and Medical Advisors and our Board of Directors.

*Stanley J. Watson, Jr., M.D., Ph.D.*, is Professor and Associate Chair for Research in the Department of Psychiatry and Co-Director of the Mental Health Research Institute at the University of Michigan. Dr. Watson is a recognized expert in neuropeptides and their receptors and their role in psychiatric diseases and behavior. Dr. Watson is also a member of the Institute of Medicine of the National Academy of Sciences.

Each of the members of our Scientific Advisory Board has signed a consulting agreement that contains confidentiality provisions and restricts him or her from competing with us for the term of the agreement. Each member of our Scientific Advisory Board receives either a per diem consulting fee or a retainer fee. Each member also has received Neurocrine stock or stock options, which vest over time. All members of our Scientific Advisory Board are full-time employees of a university or research institute that has regulations and policies which limit their ability to act as part-time consultants or in other capacities for any commercial enterprise, including us. A change in these regulations or policies could adversely affect our relationship with any of our Scientific Advisory Board members.

### **Available Information**

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

## RISK FACTORS

### Risks Related to the Company

**We expect to rely on our collaboration with Pfizer for the funding of the completion of our indiplon clinical program and for commercialization of indiplon.**

Pfizer will:

- fund substantially all out of pocket costs related to future indiplon development, manufacturing and commercialization activities;
- fund a 200 person Neurocrine sales force to detail Zoloft® and, following FDA approval, indiplon in the United States;
- be responsible for obtaining all regulatory approvals outside of the United States and regulatory approvals in the United States after approval of the first indiplon NDA; and
- be responsible for sales and marketing of indiplon worldwide.

While our agreement with Pfizer requires Pfizer to use commercially reasonable efforts in the development and commercialization of indiplon, we cannot control the amount and timing of resources Pfizer may devote to our collaboration following NDA approval in the United States nor can we control when Pfizer will seek regulatory approvals outside of the United States. If the indiplon Phase III clinical program is significantly delayed or fails to demonstrate that indiplon is safe and efficacious for the targeted patient populations or if the FDA does not approve the proposed indiplon product labeling, the indiplon market opportunity we share with Pfizer and our business may be negatively affected. In addition, if Pfizer's development activities in pursuing new indications and uses of indiplon are not successful or Pfizer's sales and marketing activities for indiplon are not effective, indiplon sales and our business may be negatively affected.

Pfizer may terminate the collaboration at any time upon 180-days notice, subject to payment of certain amounts related to ongoing clinical development activities. If Pfizer elects to terminate the collaboration prior to FDA approval, we will be responsible for Phase III indiplon development expenses while we seek another partner to assist us in the worldwide development and commercialization of indiplon. This could cause delays in obtaining marketing approvals and sales, and negatively impact our business. If Pfizer elects to terminate the collaboration after receipt of FDA approval, we would be forced to fund the Neurocrine sales force and/or seek new marketing partners for indiplon. This could lead to loss of sales and negatively impact our business. In the event the collaboration is terminated by Pfizer, we may not be successful in finding another collaboration partner on favorable terms, or at all, and any failure to obtain a new partner on favorable terms could adversely affect indiplon development and commercialization and our business.

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

Any failure or substantial delay in completing clinical trials for our product candidates may severely harm our business. Before obtaining regulatory approval for the sale of any of our potential products, we must subject these product candidates to extensive pre-clinical and clinical testing to demonstrate their safety and efficacy for humans. Clinical trials are expensive, time-consuming and may take years to complete. We are currently conducting Phase III clinical trials in our indiplon development program for insomnia. This is our most advanced clinical program and represents a significant portion of our total clinical development activities and expenditures. If our Phase III indiplon program is not successful, our business and reputation would be harmed and our stock price may be affected.

In connection with the indiplon clinical trials, as well as those clinical trials of our multiple sclerosis APL, Type I diabetes APL, anxiety CRF R1 antagonist, IL-4 fusion toxin, and GnRH antagonist clinical programs, we face the risks that:

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- the product may not prove to be efficacious;
- we may discover that a product candidate may cause harmful side effects;
- the results may not replicate the results of earlier, smaller trials;
- we or the FDA may suspend the trials;
- the results may not be statistically significant;
- patient recruitment may be slower than expected; and
- patients may drop out of the trials.

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

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

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

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

We plan to file a NDA for indiplon in late December 2003 or early 2004. We face the risk that the FDA could reject our NDA filing, find it incomplete or find it insufficient for marketing approval for indiplon, which may cause our business and reputation to be harmed and could adversely affect our stock price.

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

Since our inception, we have incurred significant net losses, including net losses of \$94.5 million and \$36.9 million for the year ended December 31, 2002 and 2001, respectively. As a result of ongoing operating losses, we had an accumulated deficit of \$201.9 million and \$107.4 million as of December 31, 2002 and 2001, respectively. We were not profitable for the year ended December 31, 2002 and we do not expect to be profitable in 2003. We have not yet completed the development, including obtaining regulatory approvals, of any products and, consequently, have not generated revenues from the sale of products. Even if we succeed in developing and commercializing one or more of our drugs, we expect to incur substantial losses for the foreseeable future. We also expect to continue to incur significant operating and capital expenditures and anticipate that our expenses will increase substantially in the foreseeable future as we:

- seek regulatory approvals for our product candidates;
- develop, formulate, manufacture and commercialize our drugs;
- implement additional internal systems and infrastructure; and

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- hire additional clinical and scientific personnel.

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

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

Our quarterly revenues, expenses and operating results have fluctuated in the past and are likely to fluctuate significantly in the future. Our revenues are unpredictable and may fluctuate, for among other reasons, due to our achievement of product development objectives and milestones, clinical trial enrollment and expenses, research and development expenses and the timing and nature of contract manufacturing and contract research payments. A high proportion of our costs are fixed, due in part to our significant research and development costs. Thus, small declines in revenue could disproportionately affect operating results in a quarter. Because of these factors, our operating results in one or more future quarters may fail to meet the expectations of securities analysts or investors, which could cause our stock price to decline.

### **We depend on continuing our current strategic alliances and developing additional strategic alliances to develop and commercialize our compounds.**

We depend upon our corporate collaborators to provide adequate funding for a number of our programs. Under these arrangements, our corporate collaborators are responsible for:

- selecting compounds for subsequent development as drug candidates;
- conducting pre-clinical studies and clinical trials and obtaining required regulatory approvals for these drug candidates; and
- manufacturing and commercializing any resulting drugs.

Our strategy for developing and commercializing our products is dependent upon maintaining our current arrangements and establishing new arrangements with research collaborators, corporate collaborators and others. We have collaborations with Pfizer, GlaxoSmithKline and Wyeth. Because we rely heavily on our corporate collaborators, the development of our projects would be substantially delayed if our collaborators:

- fail to select a compound we have discovered for subsequent development into marketable products;
- fail to gain the requisite regulatory approvals of these products;
- do not successfully commercialize products that we originate;
- do not conduct their collaborative activities in a timely manner;
- do not devote sufficient time and resources to our partnered programs or potential products;
- terminate their alliances with us;
- develop, either alone or with others, products that may compete with our products;
- dispute our respective allocations of rights to any products or technology developed during our collaborations; or
- merge with a third party that may wish to terminate the collaboration.

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

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

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We are dependent on licenses from third parties for some of our key technologies. These licenses typically subject us to various commercialization, reporting and other obligations. If we fail to comply with these obligations, we could lose important rights. For example, we have licensed indiplon from DOV Pharmaceutical and IL-4 fusion toxin, which we call NBI-3001, from the National Institutes of Health. In addition, we license some of the core research tools used in our collaborations from third parties, including the CRF receptor which we license from The Salk Institute and use in our CRF program collaboration with GSK and the excitatory amino acid transporters which we license from Oregon Health Sciences University and use in our EAATs collaboration with Wyeth. Other in-licensed technologies, such as the GnRH receptor which we license from Mount Sinai School of Medicine and Melanocortin subtype 4 which we license from the University of Michigan, will be important for future collaborations for our GnRH and Melanocortin programs. If we were to default on our obligations under any of our product licenses, such as our license to indiplon, we could lose some or all of our rights to develop, market and sell the product. Likewise, if we were to lose our rights under a license to use proprietary research tools, it could adversely affect our existing collaborations or adversely affect our ability to form new collaborations. We also face the risk that our licensors could, for a number of reasons, lose patent protection or lose their rights to the technologies we have licensed thereby impairing or extinguishing our rights under our licenses with them.

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

All of our product candidates are in research or development and we do not expect any of our product candidates to be commercially available within a year, if at all. Only a small number of research and development programs ultimately result in commercially successful drugs. Potential products that appear to be promising at early stages of development may not reach the market for a number of reasons. These reasons include the possibilities that the potential products may:

- be found ineffective or cause harmful side effects during pre-clinical studies or clinical trials;
- fail to receive necessary regulatory approvals on a timely basis or at all;
- be precluded from commercialization by proprietary rights of third parties;
- be difficult to manufacture on a large scale; or
- be uneconomical or fail to achieve market acceptance.

If any of these potential problems occurs, we may never successfully market any products.

We are currently conducting Phase III clinical trials for indiplon, our insomnia product under development. Since this is our most advanced product program, our business and reputation would be particularly harmed, and our stock price may be affected, if the product does not prove to be efficacious in these clinical trials or we fail to receive necessary regulatory approvals on a timely basis or achieve market acceptance.

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

We may require additional funding in order to continue our research and product development programs, including pre-clinical testing and clinical trials of our product candidates, for operating expenses, and to pursue regulatory approvals for product candidates. We also may require additional funding to establish manufacturing and marketing capabilities in the future. We believe that our existing capital resources, together with interest income and future payments due under our strategic alliances, will be sufficient to satisfy our current and projected funding requirements for at least the next 12 months. However, these resources might be insufficient to conduct research and development programs as planned. If we cannot obtain adequate funds, we may be required to curtail significantly one or more of our research and development programs or obtain funds through additional arrangements with corporate collaborators or others that may require us to relinquish rights to some of our technologies or product candidates.

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 pre-clinical testing and clinical trials;
- the time and costs involved in obtaining regulatory approvals;

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- the costs involved in filing and pursuing patent applications and enforcing patent claims;
- competing technological and market developments;
- the establishment of additional strategic alliances;
- the cost of manufacturing facilities and of commercialization activities and arrangements; and
- the cost of product in-licensing and any possible acquisitions.

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

**We have no marketing experience, sales force or distribution capabilities, and if our products are approved, we may not be able to commercialize them successfully.**

Although we do not currently have any marketable products, our ability to produce revenues ultimately depends on our ability to sell our products if and when they are approved by the FDA. We currently have no experience in marketing or selling pharmaceutical products. We are currently initiating marketing activities for indiplon by hiring staff with experience in pharmaceutical sales, marketing and distribution. We will rely on Pfizer to co-promote indiplon with us in the United States and rely exclusively on Pfizer to market indiplon outside of the United States. We will also rely on Pfizer to provide distribution, customer service, order entry, shipping, billing, customer reimbursement assistance and managed care sales support related to indiplon. If we fail to establish successful marketing and sales capabilities or fail to enter into successful marketing arrangements with third parties, our product revenues will suffer.

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

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

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

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

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

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- switching manufacturers may be difficult because the number of potential manufacturers is limited. It may be difficult or impossible for us to find a replacement manufacturer quickly on acceptable terms, or at all;
- our contract manufacturers may not perform as agreed or may not remain in the contract manufacturing business for the time required to successfully produce, store or distribute our products;
- drug manufacturers are subject to ongoing periodic unannounced inspection by the FDA, the Drug Enforcement Agency, and corresponding state agencies to ensure strict compliance with good manufacturing practices and other government regulations and corresponding foreign standards. We do not have control over third-party manufacturers' compliance with these regulations and standards; and
- if our primary contract manufacturer should be unable to manufacture indiplon for any reason, or should fail to receive FDA approval or Drug Enforcement Agency approval, commercialization of indiplon could be delayed which would delay indiplon sales and our business would be negatively impacted.

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

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

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

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

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

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

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

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

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



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

- the timing of receipt of marketing approvals;
- the safety and efficacy of the products;
- the success of existing products addressing our target markets or the emergence of equivalent or superior products; and
- the cost-effectiveness of the products.

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

### **Risks Related to Our Industry**

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

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

- other drug development technologies;
- methods of preventing or reducing the incidence of disease, including vaccines; and
- new small molecule or other classes of therapeutic agents.

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

We are performing research on or developing products for the treatment of several disorders including insomnia, anxiety, depression, malignant brain tumors and peripheral cancers, diabetes mellitus, multiple sclerosis, irritable bowel syndrome, eating disorders, pain, prostate cancer, obesity and certain female disorders, and there are a number of competitors to products in our research pipeline. If one or more of our competitors products or programs are successful, the market for our products may be reduced or eliminated.

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

- capital resources;
- research and development resources, including personnel and technology;
- regulatory experience;
- pre-clinical study and clinical testing experience;
- manufacturing and marketing experience; and
- production facilities.

Any of these competitive factors could reduce demand for our products.

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

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

- obtain patent protection for our products;
- preserve our trade secrets;
- prevent third parties from infringing upon our proprietary rights; and
- operate without infringing upon the proprietary rights of others, both in the United States and internationally.

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

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

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

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

We cannot assure you that third parties will not assert patent or other intellectual property infringement claims against us or our collaboration partners with respect to technologies used in potential products. Any claims that might be brought against us relating to infringement of patents may cause us to incur significant expenses and, if successfully asserted against us, may cause us to pay substantial damages. Even if we were to prevail, any litigation could be costly and time-consuming and could divert the attention of our management and key personnel from our business operations. Furthermore, as a result of a patent infringement suit brought against us or our collaboration partners, we or our collaboration partners may be forced to stop or delay developing, manufacturing or selling potential products that are claimed to infringe a third party's intellectual property unless that party grants us or our collaboration partners rights to use its intellectual property. In such cases, we may be required to obtain licenses to patents or proprietary rights of others in order to continue to commercialize our products. However, we may not be able to obtain any licenses required under any patents or proprietary rights of third parties on acceptable terms, or at all. Even if our collaboration partners or we were able to obtain rights to the third party's intellectual property, these rights may be non-exclusive, thereby giving our competitors access to the same intellectual property. Ultimately, we may be unable to commercialize some of our potential products or may have to cease some of our business operations as a result of patent infringement claims, which could severely harm our business.

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

The use of any of our potential products in clinical trials, and the sale of any approved products, may expose us to liability claims. These claims might be made directly by consumers, health care providers, pharmaceutical companies or others selling our products. We have obtained limited product liability insurance coverage for our clinical trials in the amount of \$10 million per occurrence and \$10 million in the aggregate. However, our insurance may not reimburse us or may not be sufficient to reimburse us for any expenses or losses we may suffer. Moreover, insurance coverage is becoming increasingly expensive, and we may not be able to maintain insurance coverage at a reasonable cost or in sufficient amounts to protect us against losses due to liability. We intend to expand our insurance coverage to include the sale of commercial products if we obtain marketing approval for product candidates

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in development, but we may be unable to obtain commercially reasonable product liability insurance for any products approved for marketing. On occasion, juries have awarded large judgments in class action lawsuits based on drugs that had unanticipated side effects. A successful product liability claim or series of claims brought against us would decrease our cash reserves and could cause our stock price to fall.

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

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

## **ITEM 2. PROPERTIES**

We lease approximately 93,000 square feet of space at our headquarters in San Diego, California, of which approximately 65% is laboratory space dedicated to research and development. This facility was constructed in 1998 and is under lease through August 2013. The lease payments are \$216,000 per month with annual increases of 4% on September 1st of each year. We have an ownership interest in this property through Science Park Center, LLC, which is described below under the heading "Item 7-Management's Discussion and Analysis of Financial Condition and Results of Operations - Synthetic Lease for Current Facility."

We believe that our property and equipment are generally well maintained, in good operating condition and adequate for our current needs.

## **ITEM 3. LEGAL PROCEEDINGS**

We are currently not subject to any material legal proceedings.

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

Not Applicable.

**PART II****ITEM 5. MARKET FOR REGISTRANT'S COMMON EQUITY AND RELATED STOCKHOLDER MATTERS**

Our common stock has been traded on the Nasdaq National Market System under the symbol NBIX since our initial public offering on May 23, 1996. Prior to that time there was no established public trading market for our common stock. 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
	_____	_____
<b>Year Ended December 31, 2001</b>		
1st Quarter	\$36.50	\$14.25
2nd Quarter	39.99	16.75
3rd Quarter	40.71	27.93
4th Quarter	54.26	30.36
<b>Year Ended December 31, 2002</b>		
1st Quarter	\$52.21	\$32.15
2nd Quarter	43.88	23.25
3rd Quarter	42.65	24.04
4th Quarter	50.00	37.92

As of February 21, 2003, there were approximately 99 stockholders of record of our common stock. We have not paid any cash dividends on our common stock since inception and do not anticipate paying cash dividends in the foreseeable future.

**ITEM 6. SELECTED FINANCIAL DATA**

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

	2002	2001	2000	1999(2)	1998 (1) (2)
(in thousands, except for loss per share data)					
<b>STATEMENT OF OPERATIONS DATA</b>					
Revenues:					
Sponsored research and development	\$ 12,364	\$ 16,880	\$ 6,881	\$ 12,662	\$ 12,361
Milestones and license fees	3,516	22,937	6,345	3,000	2,500
Grant income and other revenues	2,165	1,425	1,362	1,129	1,176
Total revenues	18,045	41,242	14,588	16,791	16,037
Operating expenses:					
Research and development	108,939	74,267	40,227	29,169	21,803
General and administrative	12,721	10,857	9,962	7,476	6,594
Write-off of acquired in-process research and development and licenses	—	—	—	—	4,910
Total operating expenses	121,660	85,124	50,189	36,645	33,307
Loss from operations	(103,615)	(43,882)	(35,601)	(19,854)	(17,270)
Other income (expense):					
Interest income, net	8,864	6,662	6,048	2,851	4,000
Other income	215	430	1,047	1,066	504
Equity in NPI losses and other adjustments, net	—	—	—	(885)	(7,188)
Total other income (expense)	9,079	7,092	7,095	3,032	(2,684)
Loss before income taxes	(94,536)	(36,790)	(28,506)	(16,822)	(19,954)
Income taxes	—	120	302	—	1
Loss	\$ (94,536)	\$ (36,910)	\$ (28,808)	\$ (16,822)	\$ (19,955)
Loss per share					
Basic and diluted	\$ (3.10)	\$ (1.42)	\$ (1.30)	\$ (0.88)	\$ (1.10)
Shares used in calculation of loss per share					
Basic and diluted	30,488	26,028	22,124	19,072	18,141
<b>BALANCE SHEET DATA</b>					
Cash, cash equivalents and short-term investments	\$ 244,710	\$ 319,982	\$ 164,670	\$ 91,098	\$ 62,670
Working capital	215,615	306,754	157,446	86,168	60,064
Total assets	266,539	346,350	185,962	109,222	80,529
Long-term debt and capital lease obligations	5,277	3,600	2,283	2,139	2,247
Accumulated deficit	(201,926)	(107,390)	(70,480)	(41,672)	(24,850)
Total stockholders’ equity	224,254	310,393	163,208	96,354	71,958

(1) Includes results of operations and financial position of Northwest NeuroLogic, Inc. from May 28, 1998, the date of acquisition.

(2) Sponsored research and development includes \$491 and \$3,610 in revenues from a related party for the years ended December 31, 1999 and 1998, respectively.

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

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

### Overview

We incorporated in California in 1992 and reincorporated in Delaware in 1996. Since we were founded, we have been engaged in the discovery and development of novel pharmaceutical products for neurologic and endocrine diseases and disorders. Many of our product candidates address some of the largest pharmaceutical markets in the world, including insomnia, anxiety, depression, malignant brain tumors and peripheral cancers, diabetes mellitus, multiple sclerosis, irritable bowel syndrome, eating disorders, pain, prostate cancer, obesity and certain female health disorders. To date, we have not generated any revenues from the sale of products, and we do not expect to generate any product revenues in the foreseeable future. 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 a number of 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 significant increases in operating expenses as product candidates are advanced through the various stages of clinical development. As of December 31, 2002, we have incurred a cumulative deficit of \$201.9 million and expect to incur operating losses in the future, which may be greater than losses in prior 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 (R&D expense), facility lease, 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:

Revenues under collaborative research agreements and grants are recognized as research 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. Up-front, 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 require substantive effort. Revenues from government grants are recognized based on a percentage-of-completion basis as the related costs are incurred.

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 at other companies and research institutions under agreements,

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which are generally cancelable. We review and accrue clinical trials expenses based on work performed, which relies on estimates of total costs incurred based on completion of patient studies and other events. We follow this method since reasonably dependable estimates of the costs applicable to various stages of a research agreement or clinical trial can be made. Accrued clinical costs are subject to revisions as trials progress to completion. Revisions are charged to expense in the period in which the facts that give rise to the revision become known.

We record an investment impairment charge when we believe an investment has experienced a decline in value that is other than temporary. Future adverse changes in market conditions or poor operating results of underlying investments could result in losses or an inability to recover the carrying value of the investments that may not be reflected in an investment's current carrying value, thereby possibly requiring an impairment charge in the future.

We review long-lived assets, including leasehold improvements and property and equipment, for impairment whenever events or changes in business circumstances indicate that the carrying amount of the assets may not be fully recoverable. Long-lived assets and certain identifiable intangible assets to be disposed of are reported at the lower of the carrying amount or fair value less the cost to dispose.

### **Results of Operations for Years ended December 31, 2002, 2001 and 2000**

Our revenues for the year ended December 31, 2002 were \$18.0 million compared with \$41.2 million in 2001, and \$14.6 million in 2000. The \$23.2 million decrease in revenues from 2001 to 2002 resulted primarily from \$21.0 million of milestones achieved in 2001 under the Taisho and GSK collaborations.

The increase in revenues from 2000 to 2001 was primarily the result of the Taisho and GSK collaborations, which were effective July 2000 and July 2001, respectively. Under the Taisho agreement, we recognized \$16.6 million during 2001, which included a \$5.5 million milestone achievement, compared with \$7.1 million in 2000. Under the GSK agreement, we recognized \$19.2 million during 2001, which included a \$15.5 million milestone achievement. The increase in revenues from these agreements was partially offset by the completion of the sponsored research portion of an agreement with Janssen that concluded, as scheduled, in February 2001. Under the Janssen agreement, we recognized \$525,000 during 2001 and \$3.0 million during 2000.

Research and development expenses increased to \$108.9 million during 2002 compared with \$74.3 million during 2001 and \$40.2 million in 2000. Increased expenses over the three years primarily reflect advancement of our drug candidates through progressive clinical development phases and the higher costs associated with expanding development activities and increased enrollment in clinical trials, in particular, the indiplon Phase III program. Additionally, personnel and laboratory costs, related to the expansion of research and development activities, have increased over the same period. We expect to incur increases in research and development expense in future periods as later phases of development typically involve an increase in the scope of studies, the number of patients treated and the number of scientific personnel required to manage the trials.

General and administrative expenses increased to \$12.7 million during 2002 compared with \$10.9 million during 2001 and \$10.0 million during 2000. The increase in administrative expenses from 2001 to 2002 resulted primarily from increased marketing research and marketing related costs, increased recruiting and relocation costs for new employees, increased insurance costs, and the addition of administrative personnel needed to support expanding research and development activities. The increase in expenses from 2000 to 2001 resulted primarily from additional patent legal expenses, marketing research and the addition of administrative personnel needed to support expanding research and development activities.

Interest income increased to \$9.3 million during 2002 compared with \$7.0 million during 2001 and \$6.3 million during 2000. The increase in 2002, compared with 2001 and 2000, primarily resulted from higher investment balances achieved through public and private offerings of our common stock offset by lower investment yields. In December 2001, we sold 4.0 million shares of our common stock in a public offering resulting in net proceeds of \$175.6 million. In December 2000, we sold 3.2 million shares of our common stock in a public offering resulting in net proceeds of \$90.4 million.

Other income consists primarily of sublease income from unrelated parties. The fluctuations in sublease income from year to year reflect facility capacity in excess of our needs. Excess space is subleased until it is needed

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to support company growth. During 2002, sublease income decreased significantly as we ceased subleasing portions of our facility to enable us to use all of our laboratory and office space in conjunction with increased research and development activities.

Our net loss for 2002 was \$94.5 million, or \$3.10 per share, compared with \$36.9 million, or \$1.42 per share, in 2001 and \$28.8 million, or \$1.30 per share, in 2000. The increase in net loss primarily resulted from an increase in scientific personnel and expanded clinical development activities, primarily related to the indiplon program. We expect operating losses to increase for the foreseeable future as we continue to expand our clinical development efforts.

### **Liquidity and Capital Resources**

At December 31, 2002, our cash, cash equivalents, and short-term investments totaled \$244.7 million compared with \$320.0 million at December 31, 2001. The decrease in cash balances from December 31, 2001 to December 31, 2002 is primarily due to funding our increase in scientific and clinical development personnel and expanded clinical trials, in particular, our indiplon Phase III program. Additionally, the cash, cash equivalents, and short-term investments as of December 31, 2002 do not include the initial payment from Pfizer of \$100 million for the indiplon collaboration. This amount is expected to be received in early 2003.

Net cash used in operating activities during fiscal year 2002 was \$79.4 million compared with \$21.9 million in 2001 and \$18.6 million during 2000. The increase in cash used in operations for 2002 compared to the prior periods resulted primarily from the increase in clinical development activities, primarily our indiplon program, and the addition of scientific and clinical development personnel.

Net cash used in investing activities during fiscal year 2002 was \$46.0 million compared to \$16.6 million during 2001 and \$75.7 million in 2000. These fluctuations resulted primarily from the timing differences in investment purchases, sales, 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 2002, 2001 and 2000 were \$5.3 million, \$3.8 million and \$2.4 million, respectively, and were financed primarily through capital leasing arrangements. Capital equipment purchases for 2003 also will be financed primarily through leasing agreements and are expected to be approximately \$6.0 million.

Net cash provided by financing activities during fiscal year 2002 was \$5.8 million compared with \$181.3 million in 2001 and \$94.1 million during 2000. Cash provided during 2001 and 2000 includes net proceeds from public and private offerings of our common stock of \$175.6 million and \$90.4 million, respectively.

### **Synthetic Lease for Current Facility**

We lease our current facility under an operating lease that generally requires us to pay taxes, insurance and maintenance. Based on the structure of the arrangement, our operating lease is commonly referred to as a "synthetic lease." A synthetic lease is a form of off-balance sheet financing under which an unrelated third party funds up to 100% of the costs for the acquisition and/or construction of the facility into a special purpose entity (SPE) and leases the facility to a lessee. At least 3% of the third party funds must represent at-risk equity at all times. If at any time the third party fails to maintain at least 3% at-risk equity, we will need to consolidate the SPE, which will result in debt and equity being recorded in our financial statements. Our synthetic lease is treated as an operating lease for accounting purposes and a financing lease for tax purposes. We selected the synthetic lease for the financing advantages. Also, the agreement provides that at our option, we may purchase the building by repaying the first mortgage balance. We periodically review the fair value of the property leased to determine potential accounting ramifications.

### **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



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managerially responsible for clinical development and commercialization. In these cases, the estimated completion date would largely be under the control of the collaborator. We cannot forecast, with any degree of certainty, which 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, 2002 and the effect such obligations are expected to have on our liquidity and cash flow in future periods. Our license, research and clinical development agreements are generally cancelable with written notice in 0-180 days. In addition to the minimum payments due under our license and research agreements, we may be required to pay up to \$16.6 million in milestone payments, plus sales royalties, in the event that all scientific research under these agreements is successful. Some of our clinical development agreements contain incentives for time-sensitive activities.

<b>Contractual Obligations</b>	<b>Total</b>	<b>Less than 1 year</b>	<b>1 – 3 years</b>	<b>3-5 years</b>	<b>More than 5 years</b>
			<b>(in thousands)</b>		
Capital lease obligations	\$ 8,835	\$ 3,132	\$ 4,875	\$ 828	\$ —
Operating lease	35,451	2,731	5,795	6,267	20,658
License & research agreements	1,375	1,135	120	120	—
Clinical development agreements	71,168	65,468	5,700	—	—
Total contractual obligations	\$ 116,829	\$ 72,466	\$ 16,490	\$ 7,215	\$ 20,658

The funding necessary to execute our business strategies is subject to numerous uncertainties, which may adversely affect our liquidity and capital resources. As of December 31, 2002, seven of our product candidates were in various stages of clinical trials. Completion of clinical trials may take several years or more, but the length of time generally varies substantially according to the type, complexity, novelty and intended use of a product candidate. It is also important to note that if a clinical candidate is identified, the further development of that candidate can be halted or abandoned at any time due to a number of factors. These factors include, but are not limited to, funding constraints, safety or a change in market demand.

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

The nature and efforts required to develop our product candidates into commercially viable products include research to identify a clinical candidate, pre-clinical development, clinical testing, FDA approval and commercialization. This process may cost in excess of \$100 million and can take as long as 10 years to complete for each product candidate.

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

- we or the FDA 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

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uncertainties associated with research and development of these programs, we may not be successful in achieving commercialization. As such, the ultimate timeline and costs to commercialize a product cannot be accurately estimated.

Our product candidates have not yet achieved FDA regulatory approval, which is required before we can market them as therapeutic products. In 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. The results from pre-clinical testing and early clinical 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.

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 pre-clinical testing and clinical trials;
- the time and costs involved in obtaining regulatory approvals;
- the costs involved in filing and pursuing patent applications and enforcing patent claims;
- competing technological and market developments;
- the establishment of additional strategic alliances;
- the cost of 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 these capital resources and payments will be sufficient to conduct all of our research and development programs as planned. The amount and timing of expenditures will vary depending upon a number of factors, including progress of our research and development programs.

We may require additional funding to continue our research and product development programs, to conduct pre-clinical 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, the cost of product in-licensing and 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. If adequate funds are not available, 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.

We expect to incur operating losses over the next several years as our research, development, pre-clinical studies and clinical trial activities increase. 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 40 months. If a 10% change in interest rates were to have occurred on December 31, 2002, 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.

## **Cautionary Note on Forward-Looking Statements**

Our business is subject to significant risks, including but not limited to, the risks inherent in our research and development activities, including the successful continuation of our strategic collaborations, the successful completion of clinical trials, the lengthy, expensive and uncertain process of seeking regulatory approvals, uncertainties associated both with the potential infringement of patents and other intellectual property rights of third parties, and with obtaining and enforcing our own patents and patent rights, uncertainties regarding government reforms and of product pricing and reimbursement levels, technological change, competition, manufacturing uncertainties and dependence on third parties. Even if our product candidates appear promising at an early stage of development, they may not reach the market for numerous reasons. Such reasons include the possibilities that the product will be ineffective or unsafe during clinical trials, will fail to receive necessary regulatory approvals, will be difficult to manufacture on a large scale, will be uneconomical to market or will be precluded from commercialization by proprietary rights of third parties. For more information about the risks we face, see “Item 1. Business – Risk Factors” included in this report.

## **New Accounting Pronouncements**

In November 2002, the Emerging Issues Task Force (EITF) reached a consensus on Issue No. 00-21, “Revenue Arrangements with Multiple Deliverables.” EITF Issue No. 00-21 provides guidance on how to account for arrangements that involve the delivery or performance of multiple products, services and/or rights to use assets. We will be required to adopt this provision for revenue arrangements entered into on or after June 15, 2003. Management is currently evaluating the effect that the adoption of EITF 00-21 will have on our results of operations and financial condition.

In December 2002, the Financial Accounting Standards Board (FASB) issued Statement of Financial Accounting Standards (SFAS) No. 148, “Accounting for Stock-Based Compensation, Transition and Disclosure.” SFAS No. 148 provides alternative methods of transition for a voluntary change to the fair value based method of accounting for stock-based employee compensation. SFAS No. 148 also requires that disclosures of the pro forma effect of using the fair value method of accounting for stock-based employee compensation be displayed more prominently and in a tabular format. Additionally, SFAS No. 148 requires disclosure of the pro forma effect in interim financial statements. The transition and annual disclosure requirements of SFAS No. 148 are effective immediately. The interim disclosure requirements are effective for the first quarter of 2003. The adoption of SFAS No. 148 did not have a material effect on our results of operations or financial condition.

In January 2003, the FASB issued FASB Interpretation No. 46 (FIN 46), “Consolidation of Variable Interest Entities, an Interpretation of Accounting Research Bulletin No. 51.” FIN 46 requires certain variable interest entities to be consolidated by the primary beneficiary of the entity if the equity investors in the entity do not have the characteristics of a controlling financial interest or do not have sufficient equity at risk for the entity to finance its activities without additional subordinated financial support from other parties. FIN 46 is effective for all new variable interest entities created or acquired after January 31, 2003. For variable interest entities created or acquired prior to February 1, 2003, the provisions of FIN 46 must be applied for the first interim or annual period beginning after June 15, 2003. Management is currently analyzing the effect that the adoption of FIN 46 will have on its results of operations and financial position, but expects that upon the implementation date, we will consolidate the special purpose entity described in Item 7. Management’s Discussion and Analysis of Financial Condition and Results of Operations — Synthetic Lease for Current Facility.

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

Quantitative and Qualitative Disclosures about Market Risk is contained in “Item 7. Management’s Discussion and Analysis of Financial Condition and Results of Operations — Interest Rate Risk.”

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

See the list of the Company’s Financial Statements filed with this Form 10-K under Item 15 below.

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

Not Applicable.

**PART III**

**ITEM 10. EXECUTIVE OFFICERS AND DIRECTORS OF THE REGISTRANT**

Information required by this item will be contained in our Definitive Proxy Statement for our 2003 Annual Meeting of Stockholders, to be filed pursuant to Regulation 14A with the Securities and Exchange Commission within 120 days of December 31, 2002. Such information is incorporated herein by reference.

**ITEM 11. EXECUTIVE COMPENSATION**

Information required by this item will be contained in our Definitive Proxy Statement for our 2003 Annual Meeting of Stockholders, to be filed pursuant to Regulation 14A with the Securities and Exchange Commission within 120 days of December 31, 2002. Such information is incorporated herein by reference.

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

Information required by this item will be contained in our Definitive Proxy Statement for our 2003 Annual Meeting of Stockholders, to be filed pursuant to Regulation 14A with the Securities and Exchange Commission within 120 days of December 31, 2002. Such information is incorporated herein by reference.

**ITEM 13. CERTAIN RELATIONSHIPS AND RELATED TRANSACTIONS**

Information required by this item will be contained in our Definitive Proxy Statement for our 2003 Annual Meeting of Stockholders, to be filed pursuant to Regulation 14A, with the Securities and Exchange Commission within 120 days of December 31, 2002. Such information is incorporated herein by reference.

**ITEM 14. CONTROLS AND PROCEDURES**

We maintain disclosure controls and procedures that are designed to ensure that information required to be disclosed in our reports pursuant to the Securities Exchange Act of 1934, as amended, is recorded, processed, summarized and reported within the time periods specified in the Securities and Exchange Commission’s rules and forms, and that such information is accumulated and communicated to our management, including our Chief Executive Officer and Chief Financial Officer, as appropriate, to allow timely disclosure. In designing and evaluating

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

- a Within 90 days prior to the date of this report, we carried out an evaluation, under the supervision and with the participation of our management, including our Chief Executive Officer and Chief Financial Officer, of the effectiveness of the design and operation of our disclosure controls and procedures, as defined in Rules 13a-14(c) and 15d-14(c) under the Securities Exchange Act of 1934. Based on the foregoing, our Chief Executive Officer and Chief Financial Officer concluded that our disclosure controls and procedures were effective as of the evaluation date.
- b There have been no significant changes in our internal controls or in other factors that could significantly affect these controls subsequent to the date we carried out this evaluation.

**PART IV**

**ITEM 15. EXHIBITS, FINANCIAL STATEMENT SCHEDULES AND REPORTS ON FORM 8-K**

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

1. List of Financial Statements. The following financial statements of Neurocrine Biosciences, Inc. and Report of Ernst & Young LLP, Independent Auditors, are included in this report:  
Report of Ernst & Young LLP, Independent Auditors  
Balance Sheets as of December 31, 2002 and 2001  
Statements of Operations for the years ended December 31, 2002, 2001 and 2000  
Statements of Stockholders' Equity for the years ended December 31, 2002, 2001 and 2000  
Statements of Cash Flows for the years ended December 31, 2002, 2001 and 2000  
Notes to the Financial Statements (includes unaudited Selected Quarterly Financial Data)
2. List of all Financial Statement schedules. All schedules are omitted because they are not applicable or the required information is shown in the Financial Statements or notes thereto.
3. List of Exhibits required by Item 601 of Regulation S-K. See part (c) below.

(b) *Reports on Form 8-K.* Current Reports filed pursuant to Sections 13(a) or 15(d) of the Exchange Act on Form 8-K dated December 20, 2002.

1. The Registrant filed a Current Report on Form 8-K dated December 20, 2002, to report, pursuant to Item 5 (Other Events), that the Company had entered into a license, collaboration and loan agreement with Pfizer for indiplon.

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

<b>Exhibit Number</b>	<b>Description</b>
2.1	Agreement and Plan of Reorganization dated May 1, 1998, between Northwest NeuroLogic, Inc., NBI Acquisition Corporation and the Registrant (6)
2.2	Form of Milestone Warrant pursuant to the Agreement and Plan of Reorganization dated May 1, 1998 (6)
3.1	Restated Certificate of Incorporation (1)
3.2	Bylaws (1)
3.3	Certificate of Amendment of Bylaws (1)
4.1	Form of Common Stock Certificate (1)
4.2	Form of warrant issued to existing warrant holders (1)
4.3	Information and Registration Rights Agreement dated September 15, 1992, as amended (1)
4.4*	Registration Rights Agreement dated May 28, 1998, between certain investors and the Registrant (6)
4.5	Amended and Restated Preferred Shares Rights Agreement by and between the Registrant and American Stock Transfer & Trust Company, as Rights Agent, dated as of January 11, 2002 (19)
4.6	Stock Purchase Agreement dated December 20 through 23, 1999, between Neurocrine Biosciences, Inc. and each of the Purchasers named therein (10)
10.1	Purchase and Sale Agreement and Escrow Instructions between MS Vickers II, LLC and the Registrant dated February 13, 1997 (3)
10.2	1992 Incentive Stock Plan, as amended (16)
10.3	1996 Employee Stock Purchase Plan, as amended (16)
10.4	1996 Director Stock Option Plan, as amended, and form of stock option agreement (12)
10.5	Form of Director and Officer Indemnification Agreement (1)
10.6	Employment Agreement dated March 1, 1997, between the Registrant and Gary A. Lyons, as amended May 24, 2000 (4) (11)

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<b>Exhibit Number</b>	<b>Description</b>
10.7	Employment Agreement dated March 1, 1997, between the Registrant and Paul W. Hawran, as amended May 24, 2000 (4) (11)
10.8	Consulting Agreement dated September 25, 1992, between the Registrant and Wylie A. Vale, Ph.D. (1)
10.9	Consulting Agreement effective January 1, 1992, between the Registrant and Lawrence J. Steinman, MD (1)
10.10	License Agreement dated July 17, 1992, by and between The Salk Institute for Biological Studies and the Registrant (1)
10.11	License Agreement dated November 16, 1993, by and between The Salk Institute for Biological Studies and the Registrant (1)
10.12	License Agreement dated October 19, 1992, by and between the Board of Trustees of the Leland Stanford Junior University and the Registrant (1)
10.13	Agreement dated January 1, 1995, by and between the Registrant and Janssen Pharmaceutica, N.V. (1)
10.14*	Research and License Agreement dated October 15, 1996, between the Registrant and Eli Lilly and Company (2)
10.15*	Lease between Science Park Center LLC and the Registrant dated July 31, 1997 (5)
10.16*	Option Agreement between Science Park Center LLC (Optionor) and the Registrant dated July 31, 1997 (Optionee) (5)
10.17*	Construction Loan Agreement Science Park Center LLC and the Registrant dated July 31, 1997 (5)
10.18	Secured Promissory Note Science Park Center LLC and the Registrant dated July 31, 1997 (5)
10.19*	Operating Agreement for Science Park Center LLC between Nexus Properties, Inc. and the Registrant dated July 31, 1997 (5)
10.20	Form of incentive stock option agreement and nonstatutory stock option agreement for use in connection with 1992 Incentive Stock Plan (1)
10.21*	Patent License Agreement dated May 7, 1998, between the US Public Health Service and the Registrant (6)
10.22*	Patent License Agreement dated April 28, 1998, between and among Ira Pastan, David Fitzgerald and the Registrant (6)
10.23*	Sub-License and Development Agreement dated June 30, 1998, by and between DOV Pharmaceutical, Inc. and the Registrant (6)
10.24*	Warrant Agreement dated June 30, 1998, between DOV Pharmaceutical, Inc. and the Registrant (6)
10.25*	Warrant Agreement dated June 30, 1998, between Jeff Margolis and the Registrant (6)
10.26*	Warrant Agreement dated June 30, 1998, between Stephen Ross and the Registrant (6)
10.27*	Collaboration and License Agreement dated January 1, 1999, by and between American Home Products Corporation acting through its Wyeth Laboratories Division and the Registrant (7)
10.28	Employment Agreement dated October 1, 1998, between the Registrant and Margaret Valeur-Jensen, as amended May 24, 2000 (7) (11)
10.29	Employment Agreement dated January 1, 1998, between the Registrant and Bruce Campbell, as amended May 24, 2000 (7) (11)
10.30*	Agreement by and among Dupont Pharmaceuticals Company, Janssen Pharmaceutica, N.V. and Neurocrine Biosciences, Inc. dated September 28, 1999 (9)
10.31*	Amendment Number One to the Agreement between Neurocrine Biosciences, Inc. and Janssen Pharmaceutica, N.V. dated September 24, 1999 (9)
10.32*	License Agreement between the Registrant and Taisho Pharmaceutical Co., Ltd. dated July 21, 2000 (11)
10.33**	Amendment No. 1 dated November 30, 2000 to the License Agreement between the Registrant and Taisho Pharmaceutical Co., Ltd. dated July 21, 2000 (13) (15)
10.34*	2001 Stock Option Plan (14)
10.35*	Collaboration and License Agreement between the Registrant and Glaxo Group Limited dated July 20, 2001(17)
10.36	Employment Agreement dated October 17, 2001, between the Registrant and Henry Pan, MD, PhD. (18)
10.37	2001 Stock Option Plan, as amended August 6, 2002 and October 15, 2002
10.38*	License Agreement between the Registrant and Pfizer dated December 18, 2002(20)

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<b>Exhibit Number</b>	<b>Description</b>
10.39*	Collaboration Agreement between the Registrant and Pfizer dated December 18, 2002(20)
10.40*	Loan Agreement between the Registrant and Pfizer dated December 18, 2002(20)
10.41*	Restructuring Agreement between the Registrant and Taisho Pharmaceutical Co., Ltd. dated September 30, 2002 (21)
10.42	Nonqualified Deferred Compensation Plan, as amended and restated February 22, 2000
21.1	Subsidiaries of the Company
23.1	Consent of Ernst & Young LLP, Independent Auditors

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(1)	Incorporated by reference to the Company's Registration Statement on Form S-1 (Registration No. 333-03172)
(2)	Incorporated by reference to the Company's Report on Form 10-K for the fiscal year ended December 31, 1996 filed on March 31, 1997
(3)	Incorporated by reference to the Company's amended Quarterly Report on Form 10-Q filed on August 15, 1997
(4)	Incorporated by reference to the Company's Quarterly Report on Form 10-Q filed on August 14, 1997
(5)	Incorporated by reference to the Company's Quarterly Report on Form 10-Q filed on November 14, 1997
(6)	Incorporated by reference to the Company's Quarterly Report on Form 10-Q filed on August 14, 1998
(7)	Incorporated by reference to the Company's Report on Form 10-K for the fiscal year ended December 31, 1998 filed on March 31, 1999
(8)	Incorporated by reference to the Company's Quarterly Report on Form 10-Q filed on August 11, 1999
(9)	Incorporated by reference to the Company's Quarterly Report on Form 10-Q filed on November 12, 1999
(10)	Incorporated by reference to the Company's Report on Form S-3 filed on January 20, 2000
(11)	Incorporated by reference to the Company's Quarterly Report on Form 10-Q filed on August 11, 2000
(12)	Incorporated by reference to the Company's Report on Form S-8 filed on August 17, 2000
(13)	Incorporated by reference to the Company's Current Report on Form 8-K filed on December 15, 2000
(14)	Incorporated by reference to the Company's Registration Statement on Form S-8 filed March 15, 2001
(15)	Incorporated by reference to the Company's Report on Form 10-K for the fiscal year ended December 31, 2000 filed on March 30, 2001
(16)	Incorporated by reference to the Company's Report on Form S-8 filed on July 16, 2001
(17)	Incorporated by reference to the Company's Quarterly Report on Form 10-Q filed on August 14, 2001
(18)	Incorporated by reference to the Company's Quarterly Report on Form 10-Q filed on November 13, 2001
(19)	Incorporated by reference to the Company's Current Report on Form 8-K filed on January 14, 2002
(20)	Incorporated by reference to the Company's Current Report on Form 8-K filed on December 20, 2002
(21)	Incorporated by reference to the Company's Quarterly Report on Form 10-Q filed on November 13, 2002
*	Confidential treatment has been granted with respect to certain portions of the exhibit
**	Confidential treatment has been requested with respect to certain portions of the exhibit

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



**SIGNATURES**

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

NEUROCRINE BIOSCIENCES, INC.  
A Delaware Corporation

Date: March 4, 2003

By: /s/ Gary A. Lyons \_\_\_\_\_

Gary A. Lyons  
President and Chief Executive Officer

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

<u>Signature</u>	<u>Title</u>	<u>Date</u>
<u>/s/ Gary A. Lyons</u> Gary A. Lyons	President, Chief Executive Officer and Director (Principal Executive Officer)	March 4, 2003
<u>/s/ Paul W. Hawran</u> Paul W. Hawran	Chief Financial Officer (Principal Financial and Accounting Officer)	March 4, 2003
<u>/s/ Joseph A. Mollica</u> Joseph A. Mollica	Chairman of the Board of Directors	March 4, 2003
<u>/s/ W. Thomas Mitchell</u> W. Thomas Mitchell	Director	March 4, 2003
<u>/s/ Richard F. Pops</u> Richard F. Pops	Director	March 4, 2003
<u>/s/ Stephen A. Sherwin</u> Stephen A. Sherwin	Director	March 4, 2003
<u>/s/ Lawrence Steinman</u> Lawrence Steinman	Director	March 4, 2003
<u>/s/ Wylie W. Vale</u> Wylie W. Vale	Director	March 4, 2003

### Certifications

I, Gary A. Lyons, President and Chief Executive Officer of Neurocrine Biosciences, Inc., certify that:

1. I have reviewed this annual report on Form 10-K of Neurocrine Biosciences, Inc.;
2. Based on my knowledge, this annual report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this annual report;
3. Based on my knowledge, the financial statements, and other financial information included in this annual report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this annual report;
4. The registrant's other certifying officer and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-14 and 15d-14) for the registrant and have:
  - a) designed such disclosure controls and procedures to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during this period in which the annual report is being prepared;
  - b) evaluated the effectiveness of the registrant's disclosure controls and procedures as of a date within 90 days prior to the filing date of this annual report (the "Evaluation Date"); and
  - c) presented in this annual report our conclusions about the effectiveness of the disclosure controls and procedures based on our evaluation as of the Evaluation Date;
5. The registrant's other certifying officer and I have disclosed, based on our most recent evaluation, to the registrant's auditors and the audit committee of registrant's board of directors (or persons performing the equivalent functions):
  - a) all significant deficiencies in the design or operation of internal controls which could adversely affect the registrant's ability to record, process, summarize and report financial data and have identified for the registrant's auditors any material weaknesses in internal controls; and
  - b) any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal controls; and
6. The registrant's other certifying officer and I have indicated in this annual report whether or not there were significant changes in internal controls or in other factors that could significantly affect internal controls subsequent to the date of our most recent evaluation, including any corrective actions with regard to significant deficiencies and material weaknesses.

Dated: March 4, 2003

/s/ Gary A. Lyons

\_\_\_\_\_  
Gary A. Lyons  
President and Chief Executive Officer

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I, Paul W. Hawran, Executive Vice President and Chief Financial Officer of Neurocrine Biosciences, Inc., certify that:

1. I have reviewed this annual report on Form 10-K of Neurocrine Biosciences, Inc.;
2. Based on my knowledge, this annual report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this annual report;
3. Based on my knowledge, the financial statements, and other financial information included in this annual report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this annual report;
4. The registrant's other certifying officer and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-14 and 15d-14) for the registrant and have:
  - a) designed such disclosure controls and procedures to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during this period in which the annual report is being prepared;
  - b) evaluated the effectiveness of the registrant's disclosure controls and procedures as of a date within 90 days prior to the filing date of this annual report (the "Evaluation Date"); and
  - c) presented in this annual report our conclusions about the effectiveness of the disclosure controls and procedures based on our evaluation as of the Evaluation Date;
5. The registrant's other certifying officer and I have disclosed, based on our most recent evaluation, to the registrant's auditors and the audit committee of registrant's board of directors (or persons performing the equivalent functions):
  - a) all significant deficiencies in the design or operation of internal controls which could adversely affect the registrant's ability to record, process, summarize and report financial data and have identified for the registrant's auditors any material weaknesses in internal controls; and
  - b) any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal controls; and
6. The registrant's other certifying officer and I have indicated in this annual report whether or not there were significant changes in internal controls or in other factors that could significantly affect internal controls subsequent to the date of our most recent evaluation, including any corrective actions with regard to significant deficiencies and material weaknesses.

Dated: March 4, 2003

/s/ Paul W. Hawran

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Paul W. Hawran  
Executive Vice President and  
Chief Financial Officer

**NEUROCRINE BIOSCIENCES, INC.**  
**INDEX TO THE FINANCIAL STATEMENTS**

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**REPORT OF ERNST & YOUNG LLP, INDEPENDENT AUDITORS**

The Board of Directors and Stockholders  
Neurocrine Biosciences, Inc.

We have audited the accompanying balance sheets of Neurocrine Biosciences, Inc. as of December 31, 2002 and 2001, and the related statements of operations, stockholders' equity, and cash flows for each of the three years in the period ended December 31, 2002. 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 auditing standards generally accepted in the 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 financial statements referred to above present fairly, in all material respects, the financial position of Neurocrine Biosciences, Inc. at December 31, 2002 and 2001, and the results of its operations and its cash flows for each of the three years in the period ended December 31, 2002, in conformity with accounting principles generally accepted in the United States.

/s/ ERNST & YOUNG LLP

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ERNST & YOUNG LLP

San Diego, California  
January 24, 2003

**NEUROCRINE BIOSCIENCES, INC.**  
**Balance Sheets**  
**(in thousands, except for par value and share totals)**

	December 31,	
	2002	2001
<b>ASSETS</b>		
Current assets:		
Cash and cash equivalents	\$ 44,313	\$ 163,888
Short-term investments, available-for-sale	200,397	156,094
Receivables under collaborative agreements	247	9,949
Other current assets	3,137	1,584
	<u>248,094</u>	<u>331,515</u>
Property and equipment, net	14,102	12,088
Licensed technology and patent applications costs, net	—	188
Other non-current assets	4,343	2,559
	<u>266,539</u>	<u>346,350</u>
<b>LIABILITIES AND STOCKHOLDERS' EQUITY</b>		
Current liabilities:		
Accounts payable	\$ 1,959	\$ 1,539
Accrued liabilities	22,163	15,753
Deferred revenues	5,699	5,382
Current portion of long-term debt	—	149
Current portion of capital lease obligations	2,658	1,938
	<u>32,479</u>	<u>24,761</u>
Capital lease obligations, net of current portion	5,277	3,600
Deferred rent	2,645	2,196
Deferred revenues	833	4,417
Other liabilities	1,051	983
	<u>42,285</u>	<u>35,957</u>
Commitments and contingencies (See Note 5)		
Stockholders' equity:		
Preferred stock, \$0.001 par value; 5,000,000 shares authorized; no shares issued and outstanding	—	—
Common stock, \$0.001 par value; 50,000,000 shares authorized; issued and outstanding shares were 30,662,273 in 2002 and 30,347,744 in 2001	31	30
Additional paid-in capital	424,084	420,018
Deferred compensation	(1,240)	(1,815)
Notes receivable from stockholders	(208)	(381)
Accumulated other comprehensive income (loss)	3,513	(69)
Accumulated deficit	(201,926)	(107,390)
	<u>224,254</u>	<u>310,393</u>
Total liabilities and stockholders' equity	<u>\$ 266,539</u>	<u>\$ 346,350</u>

See accompanying notes.

## NEUROCRINE BIOSCIENCES, INC.

Statements of Operations  
(in thousands, except loss per share data)

	Years Ended December 31,		
	2002	2001	2000
<b>Revenues:</b>			
Sponsored research and development	\$ 12,364	\$ 16,880	\$ 6,881
Milestones and license fees	3,516	22,937	6,345
Grant income and other revenues	2,165	1,425	1,362
<b>Total revenues</b>	<b>18,045</b>	<b>41,242</b>	<b>14,588</b>
<b>Operating expenses:</b>			
Research and development	108,939	74,267	40,227
General and administrative	12,721	10,857	9,962
<b>Total operating expenses</b>	<b>121,660</b>	<b>85,124</b>	<b>50,189</b>
Loss from operations	(103,615)	(43,882)	(35,601)
<b>Other income and (expenses):</b>			
Interest income	9,349	6,978	6,276
Interest expense	(485)	(316)	(228)
Other income	215	430	1,047
<b>Total other income</b>	<b>9,079</b>	<b>7,092</b>	<b>7,095</b>
Loss before taxes	(94,536)	(36,790)	(28,506)
Income taxes	—	120	302
<b>Net loss</b>	<b>\$ (94,536)</b>	<b>\$ (36,910)</b>	<b>\$ (28,808)</b>
<b>Loss per common share:</b>			
Basic and diluted	\$ (3.10)	\$ (1.42)	\$ (1.30)
<b>Shares used in the calculation of loss per common share:</b>			
Basic and diluted	30,488	26,028	22,124

See accompanying notes.

**NEUROCRINE BIOSCIENCES, INC.**  
**Statements of Stockholders' Equity**  
(in thousands)

	Common stock		Additional paid-in capital	Deferred compensation	Notes receivable from stockholders	Accumulated other comprehensive income (loss)	Accumulated deficit	Total stockholders' equity
	Shares	Amount						
BALANCE AT DECEMBER 31, 1999	21,608	\$22	\$138,798	\$ (411)	\$(119)	\$ (264)	\$ (41,672)	\$ 96,354
Net loss	—	—	—	—	—	—	(28,808)	(28,808)
Unrealized gain on short-term investments	—	—	—	—	—	525	—	525
Comprehensive loss	—	—	—	—	—	—	—	(28,283)
Issuance of common stock from exercise of warrants	23	—	—	—	—	—	—	—
Issuance of common stock for notes	6	—	1	—	—	—	—	1
Issuance of common stock from option exercises	354	—	2,328	—	—	—	—	2,328
Issuance of common stock pursuant to the Employee Stock Purchase Plan	98	—	1,339	—	—	—	—	1,339
Issuance of common stock, net of offering costs	3,225	3	90,353	—	—	—	—	90,356
Payments received on stockholder notes	—	—	—	—	15	—	—	15
Reversal of accrued 12/99 private placement costs	—	—	182	—	—	—	—	182
Amortization of deferred compensation, net	—	—	564	352	—	—	—	916
BALANCE AT DECEMBER 31, 2000	25,314	25	233,565	(59)	(104)	261	(70,480)	163,208
Net loss	—	—	—	—	—	—	(36,910)	(36,910)
Unrealized loss on short-term investments	—	—	—	—	—	(330)	—	(330)
Comprehensive loss	—	—	—	—	—	—	—	(37,240)
Issuance of common stock from exercise of warrants	43	—	1,902	—	—	—	—	1,902
Issuance of common stock for notes	7	—	277	—	(277)	—	—	—
Issuance of common stock from option exercises	781	1	2,436	—	—	—	—	2,437
Issuance of common stock pursuant to the Employee Stock Purchase Plan	178	—	3,382	—	—	—	—	3,382
Issuance of common stock, net of offering costs	4,025	4	175,558	—	—	—	—	175,562
Amortization of deferred compensation, net	—	—	2,898	(1,756)	—	—	—	1,142
BALANCE AT DECEMBER 31, 2001	30,348	30	420,018	(1,815)	(381)	(69)	(107,390)	310,393
Net loss	—	—	—	—	—	—	(94,536)	(94,536)
Unrealized gain on short-term investments	—	—	—	—	—	3,582	—	3,582
Comprehensive loss	—	—	—	—	—	—	—	(90,954)
Issuance of common stock for option exercises	264	1	2,195	—	—	—	—	2,196
Issuance of common stock pursuant to the Employee Stock Purchase Plan	50	—	1,175	—	—	—	—	1,175
Reversal of offering expenses	—	—	88	—	—	—	—	88
Amortization of deferred compensation, net	—	—	447	575	—	—	—	1,022
NPI Warrants	—	—	161	—	—	—	—	161
Shareholder note repayment	—	—	—	—	104	—	—	104
Shareholder note forgiveness	—	—	—	—	69	—	—	69
BALANCE AT DECEMBER 31, 2002	30,662	\$31	\$424,084	\$(1,240)	\$(208)	\$3,513	\$(201,926)	\$224,254





**NEUROCRINE BIOSCIENCES, INC.**  
**Statements of Cash Flows**  
**(in thousands)**

	Years Ended December 31,		
	2002	2001	2000
<b>CASH FLOW FROM OPERATING ACTIVITIES</b>			
Net loss	\$ (94,536)	\$ (36,910)	\$ (28,808)
Adjustments to reconcile net loss to net cash used in operating activities:			
Depreciation and amortization	3,098	2,651	2,198
Loss on abandonment of assets	5	198	80
Deferred revenues	(3,267)	5,737	3,907
Deferred rent	577	597	868
Loan forgiveness on notes receivable from stockholders	69	—	—
Non-cash compensation expense	1,183	4,024	2,677
Change in operating assets and liabilities:			
Accounts receivable and other current assets	8,149	(3,798)	(4,020)
Other non-current assets	(1,413)	(322)	1,014
Accounts payable and accrued liabilities	6,770	5,967	3,439
Net cash used in operating activities	(79,365)	(21,856)	(18,645)
<b>CASH FLOW FROM INVESTING ACTIVITIES</b>			
Purchases of short-term investments	(401,589)	(175,886)	(151,582)
Sales/maturities of short-term investments	360,868	163,054	78,348
Purchases of property and equipment, net	(5,300)	(3,805)	(2,440)
Net cash used in investing activities	(46,021)	(16,637)	(75,674)
<b>CASH FLOW FROM FINANCING ACTIVITIES</b>			
Issuance of common stock	3,459	179,486	93,360
Proceeds received from long-term obligations	4,561	3,483	1,741
Principal payments on long-term obligations	(2,313)	(1,666)	(984)
Payments received on notes receivable from stockholders	104	—	15
Net cash provided by financing activities	5,811	181,303	94,132
Net (decrease) increase in cash and cash equivalents	(119,575)	142,810	(187)
Cash and cash equivalents at beginning of the year	163,888	21,078	21,265
Cash and cash equivalents at end of the year	\$ 44,313	\$ 163,888	\$ 21,078
<b>SUPPLEMENTAL DISCLOSURES</b>			
Supplemental disclosures of cash flow information:			
Interest paid	\$ 410	\$ 312	\$ 228
Taxes paid	\$ —	\$ 120	\$ 302

See accompanying notes.

**NEUROCRINE BIOSCIENCES, INC.**  
**NOTES TO THE FINANCIAL STATEMENTS**  
**December 31, 2002**

**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. Since the Company was founded, it has been engaged in the discovery and development of novel pharmaceutical products for neurologic and endocrine diseases and disorders. Many of its product candidates address some of the largest pharmaceutical markets in the world, including insomnia, anxiety, depression, malignant brain tumors and peripheral cancers, diabetes mellitus, multiple sclerosis, irritable bowel syndrome, eating disorders, pain, prostate cancer, obesity and certain female health disorders.

**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 Statement of Financial Accounting Standards (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 comprehensive income. 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 interest 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.

During the years ended December 31, 2002, 2001 and 2000, the Company had collaborative research agreements that accounted for 88%, 97% and 91%, respectively, of total revenue.

**Property and Equipment.** Property and equipment are stated at cost and depreciated over the estimated useful lives of the assets (generally three to seven years) using the straight-line method. Amortization of leasehold improvements is computed over the shorter of the lease term or the estimated useful life of the related assets.

**Licensed Technology and Patent Application Costs.** Licensed technology consists of worldwide licenses to patents related to the Company's platform technology, which are capitalized at cost and amortized over periods of 7 to 11 years. These costs are regularly reviewed to determine that they include costs for patent applications the Company is pursuing. Costs related to applications that are not being actively pursued are generally written-off. All costs were fully amortized as of December 31, 2002 and accumulated amortization at December 31, 2002 was \$647,000.

**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 impairment is indicated, the Company measures the amount of such impairment by comparing the carrying value of the asset to the present value of the expected future cash flows

**NEUROCRINE BIOSCIENCES, INC.**  
**NOTES TO THE FINANCIAL STATEMENTS**  
**December 31, 2002**

associated with the use of the asset. While the Company's current and historical operating and cash flow losses are indicators of impairment, the Company believes the future cash flows to be received from the long-lived assets will exceed the assets' carrying value, and accordingly the Company has not recognized any impairment losses through December 31, 2002.

**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.

**Industry Segment and Geographic Information.** The Company operates in a single industry segment – the discovery and development of therapeutics for the treatment of neurologic and endocrine diseases and disorders. The Company has no foreign operations for the years ended December 31, 2002, 2001 and 2000.

**Revenue Recognition.** Revenues under collaborative research agreements and grants are recognized as research 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. Up-front, 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 require substantive effort. Revenues from government grants are recognized based on a percentage-of-completion basis as the related costs are incurred.

Up-front payments have been received for program cost reimbursements incurred during a negotiation period. 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.

**Research and Development Expenses.** Research and development costs are expensed as incurred. Such costs include: personnel expenses, contractor fees, laboratory supplies, facilities, miscellaneous expenses and allocations of corporate costs. These expenses are incurred during proprietary research and development activities, as well as in providing services under collaborative research agreements and grants.

**Stock-Based Compensation.** As permitted by SFAS No. 123, "Accounting for Stock-Based Compensation," the Company has elected to follow Accounting Principles Board (APB) Opinion No. 25, "Accounting for Stock Issued to Employees", and related interpretations in accounting for stock-based employee compensation. Deferred compensation is recorded for employee options only in the event that the fair market value of the stock on the date of the option grant exceeds the exercise price of the options. The deferred compensation is amortized over the vesting period of the options.

Compensation charges for options granted to non-employees have been determined in accordance with SFAS No. 123 and Emerging Issues Task Force (EITF) 96-18, "Accounting for Equity Instruments that Are Issued to Other Than Employees for Acquiring, or in Conjunction with Selling, Goods or Services," as the fair value of the consideration received or the fair value of the equity instruments issued, whichever is more reliably measured. Compensation for options granted to non-employees is periodically measured as the underlying options vest.

**Earnings (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

**NEUROCRINE BIOSCIENCES, INC.**  
**NOTES TO THE FINANCIAL STATEMENTS**  
**December 31, 2002**

weighted average number of common and common equivalent shares outstanding during the period. Potentially dilutive securities composed 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, warrants for common stock, and restricted stock that has not yet fully vested. Potentially dilutive securities totaled 2.1 million, 2.0 million and 2.6 million for the years ended December 31, 2002, 2001 and 2000, respectively, and were excluded from the diluted earnings per share because of their anti-dilutive effect.

**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 consisted of gains and losses on short-term investments and is reported in the statements of stockholders' equity.

**Impact of Recently Issued Accounting Standards.** In November 2002, the Emerging Issues Task Force (EITF) reached a consensus on Issue No. 00-21, "Revenue Arrangements with Multiple Deliverables." EITF Issue No. 00-21 provides guidance on how to account for arrangements that involve the delivery or performance of multiple products, services and/or rights to use assets. The Company will be required to adopt this provision for revenue arrangements entered into on or after June 15, 2003. Management is currently evaluating the effect that the adoption of EITF 00-21 will have on the Company's results of operations and financial condition.

In December 2002, the FASB issued Statement of Financial Accounting Standards (SFAS) No. 148, "Accounting for Stock-Based Compensation, Transition and Disclosure." SFAS No. 148 provides alternative methods of transition for a voluntary change to the fair value based method of accounting for stock-based employee compensation. SFAS No. 148 also requires that disclosures of the pro forma effect of using the fair value method of accounting for stock-based employee compensation be displayed more prominently and in a tabular format. Additionally, SFAS No. 148 requires disclosure of the pro forma effect in interim financial statements. The transition and annual disclosure requirements of SFAS No. 148 are effective immediately. The interim disclosure requirements are effective for the first quarter of 2003. The adoption of SFAS No. 148 did not have a material effect on our results of operations or financial condition.

In January 2003, the FASB issued FASB Interpretation No. 46 (FIN 46), "Consolidation of Variable Interest Entities, an Interpretation of Accounting Research Bulletin No. 51." FIN 46 requires certain variable interest entities to be consolidated by the primary beneficiary of the entity if the equity investors in the entity do not have the characteristics of a controlling financial interest or do not have sufficient equity at risk for the entity to finance its activities without additional subordinated financial support from other parties. FIN 46 is effective for all new variable interest entities created or acquired after January 31, 2003. For variable interest entities created or acquired prior to February 1, 2003, the provisions of FIN 46 must be applied for the first interim or annual period beginning after June 15, 2003. Management is currently analyzing the effect that the adoption of FIN 46 will have on its results of operations and financial position, but expects that upon the implementation date, the Company will consolidate the entity Science Park Center, LLC which is described in Note 6.

**NEUROCRINE BIOSCIENCES, INC.**  
**NOTES TO THE FINANCIAL STATEMENTS**  
**December 31, 2002**

**NOTE 2. SHORT-TERM INVESTMENTS**

Cash, cash equivalents, and short-term investments totaled \$244.7 million and \$320.0 million as of December 31, 2002 and 2001, 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, 2002</b>				
US Government securities	\$ 82,688	\$ 141	\$(33)	\$ 82,796
Corporate debt securities	103,861	2,293	(23)	106,131
Other debt securities	10,335	39	(1)	10,373
<b>Total debt securities</b>	<b>196,884</b>	<b>2,473</b>	<b>(57)</b>	<b>199,300</b>
Equity securities	—	1,097	—	1,097
<b>Total securities</b>	<b>\$196,884</b>	<b>\$3,570</b>	<b>\$(57)</b>	<b>\$200,397</b>
<b>December 31, 2001</b>				
US Government securities	\$ 6,000	\$ 17	\$ —	\$ 6,017
Corporate debt securities	150,163	—	(86)	150,077
<b>Total securities</b>	<b>\$156,163</b>	<b>\$ 17</b>	<b>\$(86)</b>	<b>\$156,094</b>

The amortized cost and estimated fair value of debt securities by contractual maturity at December 31, 2002 are shown below (in thousands):

	Amortized Cost	Estimated Fair Value
Due in 12 months or less	\$ 34,144	\$ 35,335
Due between 12 months and 44 months	162,740	165,062
	<b>\$196,884</b>	<b>\$200,397</b>

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

	Years Ended December 31,		
	2002	2001	2000
Proceeds from sales	\$360,868	\$163,054	\$78,348
Gross realized gains on sales	\$ 869	\$ 583	\$ 304
Gross realized losses on sales	\$ (25)	\$ (870)	\$ (32)

**NEUROCRINE BIOSCIENCES, INC.**  
**NOTES TO THE FINANCIAL STATEMENTS**  
**December 31, 2002**

**NOTE 3. PROPERTY AND EQUIPMENT**

Property and equipment at December 31, 2002 and 2001 consist of the following (in thousands):

	2002	2001
Land	\$ 4,290	\$ 4,661
Furniture and fixtures	1,761	1,583
Equipment	17,249	12,734
Leasehold improvements	1,386	1,238
Construction in progress	160	—
	24,846	20,216
Less accumulated depreciation	(10,744)	(8,128)
Property and equipment, net	\$ 14,102	\$12,088

Furniture and equipment under capital leases were \$10.6 million and \$6.3 million at December 31, 2002 and 2001, respectively. Accumulated depreciation of furniture and equipment under capital leases totaled \$3.4 million and \$1.7 million at December 31, 2002 and 2001, respectively. The Company entered into \$4.6 million of additional capital leases during 2002 and \$3.5 million during 2001.

**NOTE 4. ACCRUED LIABILITIES**

Accrued liabilities at December 31, 2002 and 2001 consist of the following (in thousands):

	2002	2001
Accrued employee benefits	\$ 2,406	\$ 2,438
Accrued professional fees	762	1,300
Accrued development costs	18,499	11,150
Other accrued liabilities	496	865
	\$22,163	\$15,753

**NOTE 5. COMMITMENTS AND CONTINGENCIES**

**Capital Lease Obligations.** The Company has financed certain equipment under capital lease obligations, which expire on various dates through the year 2006 and bear interest at rates between 6.0% and 9.6%. The lease commitments are repayable in monthly installments.

**Operating Leases.** In September 1998, the Company leased an expanded laboratory and office complex under a 15-year operating lease from the Science Park Center, LLC, of which the Company owns a minority interest. The lease contains a 4% per year escalation in base rent fees, effective with each anniversary, and generally requires the Company to pay taxes, insurance and maintenance.

Rent expense is recognized on a straight-line basis resulting in deferred rent of \$2.6 million and \$2.2 million at December 31, 2002 and 2001, respectively. Rent expense was \$1.6 million, \$1.7 million and \$2.5 million for the years ended December 31, 2002, 2001 and 2000, respectively. Sublease income was \$190,000, \$698,000 and \$1.2 million for the years ended December 31, 2002, 2001 and 2000, respectively.

**Licensing and Research Agreements.** The Company has entered into licensing agreements with various universities and research organizations, which are cancelable at the option of the Company with terms ranging from

**NEUROCRINE BIOSCIENCES, INC.**  
**NOTES TO THE FINANCIAL STATEMENTS**  
**December 31, 2002**

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, certain agreements require minimum royalty payments. Certain agreements also require the Company to pay expenses arising from the prosecution and maintenance of the patents covering the licensed technology. Due to the uncertainty of the pharmaceutical development process, the Company continually reassesses the value of the license agreements and cancels them as 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 \$16.6 million over the lives of these agreements, in addition to sales royalties ranging from 1% – 7%. Due to the uncertainties of the development process, the timing and probability of the milestone and royalty payments cannot be accurately estimated.

**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 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 conduct of pre-clinical development research, manufacture of clinical compounds, enrollment of patients, recruiting of patients, monitoring of studies, data analysis and regulatory filing assistance. Payments under these agreements typically include fees for services and reimbursement of expenses. Some agreements may also 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.

Repayment schedules for commitments and contractual obligations at December 31, 2002 are as follows (in thousands):

Fiscal Year:	Capital Leases	Operating Leases	Licenses & Research Agreements	Development Agreements
2003	\$ 3,132	\$ 2,731	\$1,135	\$65,468
2004	2,888	2,841	120	2,896
2005	1,987	2,954	120	2,804
2006	828	3,072	—	—
2007	—	3,195	—	—
Thereafter	—	20,658	—	—
	—————	—————	—————	—————
Total minimum payments	\$ 8,835	\$35,451	\$1,375	\$71,168
Less: amounts representing interest	(900)			
	—————			
Future minimum payments	7,935			
Less: current portion	(2,658)			
	—————			
Future payments on capital lease obligations	\$ 5,277			



**NEUROCRINE BIOSCIENCES, INC.**  
**NOTES TO THE FINANCIAL STATEMENTS**  
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**NOTE 6. SCIENCE PARK CENTER, LLC**

In May 1997, the Company along with two unrelated parties formed Science Park Center, LLC (the LLC) in order to construct an office and laboratory facility. The LLC is a California limited liability company, of which the Company owns a nominal minority interest. In relation to the construction of the facility, the Company sold a parcel of land to the LLC in exchange for a note receivable in the amount of \$3.5 million plus interest of 8.25%. The sales price was established by the fair market value of the parcel at the time of sale.

During 1998, the LLC constructed a laboratory and office facility and leased the facility to the Company under a 15-year operating lease. The Company has the option to purchase the facility at any time during the term of the lease at the unamortized cost of the first mortgage.

Based on the structure of the arrangement with the LLC, this operating lease is commonly referred to as a "synthetic lease." A synthetic lease is a form of off-balance sheet financing under which an unrelated third party funds up to 100% of the costs for the acquisition and/or construction of the facility into a limited liability company and leases the facility to a lessee. A synthetic lease is treated as an operating lease for accounting purposes and a financing lease for tax purposes. At least 3% of the third party funds must be at-risk equity at all times and must remain at-risk to qualify as an operating lease for accounting purposes. If at any time the third party fails to maintain at least 3% at-risk equity, the Company will need to consolidate the LLC, which will result in debt and equity being recorded in its financial statements. The Company selected the synthetic lease for financing advantages and periodically reviews the fair value of the property leased to determine potential accounting ramifications.

For accounting purposes, the sale of land to the LLC does not qualify as a sale under SFAS No. 98 "Accounting for Leases," and therefore, the entire amount of the note receivable, \$2.8 million and \$3.2 million for years ended December 31, 2002 and 2001, respectively, is included in land. The interest income earned on the note receivable from the LLC totaled approximately \$244,000, \$298,000 and \$304,000 for the years ended December 31, 2002, 2001 and 2000, respectively, and is recorded as an offset to rent expense by the Company.

The following are the unaudited, condensed balance sheets and statements of income for the LLC:

**Science Park Center, LLC.**  
**Balance Sheets**  
*(unaudited, in thousands)*

	December 31,	
	2002	2001
Current assets	\$ 285	\$ 240
Building, net	13,513	14,038
Land	3,485	3,485
Deferred rent	2,645	2,196
<b>Total assets</b>	<b>\$19,928</b>	<b>\$19,959</b>
Current liabilities	\$ 107	\$ 112
Notes payable to Neurocrine	2,790	3,161
Building loan	14,104	14,280
Distribution payable	2,327	1,695
<b>Total liabilities</b>	<b>19,328</b>	<b>19,248</b>
Retained earnings	600	711
<b>Total liabilities and shareholders' equity</b>	<b>\$19,928</b>	<b>\$19,959</b>

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**Science Park Center, LLC.**  
**Statements of Income**  
*(unaudited, in thousands)*

	Years Ended December 31,		
	2002	2001	2000
Rental income	\$3,076	\$3,076	\$3,076
Operating expenses	642	632	635
Interest expense, net	1,222	1,366	1,293
Income taxes	6	10	5
	\$1,206	\$1,068	\$1,143

The Company receives cash distributions from the LLC from retained earnings above and beyond the at-risk equity of the unrelated parties. The LLC accrues the distributions payable to the Company on a monthly basis and periodically makes cash payments to reduce those payables. The distributions due the Company are offset against rent expense recorded by the Company. Distributions recorded by the Company for the years ended December 31, 2002, 2001 and 2000 were \$1.2 million, \$1.1 million and 723,000, respectively.

**NOTE 7. STOCKHOLDERS' EQUITY**

**Common Stock Issuances.** From inception through 2001, the Company has issued common stock in various private and public offerings, as well as to corporate collaborators, at prices between \$5.00 and \$46.75 per share resulting in aggregate net proceeds of approximately \$384.1 million. This total includes a December 2001 public offering, in which the Company sold 4.0 million shares of its common stock at \$46.75 per share. The net proceeds generated from this transaction were \$175.6 million.

**Options.** The Company has authorized 9.2 million shares of common stock for issuance upon exercise of options or stock purchase rights granted under the 1992 Incentive Stock Plan, 1996 Director Option Plan, 1997 Northwest Neurologic, Inc. Restated Incentive Stock Plan and 2001 Stock Option Plan (collectively, the Option Plans). The Option Plans provide for the grant of stock options and stock purchase rights to officers, directors, and employees of, and consultants and advisors to, the Company. Options under the Option Plans have terms of up to 10 years from the date of grant. Options under the 1992 Incentive Stock Plan and the Northwest Neurologic, Inc. Restated 1997 Incentive Stock Plan may be designated as incentive stock options or nonstatutory stock options. Options under the 2001 Stock Option Plan are nonstatutory stock options. Of the shares available for future issuance under the Option Plans, 4.9 million are outstanding grants and 394,000 remain available for future grant.

A summary of the Company's stock option activity, and related information for the years ended December 31 follows (in thousands, except for weighted average exercise price data):

	2002		2001		2000	
	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	3,883	\$18.59	3,911	\$12.75	3,158	\$ 5.91
Granted	1,375	37.54	980	31.17	1,136	29.66
Exercised	(268)	8.90	(850)	6.14	(354)	6.56
Canceled	(115)	28.70	(158)	19.09	(29)	11.69
	4,875	\$24.23	3,883	\$18.59	3,911	\$12.75

**NEUROCRINE BIOSCIENCES, INC.**  
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A summary of options outstanding as of December 31, 2002 follows (in thousands, except for weighted average remaining contractual life and weighted average exercise price data):

Range of Exercise Prices	Options Outstanding			Options Exercisable	
	Outstanding as of 12/31/02	Weighted Average Remaining Contractual Life	Weighted Average Exercise Price	Exercisable As of 12/31/02	Weighted Average Exercise Price
\$0.00 to \$ 5.28	669	4.0	\$ 3.85	636	\$ 3.80
\$5.29 to \$10.57	960	5.0	7.36	927	7.33
\$10.58to \$21.13	288	7.4	18.30	192	18.33
\$21.14to \$31.70	735	8.3	27.47	230	27.74
\$31.71to \$36.98	1,461	8.7	35.51	455	35.09
\$36.99to \$52.83	762	8.9	40.86	180	39.55
<b>\$0.00 to \$52.83</b>	<b>4,875</b>	<b>7.2</b>	<b>\$24.23</b>	<b>2,620</b>	<b>\$16.10</b>

The weighted average fair values (computed using Black-Scholes) of the options granted during 2002, 2001 and 2000 were \$24.51, \$20.54 and \$20.51, respectively.

Pro forma information regarding net loss is required by SFAS No. 123 and has been determined as if the Company had accounted for its employee stock options under the fair value method of that Statement. The fair value for these options was estimated at the date of grant using a Black-Scholes option pricing model using the following weighted average assumptions for 2002, 2001 and 2000, respectively: risk-free interest rates of 2.8%, 4.4% and 5.0%; a dividend yield of 0.0% (for all years); volatility factors of the expected market price of the Company's common stock of .78, .80 and .81; and a weighted average expected life of the option of 5 years (for all years presented).

For purposes of pro forma disclosures, the estimated fair value of the options granted is amortized to expense over the options' vesting period. The pro forma effect on net losses for 2002, 2001 and 2000 is not likely to be representative of the effects on reported income or loss in future years because these amounts reflect less than full vesting for options granted during these periods. The Company's reported and pro forma information for the years ended December 31, 2002, 2001 and 2000 follows (in thousands, except for loss per share data):

	2002	2001	2000
Net loss as reported	\$ (94,536)	\$(36,910)	\$(28,808)
Loss per share (basic and diluted)	(3.10)	(1.42)	(1.30)
Pro forma net loss	\$(109,358)	\$(44,188)	\$(31,057)
Pro forma loss per share (basic and diluted)	(3.59)	(1.70)	(1.40)

**Employee Stock Purchase Plan.** The Company has reserved 625,000 shares of common stock for issuance under the 1996 Employee Stock Purchase Plan, as amended (the Purchase Plan). The Purchase Plan permits eligible employees to purchase common stock through payroll deductions at a purchase price equal to 85% of the lesser of the fair market value per share of common stock on the enrollment date or on the date on which the shares are purchased. As of December 31, 2002, 420,000 shares have been issued pursuant to the Purchase Plan.

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**Warrants.** The Company has outstanding warrants to purchase 380,787 shares of common stock at the following exercise prices. At December 31, 2002, all outstanding warrants were exercisable.

Exercise Prices	Warrants Outstanding at December 31, 2002	Expiration
\$ 8.04	15,000	06/2003
\$10.50	301,000	03/2006
\$41.41	60,000	06/2003
\$52.05	4,787	12/2012
	380,787	

The following shares of common stock are reserved for future issuance at December 31, 2002 (in thousands):

Stock option plans	5,267
Employee stock purchase plan	205
Warrants	381
Total	5,853

**NOTE 8. 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 will collaborate in the completion of the indiplon Phase III clinical program. During 2003, the Company will be responsible for \$15 million in development costs, and all other external collaboration costs will be borne by Pfizer. Following the filing of a New Drug Application (NDA) with the Food and Drug Administration regarding indiplon, Pfizer will support the creation of a 200 person Neurocrine sales force. The Company's sales force will detail Pfizer's antidepressant drug Zoloft® to psychiatrists in the United States. Upon approval of the indiplon NDA, our sales force will also co-promote indiplon to psychiatrists and sleep specialists in the United States. During the first quarter of 2003, the Company will receive an upfront payment of \$100 million and will also be eligible to receive up to \$300 million in additional pre-commercialization milestone payments as indiplon moves to commercialization. Further, upon commercialization of indiplon, the Company will be entitled to a percentage of worldwide sales of indiplon for the longer of 10 years or the life of the indiplon patent rights as well as co-promotion payments on sales of Zoloft® and indiplon in the United States. In addition, Pfizer has committed to loan the Company up to \$175 million, at commercial terms, pursuant to a secured short-term credit facility, subject to prior U.S. launch of indiplon and various other conditions. Pfizer may terminate the collaboration at its discretion upon 180-days written notice to Neurocrine. In such event, the Company would be entitled to certain payments for ongoing clinical development and related activities and all indiplon product rights would revert to Neurocrine. The Company has obtained rights to indiplon pursuant to a 1998 Sublicense and Development Agreement with DOV Pharmaceuticals, Inc. (DOV) and is responsible for specified milestone payments and royalties on net sales to DOV under the license agreement. For the year ended December 31, 2002, no revenue was recognized under the Pfizer collaboration.

**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 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 the year ended December 31, 2002, the Company recognized \$7.6 million in revenue under the GSK agreement. At

**NEUROCRINE BIOSCIENCES, INC.**  
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December 31, 2002, the Company had \$2.3 million of deferred license fees that will be amortized over the remaining life of the agreement. In addition, at December 31, 2002, the Company had \$3.1 million of deferred sponsored research that will be amortized over the remaining sponsored research period.

**Taisho Pharmaceutical Co., Ltd.** In December 1999, the Company entered into an agreement with Taisho Pharmaceutical Co., Ltd. (Taisho), providing to them an exclusive option to obtain European, Asian and North American development and commercialization rights for Neurocrine's altered peptide ligand product, NBI-6024, for Type 1 diabetes in exchange for a \$2.0 million option fee. In July 2000, Taisho exercised its option as to Europe and Asia, and in December 2000, Taisho exercised its option as to North America. In September 2002, the collaboration agreement with Taisho was restructured to provide that worldwide development and commercialization rights, excluding Japan, revert to us. The restructured agreement further provides that under certain circumstances, if we enter into a business arrangement with specified third parties, then Taisho will be entitled to receive a percentage of certain consideration received by us. Generally, if we do not enter into a business discussion with one of the specified third parties on or before a specified date, the restructured agreement will expire, and at that time the rights to Japan will revert to us. For the years ended December 31, 2002, 2001 and 2000, the Company recognized \$6.8 million, \$16.6 million and \$7.1 million, respectively, in revenue under the Taisho agreement. As of December 31, 2002, the Company has \$1.1 million of deferred license fees that will be amortized over the remaining life of the agreement.

**Wyeth.** Effective January 1999, the Company entered into a collaboration and license agreement with Wyeth relating to the research, development and commercialization of compounds that control excitatory amino acid transporters for the treatment of neurodegenerative and psychiatric diseases. The Company has granted Wyeth exclusive and non-exclusive rights to the Company's excitatory amino acid transporters technology as well as exclusive rights to any products developed during the collaboration. These licenses are for the term of the patents licensed. The Company will receive royalties on product sales for the terms of the patents covering the collaboration products, subject to adjustments for royalties payable to other parties and for competition. The Company will also receive royalties for products that are not the subject of issued patents. The Company also has the option to co-promote collaboration products in Canada and the United States under some conditions. Wyeth may terminate the agreement if it decides that the research is not successful, if it decides to stop the program or if Neurocrine is acquired by another company. The agreement may also be terminated by either party for the other party's failure to meet its obligations under the agreement or bankruptcy. The three-year sponsored research portion of the Wyeth agreement was completed on schedule in December 2001 and was subsequently extended on a smaller scale through December 2002.

For the years ended December 31, 2002, 2001 and 2000, the Company recognized \$1.5 million, \$3.4 million and \$3.0 million, respectively, in revenues under the Wyeth agreement.

**Janssen Pharmaceutica, N.V.** In January 1995, the Company entered into the first of two research and development agreements with Janssen Pharmaceutica, N.V. (Janssen) to collaborate in the discovery, development and commercialization of small molecule CRF R1 antagonists for the treatment of anxiety, depression and substance abuse. Under the January 1995 agreement, Janssen funded three years of research at Neurocrine and received exclusive licenses to all CRF R1 antagonist compounds developed during the term of the funded research or during the year thereafter. The terms of the licenses are for the term of the patents licensed under the agreement. The collaborative research portion of the first Janssen agreement was completed as scheduled in 1997. In September 1999, together with Janssen, the Company entered into an amended agreement to expand the collaborative research and development efforts to identify additional small molecule CRF antagonists for the treatment of psychiatric disorders. In connection with the amended Janssen agreement, the Company received an initial payment and two years of additional research funding for our scientists working in collaboration with Janssen. This additional research was completed in February 2001.

In March 2002, Janssen notified us that it had discontinued development of the backup compound and elected to terminate both the 1995 and 1999 agreements. As a result, exclusive rights to all of the first generation CRF R<sub>1</sub> antagonist compounds developed thereunder reverted to Neurocrine. We do not expect additional payments

**NEUROCRINE BIOSCIENCES, INC.**  
**NOTES TO THE FINANCIAL STATEMENTS**  
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of any kind under the Janssen agreement. For the years ended December 31, 2001 and 2000, the Company recognized \$525,000, and \$3.0 million, respectively, in revenues under terms of the Janssen agreements.

**NOTE 9. INCOME TAXES**

At December 31, 2002, the Company had Federal and California income tax net operating loss carry-forwards of approximately \$169.4 million and \$106.5 million, respectively. The Federal and California tax loss carry-forwards will begin to expire in 2010 and 2003, respectively, unless previously utilized. The Company also has Federal and California research tax credit carry-forwards of approximately \$14.0 million and \$6.8 million, respectively, which will begin to expire in 2007 and 2012, respectively, unless previously utilized. The Company has Federal Alternative Minimum Tax credit carry-forwards of approximately \$257,000, which will carry-forward indefinitely.

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%. However, the Company does not believe such changes will have a material impact upon the utilization of these carry-forwards.

Significant components of the Company's deferred tax assets as of December 31, 2002 and 2001 are shown below. A valuation allowance of \$91.1 million and \$45.7 million at December 31, 2002 and 2001, respectively, have 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:

	2002	2001
Deferred tax assets:		
Net operating loss carry-forwards	\$ 65,400	\$ 27,975
Tax credit carry-forwards	18,688	13,283
Capitalized research and development	4,014	3,733
Other, net	3,036	729
Total deferred tax assets	91,138	45,720
Valuation allowance	(91,138)	(45,720)
Net deferred tax assets	\$ —	\$ —

The provision for income taxes on earnings subject to income taxes differs from the statutory Federal rate at December 31, 2002, 2001 and 2000, due to the following:

	2002	2001	2000
Federal income taxes at 34%	\$(32,142)	\$(12,582)	\$(9,692)
State income tax, net of Federal benefit	(5,295)	(1,736)	—
Tax effect on non-deductible expenses	(7,981)	(4,202)	335
Increase in valuation allowance	45,418	18,520	9,357
	\$ —	\$ —	\$ —

**NOTE 10. RETIREMENT PLAN**

The Company has a 401(k) defined contribution savings plan (the 401(k) Plan). The 401(k) Plan is for the benefit of all qualifying employees and permits employees voluntary contributions up to 20% of base salary limited by the IRS-imposed maximum. On January 1, 2001, the Company began matching 50% of employee contributions up to 6% of eligible compensation, which cliff vests over four years. Employer contributions were \$432,000 and \$359,000 for the years ended December 31, 2002 and 2001, respectively. No employer contributions were made in 2000.

**NEUROCRINE BIOSCIENCES, INC.**  
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**NOTE 11. SELECTED QUARTERLY FINANCIAL DATA (UNAUDITED)**

The following is a summary of the quarterly results of operations for the years ended December 31, 2002 and 2001 (unaudited, in thousands, except for earnings (loss) per share data):

	Quarters Ended				Year End Dec 31
	Mar 31	Jun 30	Sep 30	Dec 31	
<b>Fiscal Year End 2002</b>					
Revenues	\$ 4,957	\$ 4,227	\$ 4,983	\$ 3,878	\$ 18,045
Operating expenses	22,778	26,247	27,484	45,151	121,660
Net loss	(15,764)	(19,751)	(20,234)	(38,787)	(94,536)
Loss per share:					
Basic & Diluted	\$ (0.52)	\$ (0.65)	\$ (0.66)	\$ (1.27)	\$ (3.10)
Shares used in the calculation of loss per share:					
Basic & Diluted	30,384	30,433	30,522	30,611	30,488
	Quarters Ended				Year End Dec 31
	Mar 31	Jun 30	Sep 30	Dec 31	
<b>Fiscal Year End 2001</b>					
Revenues	\$ 3,488	\$ 3,328	\$ 21,593	\$ 12,833	\$ 41,242
Operating expenses	17,567	18,920	20,400	28,237	85,124
Net income (loss)	(11,463)	(13,344)	2,507	(14,610)	(36,910)
Earnings (loss) per share:					
Basic	\$ (0.45)	\$ (0.52)	\$ 0.10	\$ (0.53)	\$ (1.42)
Diluted	\$ (0.45)	\$ (0.52)	\$ 0.09	\$ (0.53)	\$ (1.42)
Shares used in the calculation of earnings (loss) per share:					
Basic	25,407	25,498	25,816	27,371	26,028
Diluted	25,407	25,498	27,972	27,371	26,028

NEUROCRINE BIOSCIENCES, INC.  
2001 STOCK OPTION PLAN  
AS AMENDED AUGUST 6, 2002 AND OCTOBER 15, 2002

1. PURPOSE OF THE PLAN. The purposes of this Incentive Stock Plan are to attract and retain the best available personnel, to provide additional incentive to the employees of Neurocrine Biosciences, Inc. (the "Company") and to promote the success of the Company's business.

2. DEFINITIONS.

(a) "Board" shall mean the Committee, if one has been appointed, or the Board of Directors of the Company, if no Committee is appointed.

(b) "Code" shall mean the Internal Revenue Code of 1986, as amended.

(c) "Committee" shall mean the Committee appointed by the Board of Directors in accordance with Section 4(a) of the Plan, if one is appointed.

(d) "Common Stock" shall mean the common stock, \$.001 per share, of the Company.

(e) "Company" shall mean Neurocrine Biosciences, Inc.

(f) "Consultant" shall mean any person who is engaged by the Company or any Parent or Subsidiary to render consulting services and is compensated for such consulting services, and any director of the Company whether compensated for such services ; provided that (i) such person renders bona fide services to the Company, (ii) the services rendered by such person are not in connection with the offer or sale of securities in a capital-raising transaction and do not directly or indirectly promote or maintain a market for the Company's securities, and (iii) such person is a natural person who has contracted directly with the Company to render such services. However, the term "Consultant" shall not include members of the Board of Directors of the Company who are either not compensated by the Company for their services as directors or who are merely paid a fee by the Company for their services as directors.

(g) "Continuous Status as an Employee or Consultant" shall mean the absence of any interruption or termination of service as an Employee or Consultant, as applicable. Continuous Status as an Employee or Consultant shall not be considered interrupted in the case of sick leave, military leave, or any other leave of absence approved by the Board; provided that such leave is for a period of not more than ninety (90) days or reemployment upon the expiration of such leave is guaranteed by contract or statute. Continuous Service shall not be deemed to have terminated merely because of a change in the capacity in which the Optionee renders service to the Company as an Employee or Consultant, provided that the Optionee's service is continuous.



(h) "Employee" means any person employed by the Company. Mere service as a member of the Board of Directors or payment of a director's fee by the Company shall not be sufficient to constitute "employment" by the Company.

(i) "Fair Market Value" means, as of any date, the value of the Common Stock determined as follows:

(i) If the Common Stock is listed on any established stock exchange or traded on the Nasdaq National Market or the Nasdaq SmallCap Market, the Fair Market Value of a share of Common Stock shall be the closing sales price for such stock (or the closing bid, if no sales were reported) as quoted on such exchange or market (or the exchange or market with the greatest volume of trading in the Common Stock) on the last market trading day prior to the day of determination, as reported by The Nasdaq Stock Market or such other source as the Board deems reliable.

(ii) In the absence of such markets for the Common Stock, the Fair Market Value shall be determined in good faith by the Board.

(j) "Nonstatutory Stock Option" shall mean an Option not intended to qualify as an incentive stock option within the meaning of Section 422 of the Code.

(k) "Officer" means a President, Secretary, Treasurer, Chairman of the Board, Vice President, Assistant Secretary or Assistant Treasurer of the Company, as such positions are described in the Company's Bylaws, any other person designated an "officer" of the Company by the Board of Directors in accordance with the Company's Bylaws or any person who is an "officer" within the meaning of Rule 16a-1(f) under the Securities Exchange Act of 1934, as amended, or Nasdaq Marketplace Rule 4350(i)(1)(A).

(l) "Option" shall mean a stock option granted pursuant to the Plan.

(m) "Optioned Stock" shall mean the Common Stock subject to an Option or Stock Purchase Right.

(n) "Optionee" shall mean an Employee or Consultant who receives an Option.

(o) "Parent" shall mean a "parent corporation," whether now or hereafter existing, as defined in Section 424(e) of the Code.

(p) "Plan" shall mean this 2001 Incentive Stock Plan.

(q) "Purchaser" shall mean an Employee or Consultant who exercises a Stock Purchase Right.

(r) "Share" shall mean a share of the Common Stock, as adjusted in accordance with Section 12 of the Plan.

(s) "Stock Purchase Right" shall mean a right to purchase Common Stock pursuant to the Plan or the right to receive a bonus of Common Stock for past services.

(t) "Subsidiary" shall mean a "subsidiary corporation," whether now or hereafter existing, as defined in Section 424(f) of the Code.

3. STOCK SUBJECT TO THE PLAN. Subject to the provisions of Section 12 of the Plan, the maximum aggregate number of shares that may be issued upon exercise of Options and Stock Purchase Rights under the Plan is one million, one hundred fifty thousand (1,150,000) shares of Common Stock. The Shares may be authorized but unissued, or reacquired Common Stock. If an Option or Stock Purchase Right should expire or become unexercisable for any reason without having been exercised in full, then the unpurchased Shares which were subject thereto shall, unless the Plan shall have been terminated, become available for future grant or sale under the Plan. Notwithstanding any other provision of the Plan, shares issued under the Plan and later repurchased by the Company shall not become available for future grant or sale under the Plan.

4. ADMINISTRATION OF THE PLAN.

(a) Procedure.

(i) Multiple Administrative Bodies. The Plan may be administered by different Committees with respect to different groups of Employees and Consultants.

(ii) Section 162(m). To the extent that the Administrator determines it to be desirable to qualify Options granted hereunder as "performance-based compensation" within the meaning of Section 162(m) of the Code, the Plan shall be administered by a Committee of two or more "outside directors" within the meaning of Section 162(m) of the Code.

(iii) Rule 16b-3. To the extent desirable to qualify transactions hereunder as exempt under Rule 16b-3, the transactions contemplated hereunder shall be structured to satisfy the requirements for exemption under Rule 16b-3.

(iv) Other Administration. Other than as provided above, the Plan shall be administered by (A) the Board or (B) a Committee, which committee shall be constituted to satisfy applicable laws.

(b) Powers of the Board. Subject to the provisions of the Plan, the Board shall have the authority, in its discretion: (i) to grant Nonstatutory Stock Options or Stock Purchase Rights; (ii) to determine, upon review of relevant information and in accordance with Section 7 of the Plan, the Fair Market Value of the Common Stock; (iii) to determine the exercise price per share of Options or Stock Purchase Rights, to be granted, which exercise price shall be determined in accordance with Section 7 of the Plan; (iv) to determine, subject to Section 5 below, the Employees or Consultants to whom, and the time or times at which, Options or Stock Purchase Rights shall be granted and the number of shares to be represented by each Option or Stock Purchase Right; (v) to interpret the Plan; (vi) to prescribe, amend and rescind rules and regulations relating to the Plan; (vii) to determine the terms and provisions of each Option and Stock Purchase Right granted (which need not be identical)

and, with the consent of the holder thereof, modify or amend any provisions (including provisions relating to exercise price) of any Option or Stock Purchase Right; (viii) to accelerate or defer (with the consent of the Optionee) the exercise date of any Option, consistent with the provisions of Section 5 of the Plan; (ix) to authorize any person to execute on behalf of the Company any instrument required to effectuate the grant of an Option or Stock Purchase Right previously granted by the Board; (x) to allow Optionees to satisfy withholding tax obligations by electing to have the Company withhold from the Shares to be issued upon exercise of an Option or Stock Purchase Right that number of Shares having a Fair Market Value equal to the statutory minimum amount required to be withheld. The Fair Market Value of the Shares to be withheld shall be determined on the date that the amount of tax to be withheld is to be determined. All elections by an Optionee to have Shares withheld for this purpose shall be made in such form and under such conditions as the Administrator may deem necessary or advisable; and (xi) to make all other determinations deemed necessary or advisable for the administration of the Plan.

(c) Effect of Board's Decision. All decisions, determinations and interpretations of the Board shall be final and binding on all Optionees, Purchasers and any other holders of any Options or Stock Purchase Rights granted under the Plan.

## 5. ELIGIBILITY.

(a) Options and Stock Purchase Rights may be granted to Employees and Consultants. An Employee or Consultant who has been granted an Option or Stock Purchase Right may, if such Employee or Consultant is otherwise eligible, be granted additional Option(s) or Stock Purchase Right(s). Notwithstanding anything herein to the contrary, the aggregate number of shares issued or reserved for issuance pursuant to Options granted to persons other than Officers must exceed fifty percent (50%) of the total number of shares issued or reserved for issuance pursuant to Options granted under the Plan as determined on the three-year anniversary of the adoption of the Plan by the Board and on each yearly anniversary of the adoption of the Plan thereafter.

(b) Each Option shall be designated in the written option agreement as a Nonstatutory Stock Option.

(c) The Plan shall not confer upon any Optionee or holder of a Stock Purchase Right any right with respect to continuation of employment by or the rendition of consulting services to the Company, nor shall it interfere in any way with his or her right or the Company's right to terminate his or her employment or services at any time, with or without cause.

(d) A Consultant shall not be eligible for the grant of an Option if, at the time of grant, a Form S-8 Registration Statement under the Securities Act ("Form S-8") is not available to register either the offer or the sale of the Company's securities to such Consultant because of the nature of the services that the Consultant is providing to the Company, or because the Consultant is not a natural person, or as otherwise provided by the rules governing the use of Form S-8, unless the Company determines both (i) that such grant (A) shall be registered in another manner under the Securities Act (e.g., on a Form S-3 Registration Statement) or (B) does not require registration under the Securities Act in order to comply with the requirements of the Securities Act, if applicable, and (ii) that such grant complies with the securities laws of all other relevant jurisdictions

6. TERM OF PLAN. The Plan shall become effective upon the earlier to occur of its adoption by the Board of Directors. It shall continue in effect for a term of ten (10) years unless sooner terminated under Section 14 of the Plan.

7. EXERCISE PRICE AND CONSIDERATION.

(a) The per Share exercise price for the Shares to be issued pursuant to exercise of an Option or Stock Purchase Right shall be such price as is determined by the Board, but shall be subject to the following:

(i) the per Share exercise price shall be no less than the par value per Share on the date of grant.

(b) The consideration to be paid for the Shares to be issued upon exercise of an Option or Stock Purchase Right, including the method of payment, shall be determined by the Board and may consist entirely of cash, check, promissory note bearing a market rate of interest, other Shares of Common Stock which (i) either have been owned by the Optionee for more than six (6) months on the date of surrender or were not acquired directly or indirectly, from the Company, and (ii) have a Fair Market Value on the date of surrender equal to the aggregate exercise price of the Shares as to which said Option shall be exercised, or any combination of such methods of payment, or such other consideration and method of payment for the issuance of Shares as may be permitted under applicable law.

8. TERM OF OPTION. The term of each Option shall be the term stated in the Option Agreement; provided, however, that the term shall be no more than ten (10) years from the date of grant thereof.

9. EXERCISE OF OPTION.

(a) Procedure for Exercise; Rights as a Shareholder.

(i) Any Option granted hereunder shall be exercisable at such times and under such conditions as determined by the Board, including performance criteria with respect to the Company and/or the Optionee, and as shall be permissible under the terms of the Plan.

(ii) An Option may not be exercised for a fraction of a Share.

(iii) An Option shall be deemed to be exercised when written notice of such exercise has been given to the Company in accordance with the terms of the Option by the person entitled to exercise the Option and full payment for the Shares with respect to which the Option is exercised has been received by the Company. Full payment may, as authorized by the Board, consist of any consideration and method of payment allowable under Section 7 of, the Plan. Until the issuance (as evidenced by the appropriate entry on the books of the Company or of a duly authorized transfer agent of the Company) of the stock certificate evidencing such Shares no right to vote or receive dividends or any other rights as a shareholder shall exist with respect to the Optioned Stock, notwithstanding the exercise of the Option. The Company shall issue

(or cause to be issued) such stock certificate promptly upon exercise of the Option. No adjustment will be made for a dividend or other right for which the record date is prior to the date the stock certificate is issued, except as provided in Section 12 of the Plan.

(iv) Exercise of an Option in any manner shall result in a decrease in the number of Shares which thereafter may be available, both for purposes of the Plan and for sale under the Option, by the number of Shares as to which the Option is exercised.

(b) Termination of Status as an Employee or Consultant. In the event of termination of an Optionee's Continuous Status as an Employee or Consultant (as the case may be), such Optionee may, but only within such period of time as is determined by the Board, with such determination not exceeding six (6) months after the date of termination, exercise the Option to the extent that such Employee or Consultant was entitled to exercise it at the date of such termination (but in no event later than the date of expiration of the term of such Option as set forth in the Option Agreement). To the extent that such Employee or Consultant was not entitled to exercise the Option at the date of such termination, or if such Employee or Consultant does not exercise such Option (which such Employee or Consultant was entitled to exercise) within the time specified herein, the Option shall terminate.

(c) Disability of Optionee. Notwithstanding the provisions of Section 8(b)(ii) above, in the event of termination of an Optionee's Continuous Status as an Employee or Consultant as a result of such Employee's or Consultant's total and permanent disability (as defined in Section 22(e)(3) of the Code), such Employee or Consultant may, but only within six (6) months (or such other period of time as is determined by the Board) from the date of such termination (but in no event later than the date of expiration of the term of such Option as set forth in the Option Agreement), exercise the Option to the extent the right to exercise would have accrued had the Optionee continued Continuous Status as an Employee or Consultant for a period of six (6) months following termination of Continuous Status by reason of disability. To the extent that such Employee or Consultant was not entitled to exercise an Option in this period, or if such Employee or Consultant does not exercise such Option (which such Employee or Consultant was entitled to exercise) within the time specified herein, the Option shall terminate.

(d) Retirement of Optionee. Notwithstanding the provisions of Section 8(b)(ii) above, in the event of termination of an Employee Optionee's Continuous Status as an Employee as a result of such Employee's retirement from the Company at age fifty five (55) or greater after having Continuous Status for (5) years or more, all Options held by such Optionee shall vest and such Employee may, but only within three (3) years from the date of such termination (but in no event later than the date of expiration of the term of such Option as set forth in the Option Agreement), exercise the Option to the extent such Employee was entitled to exercise it at the date of such termination.

(e) Death of Optionee. In the event of the death of an Optionee:

(i) during the term of the Option who is at the time of his or her death an Employee or Consultant of the Company and who shall have been in Continuous Status as an

Employee or Consultant since the date of grant of the Option, the Option may be exercised, at any time within six (6) months (or at such later time as may be determined by the Board but in no event later than the date of expiration of the term of such Option as set forth in the Option Agreement), by the Optionee's estate or by a person who acquired the right to exercise the Option by bequest or inheritance, but only to the extent that the right to exercise would have accrued had the Optionee continued living and remained in Continuous Status as an Employee or Consultant six (6) months (or such other period of time as in determined by the Board) after the date of death; or

(ii) within thirty (30) days (or such other period of time as is determined by the Board), after the termination of Continuous Status as an Employee or Consultant, the Option may be exercised, at any time within six (6) months (or such other period of time as is determined by the Board at the time of grant of the Option) following the date of death (but in no event later than the date of expiration of the term of such Option as set forth in the Option Agreement), by the Optionee's estate or by a person who acquired the right to exercise the Option by bequest or inheritance, but only to the extent that the right to exercise that had accrued at the date of termination.

10. STOCK PURCHASE RIGHTS.

(a) Rights to Purchase. After the Board of Directors determines that it will offer an Employee or Consultant a Stock Purchase Right, it shall deliver to the offeree a stock purchase agreement or stock bonus agreement, as the case may be, setting forth the terms, conditions and restrictions relating to the offer, including the number of Shares which such person shall be entitled to purchase, and the time within which such person must accept such offer, which shall in no event exceed six (6) months from the date upon which the Board of Directors or its Committee made the determination to grant the Stock Purchase Right. The offer shall be accepted by execution of a stock purchase agreement or stock bonus agreement in the form determined by the Board of Directors.

(b) Issuance of Shares. Forthwith after payment therefor, the Shares purchased shall be duly issued; provided, however, that the Board may require that the Purchaser make adequate provision for any Federal and State withholding obligations of the Company as a condition to the Purchaser purchasing such Shares.

(c) Repurchase Option. Unless the Board determines otherwise, the stock purchase agreement or stock bonus agreement shall grant the Company a repurchase option exercisable upon the voluntary or involuntary termination of the Purchaser's employment with the Company for any reason (including death or disability). If the Board so determines, the purchase price for shares repurchased may be paid by cancellation of any indebtedness of the Purchaser to the Company. The repurchase option shall lapse at such rate as the Board may determine.

(d) Other Provisions. The stock purchase agreement or stock bonus agreement shall contain such other terms, provisions and conditions not inconsistent with the Plan as may be determined by the Board of Directors.

11. NON-TRANSFERABILITY OF OPTIONS AND STOCK PURCHASE RIGHTS. Unless determined otherwise by the Administrator, an Option or Stock Purchase Right may not be sold, pledged, assigned, hypothecated, transferred, or disposed of in any manner other than by will or by the laws of descent or distribution and may be exercised, during the lifetime of the Optionee, only by the Optionee. If the Administrator makes an Option or Stock Purchase Right transferable, such Option or Stock Purchase Right shall contain such additional terms and conditions as the Administrator deems appropriate.

12. ADJUSTMENTS UPON CHANGES IN CAPITALIZATION OR MERGER.

(a) Changes in Capitalization. Subject to any required action by the shareholders of the Company, the number of shares of Common Stock covered by each outstanding Option or Stock Purchase Right, and the number of shares of Common Stock which have been authorized for issuance under the Plan but as to which no Options or Stock Purchase Rights have yet been granted or which have been returned to the Plan upon cancellation or expiration of an Option or Stock Purchase Right, as well as the price per share of Common Stock covered by each such outstanding Option or Stock Purchase Right, shall be proportionately adjusted for any increase or decrease in the number of issued shares of Common Stock resulting from a stock split, reverse stock split, stock dividend, combination or reclassification of the Common Stock, or any other increase or decrease in the number of issued shares of Common Stock effected without receipt of consideration by the Company. The conversion of any convertible securities of the Company shall not be deemed to have been "effected without receipt of consideration." Such adjustment shall be made by the Board, whose determination in that respect shall be final, binding and conclusive. Except as expressly provided herein, no issuance by the Company of shares of stock of any class, or securities convertible into shares of stock of any class, shall affect, and no adjustment by reason thereof shall be made with respect to, the number or price of shares of Common Stock subject to an Option or Stock Purchase Right.

(b) Dissolution or Liquidation. In the event of the proposed dissolution or liquidation of the Company, the Administrator shall notify the Optionee or Purchaser at least fifteen (15) days prior to such proposed action. To the extent it has not been previously exercised, the Option or Stock Purchase Right shall terminate immediately prior to the consummation of such proposed action.

(c) Merger or Asset Sale. In the event of a merger, sale of all or substantially all of the assets of the Company, tender offer or other transaction or series of related transactions resulting in a change of ownership of more than fifty percent (50%) of the voting securities of the Company ("Change in Control"), approved by the majority of the members of the Board on the Board prior to the commencement of such Change in Control, each outstanding Option shall be assumed or an equivalent option or right substituted by the successor corporation or a Parent or Subsidiary of the successor corporation; provided however, in the event that within one year of the date of the completion of the Change in Control, the successor corporation or a Parent or Subsidiary of the successor corporation terminates the employment of an Optionee without Cause (as defined below), such Optionee shall fully vest in and have the right to exercise the options assumed or substituted for the Option as to all of the Optioned Stock, including Shares as to which it would not otherwise be exercisable. In the event that the successor corporation refuses to assume or substitute for the Option, the Optionee shall fully vest in and have the right to exercise the Option as to all of the

Optioned Stock, including Shares as to which it would not otherwise be exercisable. If an Option becomes fully vested and exercisable in lieu of assumption or substitution in the event of a Change of Control, the Administrator shall notify the Optionee in writing or electronically that the Option shall be fully vested and exercisable for a period of fifteen (15) days from the date of such notice, and the Option shall terminate upon the expiration of such period. For the purposes of this paragraph, the Option shall be considered assumed if, following the Change of Control, the option confers the right to purchase, for each Share of Optioned Stock subject to the Option immediately prior to the Change in Control, the consideration (whether stock, cash, or other securities or property) received in the Change of Control by holders of Common Stock for each Share held on the effective date of the transaction (and if holders were offered a choice of consideration, the type of consideration chosen by the holders of a majority of the outstanding Shares); provided, however, that if such consideration received in the Change of Control is not solely common stock of the successor corporation or its Parent, the Administrator may, with the consent of the successor corporation, provide for the consideration to be received upon the exercise of the Option, for each Share of Optioned Stock subject to the Option, to be solely common stock of the successor corporation or its Parent equal in fair market value to the per share consideration received by holders of Common Stock in the Change of Control. For purposes of this paragraph, termination shall be for "Cause" in the event of the occurrence of any of the following: (a) any intentional action or intentional failure to act by employee which was performed in bad faith and to the material detriment of the successor corporation or its Parent or Subsidiary; (b) employee willfully and habitually neglects the duties of employment; or (c) employee is convicted of a felony crime involving moral turpitude, provided that in the event that any of the foregoing events is capable of being cured, the successor corporation or its Parent or Subsidiary shall provide written notice to the employee describing the nature of such event and the employee shall thereafter have five (5) business days to cure such event.

In the event of a Change in Control which is not approved by the majority of the members of the Board on the Board prior to the commencement of a Change in Control, each Optionee shall fully vest in and have the right to exercise all outstanding Options as to all of the Optioned Stock, including Shares as to which it would not otherwise be exercisable.

13. DATE OF GRANTING OPTIONS. The date of grant of an Option or Stock Purchase Right shall, for all purposes, be the date on which the Board makes the determination granting such Option or stock Purchase Right. Notice of the determination shall be given to each Employee or Consultant to whom an Option or Stock Purchase Right is so granted within a reasonable time after the date of such grant.

14. AMENDMENT AND TERMINATION OF THE PLAN.

(a) Amendment and Termination. The Administrator may at any time amend, alter, suspend or discontinue the Plan, but no amendment, alteration, suspension or discontinuation shall be made which would impair the rights of any Optionee under any grant theretofore made, without his or her consent. In addition, to the extent necessary and desirable to comply with Section 422 of the Code (or any other applicable laws or regulation, the requirements of the NASD or an established Stock exchange), the Company shall obtain shareholder approval of any Plan amendment in such a manner and to such a degree as required.



(b) Effect of Amendment or Termination. Any such amendment or termination of the Plan shall not affect Options or Stock Purchase Rights already granted, and such Options and Stock Purchase Rights shall remain in full force and effect as if this Plan had not been amended or terminated, unless mutually agreed otherwise between the Optionee and the Administrator, which agreement must be in writing and signed by the Optionee and the Company.

15. CONDITIONS UPON ISSUANCE OF SHARES. Shares shall not be issued pursuant to the exercise of an Option or Stock Purchase Rights unless the exercise of such Option or Stock Purchase Rights and the issuance and delivery of such Shares pursuant thereto shall comply with all relevant provisions of law, including, without limitation, the Securities Act of 1933, as amended, the Exchange Act, the rules and regulations promulgated thereunder, and the requirements of any stock exchange upon which the Shares may then be listed, and shall be further subject to the approval of counsel for the Company with respect to such compliance.

As a condition to the exercise of an Option or Stock Purchase Right, the Company may require the person exercising such Option or Stock Purchase Right to represent and warrant at the time of any such exercise that the Shares are being purchased only for investment and without any present intention to sell or distribute such Shares if, in the opinion of counsel for the Company, such a representation is required by any of the aforementioned relevant provisions of law.

16. RESERVATION OF SHARES. The Company, during the term of this Plan, will at all times reserve and keep available such number of Shares as shall be sufficient to satisfy the requirements of the Plan. The inability of the Company to obtain authority from any regulatory body having jurisdiction, which authority is deemed by the Company's counsel to be necessary to the lawful issuance and sale of any Shares hereunder, shall relieve the Company of any liability in respect of the failure to issue or sell such Shares as to which such requisite authority shall not have been obtained.

17. OPTION, STOCK PURCHASE AND STOCK BONUS AGREEMENTS. Options shall be evidenced by written option agreements in such form as the Board shall approve. Upon the exercise of Stock Purchase Rights, the Purchaser shall sign a stock purchase agreement or stock bonus agreement in such form as the Board shall approve.

18. INFORMATION TO OPTIONEES AND PURCHASERS. The Company shall provide to each Optionee and Purchaser, during the period for which such Optionee or Purchaser has one or more Options to Stock Purchase Rights outstanding, a balance sheet and an income statement at least annually. The Company shall not be required to provide such information to key employees whose duties in connection with the Company assure them access to equivalent information.

## NEUROCRINE BIOSCIENCES, INC.

## NON-QUALIFIED DEFERRED COMPENSATION PLAN

Restatement effective as of February 22, 2000

Neurocrine Biosciences, Inc. (the "Company") maintains the Neurocrine Biosciences, Inc. Nonqualified Deferred Compensation Plan (the "Plan"), consisting of the following provisions, for the exclusive benefit of the participants and their beneficiaries (and to defray reasonable administrative expenses thereunder). The Plan was originally established effective as of December 1, 1996. Effective as of February 22, 2000 (the "Effective Date"), except as otherwise stated herein, the Company hereby amends and restates the Plan. Throughout, the term "Company" shall include wherever relevant any entity that is directly or indirectly controlled by the Company, any entity in which the Company has a significant equity or investment interest, or any subsidiary of the Company, as determined by the Committee.

## RECITALS

1. The Company wishes to continue to maintain a supplemental retirement plan for the benefit of its Board of Directors and a select group of management or highly compensated employees of the Company.
2. The Company wishes to provide that the supplemental retirement plan, as restated, shall continue to be designated the Neurocrine Biosciences, Inc. Nonqualified Deferred Compensation Plan.
3. The Company wishes to provide under the Plan for the payment of accrued vested benefits to Plan participants and their beneficiaries.
4. Under the Plan, the Company is obligated to pay vested accrued benefits to the Plan participants and their beneficiaries from the Company's general assets.
5. The Company has entered into an agreement (the "Trust Agreement") appointing a trustee (the "Trustee") under an irrevocable trust (the "Trust") to be used in connection with the Plan.
6. The Company intends to make contributions to the Trust so that such contributions will be held by the Trustee and invested, reinvested and distributed, all in accordance with the provisions of the Plan and the Trust Agreement.
7. The Company intends that amounts contributed to the Trust and the income thereon shall be used by the Trustee to satisfy the liabilities of the Company under the Plan with respect to each Plan participant for whom an Account has been established and such utilization shall be in accordance with the procedures set forth herein.

8. The Company intends that the Trust be a "grantor trust" with the principal and income of the Trust treated as assets and income of the Company for Federal and state income tax purposes.

9. The Company intends that the assets of the Trust shall at all times be subject to the claims of the general creditors of the Company, as provided in the Trust Agreement.

10. The Company intends that the existence of the Trust shall not alter the characterization of the Plan as "unfunded" for purposes of the Employee Retirement Income Security Act of 1974, as amended ("ERISA"), and shall not be construed to provide income to Plan participants under the Plan prior to actual payment of the vested accrued benefits thereunder.

NOW THEREFORE, the Company hereby establishes the Plan as follows:

SECTION 1. TITLE.

This Plan shall be known as the Neurocrine Biosciences, Inc. Nonqualified Deferred Compensation Plan.

SECTION 2. DEFINITIONS.

(a) "Account(s)" means the Deferred Compensation Account, the Supplemental Contributions Account and/or the Matching Contributions Account, as the context requires.

(b) "Bonus" means any special and/or discretionary cash compensation amounts in excess of Salary, determined by the Company to be payable to a Participant with respect to services rendered.

(c) "Change of Control" means and shall be deemed to have occurred if NBI is acquired by another entity, which shall be defined herein as the merger of NBI with or into an acquiring entity, with NBI not surviving the merger; the sale of substantially all of NBI's assets; the acquisition of more than twenty-percent (20%) of NBI's outstanding common stock or other equity interest by an entity; the cash balance or asset balance of NBI becomes less than twenty million dollars (\$20 million); or any other change of control of NBI.

(d) "Committee" means the Compensation Committee of the Company's Board of Directors.

(e) "Company" means Neurocrine Biosciences, Inc.

(f) "Continuous Service" means a Participant's uninterrupted services with the Company or any affiliate after the effective date of the Plan. Service shall not be deemed interrupted by a leave of absence authorized by the Committee, an absence due to mandatory military service or an absence due to disability while the Participant is receiving benefits under any short-term or long-term disability plan or arrangement maintained or sponsored by the Company.

- (g) "Deferred Compensation" means the sum of Salary and Bonus that are the subject of an elective deferral under Section 4.
- (h) "Deferred Compensation Account" means the bookkeeping account established for a Participant under the Plan and to which Deferred Compensation amounts with respect to such Participant are credited from time to time, as adjusted from time to time as provided in the Plan.
- (i) "Deferred Compensation Election Form" means the form pursuant to which Eligible Executives elect to become Participants in the Plan and defer compensation thereunder, in such form as the Committee determines from time to time in its sole discretion.
- (j) "Disability" means mental or physical disability as determined by the Committee in accordance with standards and procedures similar to those under the Company's broad-based regular long-term disability plan, if any. At any time that the Company does not maintain such a long-term disability plan, Disability shall mean the inability of a Participant, as determined by the Committee, substantially to perform such Participant's regular duties and responsibilities due to a medically determinable physical or mental illness which has lasted (or can reasonably be expected to last) for a period of six (6) consecutive months.
- (k) "Eligible Executive" means any member of the Board of Directors and any employee of the Company who is selected for participation by the Committee.
- (l) "Matching Contributions Account" means the bookkeeping account established for a Participant under the Plan and to which the Company's matching contributions under Section 4(b) of the Plan are credited from time to time, as adjusted from time to time under the Plan.
- (m) "NBI" means Neurocrine Biosciences, Inc.
- (n) "Participant" means an Eligible Executive who has elected to defer Salary and/or Bonus amounts pursuant to the Plan.
- (o) "Plan" means Neurocrine Biosciences, Inc. Nonqualified Deferred Compensation Plan for Executives, as set forth herein and as amended from time to time.
- (p) "Plan Year" means the calendar year, except for the first Plan Year which shall be (i) from December 1, 1996 through December 31, 1996 in the case of employee Eligible Executives and (ii) March 15, 2000 through December 31, 2000 in the case of members of the Company's Board of Directors who are Eligible Executives.
- (q) "Retirement" means termination of services to the Company at any time on or after the attainment of age 60.

(r) "Salary" means the regular base compensation paid by the Company to a member of the Board of Directors or to an employee (without regard to any reduction thereof pursuant to the Plan or any thrift or savings plan maintained by the Company), exclusive of Bonus payments and any other incentive payments made by the Company to such member of the Board of Directors or employee.

(s) "Supplemental Contributions Account" means the bookkeeping account established for the Participant under the Plan and to which the Company's supplemental contributions under Section 4(c) of the Plan are credited from time to time, as adjusted from time to time under the Plan.

(t) "Unforeseeable Emergency" means a severe financial hardship to the Participant resulting from a sudden and unexpected illness or accident of the Participant or a dependent of the Participant, loss of the Participant's property due to casualty, or other similar extraordinary unforeseeable circumstances arising as a result of events beyond the control of the Participant.

SECTION 2. ELIGIBILITY. Individuals eligible to participate in the Plan shall consist of the Eligible Executives of the Company.

SECTION 3. ADMINISTRATION.

(a) The Plan shall be administered by the Committee. The Committee is authorized to construe and interpret the Plan and promulgate, amend and rescind rules and regulations relating to the implementation, administration and maintenance of the Plan. Subject to the terms and conditions of the Plan, the Committee shall make all determinations necessary or advisable for the implementation, administration and maintenance of the Plan including, without limitation, determining the Eligible Employees and correcting any technical defect(s) or technical omission(s), or reconciling any technical inconsistency (ies), in the Plan. The Committee may designate persons other than members of the Committee to carry out the day-to-day ministerial administration of the Plan under such conditions and limitations as it may prescribe; provided, however, that the Committee shall not delegate its authority with regard to the determination of Eligible Employees. The Committee's determinations under the Plan need not be uniform and may be made selectively among Participants, whether or not such Participants are similarly situated. Any determination, decision or action of the Committee in connection with the construction, interpretation, administration, implementation or maintenance of the Plan shall be final, conclusive and binding upon all Participants and any person(s) claiming under or through any Participants.

(b) The Company will indemnify and hold harmless the Committee and each member thereof against any cost or expense (including without limitation attorney's fees) or liability (including without limitation any sum paid in settlement of a claim with the approval of the Company) arising out of any act or omission to act, except in the case of willful gross misconduct or gross negligence.

SECTION 4.

PARTICIPATION; ELECTIVE DEFERRALS; MATCHING CONTRIBUTIONS.

(a) To elect to participate in the Plan for a particular Plan Year, an Eligible Executive must execute a Deferred Compensation Election Form and file such form with the Committee (or its designee) before the commencement of such Plan Year. To participate in the Plan during the year in which the Plan is first implemented, the Eligible Executive must make an election to defer Salary compensation for services to be performed subsequent to the election and/or to defer Bonus compensation, in each case, within 30 days after the effective date of the Plan. To participate in the Plan during the first year in which an individual becomes eligible to participate in the Plan, the new Eligible Executive must make an election to defer Salary compensation for services to be performed subsequent to the election and/or to defer Bonus compensation, in each case, within 30 days after the date the new Eligible Executive becomes eligible. Such election shall:

- (i) contain a statement that the Eligible Executive elects to defer a portion of the Eligible Executive's Salary (up to one hundred percent (100%) thereof, in increments of one-percent (1%)) and/or Bonus (up to 100% thereof, in increments of one-percent (1%)) for a specified Plan Year that becomes payable to the Eligible Executive after the filing of such;
- (ii) apply only to the Salary otherwise payable to the Eligible Executive during the Plan Year for which such election is made and to any Bonus payment that is attributable to the Eligible Executive's services rendered to the Company during the Plan Year for which such election is made (whether or not actually payable in such Plan Year); and
- (iii) be irrevocable with respect to the Plan Year to which it applies.

Upon receipt of an Eligible Executive's deferral election, the Company shall establish as an accounting entry an individual Deferred Compensation Account for such Eligible Executive and such Eligible Executive shall become a Participant under the Plan. Thereafter, the Company shall credit the Executive's Deferred Compensation Account with all Deferred Compensation which would otherwise have been payable to the Eligible Executive in the absence of an election under the Plan. The Deferred Compensation Account shall be credited no less frequently than the first day of each month in an amount equal to the sum of the Deferred Compensation that would otherwise have been paid by the Company in accordance with the Company's normal payroll practices for the immediately preceding month.

(b) At the beginning of each month, the Company may, in its sole discretion, if on the first day of any such month the Participant is employed by the Company, credit matching contributions to the Participant's Matching Contributions Account.

(c) From time to time, the Company may, in its sole discretion, credit Supplemental Contributions to the Participant's Supplemental and Matching Contributions Account in such amounts as the Company shall determine in its sole discretion.

SECTION 5. PAYMENT OF DEFERRED COMPENSATION. The vested accrued balances in a Participant's Account shall be paid to a Participant, or, in the case of any Participant's death prior to payment, the Participant's designated beneficiary (ies), in cash in one lump sum or annually up to fifteen (15) years no later than fifteen (15) business days after the end of the month in which the termination of the Participant's services to the Company occurs. Such election shall be made at the time of deferral and may be changed at any time prior to the Participant's termination of services to the Company as long as it is made twelve (12) months prior to Retirement if the Participant's termination of services to the Company is due to the Participant's Retirement from the Company.

SECTION 6. INVESTMENT OF ACCOUNT BALANCES. During and for each Plan Year, the accrued balances in each Deferred Compensation Account, Supplemental Contributions Account and Matching Contributions Account will be deemed to be invested, as of the first day of the month immediately succeeding the month in which elective deferrals, supplemental contributions and matching contributions are credited to their respective Accounts under the Plan, in one or a combination of more than one of the following investments; (a) Company's common stock including dividends; (b) mutual funds available under the Company's 401(k) savings plan; (c) guaranteed account (six percent (6%) annual appreciation compounded monthly). At the end of each Plan Year, the Accounts shall be adjusted and increased by the results of such deemed investment for such Plan Year pursuant to Section 7 below and such adjusted Account balances shall then be reinvested for the immediately succeeding Plan Year.

SECTION 7. VALUATION. At the end of each Plan Year, the vested and unvested balances in the Account of each Participant shall be determined by the Company, taking into account any increase therein for such Plan Year under Section 6. The balance determined, as of the end of each Plan Year, shall be communicated in writing to each Participant as soon as practicable after the end of the Plan Year. In the case of any termination under Section 5 above, the vested and unvested balances in the Account of any affected Participant shall be determined by the Company as of the end of the date in which occurs any such termination, also taking into account any increase therein for such Plan Year to date under Section 6.

SECTION 8. DISTRIBUTION IN CASES OF HARDSHIP. The Committee may make distributions to a Participant from the vested balances in such Participant's Deferred Compensation Account, Supplemental Contributions Account or Matching Contributions Account upon a showing by such Participant that an Unforeseeable Emergency has occurred. Such distributions shall be limited to the amount shown to be necessary to meet the Unforeseeable Emergency.

SECTION 9. VESTING. Notwithstanding anything contained herein to the contrary, a Participant's accrued balance in such Participant's Deferred Compensation Account (and the amounts payable with respect thereto) shall be fully vested at all times. A Participant's accrued balance in such Participant's Matching Contributions Account (and the amounts payable with respect thereto) and in such Participant's Supplemental Contributions Account (and the amounts payable with respect thereto) shall, in each case, be vested in twenty-five percent (25%) increments for each of the first four (4) years of a Participant's uninterrupted service with the Company commencing on the last date

of hire. Notwithstanding the immediately preceding sentence, if (a) the Participant dies, (b) the Participant's services to the Company is terminated due to Disability or (c) a Change of Control occurs, such Participant's accrued balance in the Matching Contributions Account and Supplemental Contributions Account shall be fully vested as of the date of death, the date of such termination or the date of any such Change of Control, as the case may be.

SECTION 10. FORFEITURE. If a Participant's services to the Company are terminated for any reason (other than death) prior to such Participant's vesting under Section 9, such unvested Participant's accrued balance in such Participant's Matching Contributions Accounts (and the amounts payable with respect thereto) and in such Participant's Supplemental Contributions Account (and the amounts payable with respect thereto) shall, in each case, be forfeited by such Participant.

SECTION 11. AMENDMENT. The Plan may be amended, modified or terminated at any time by the Committee except that no such amendment, modification or termination shall have a material adverse effect on the accrued balance of any Participant's Deferred Compensation Account, Supplemental Contributions Account and/or Matching Contributions Account as of the effective date of any such amendment, modification or termination (without the consent of the Participant (or, if the Participant is dead, his or her beneficiary (ies))).

SECTION 12. PARTICIPANT'S RIGHT UNSECURED; NO DUTY TO INVEST. The right of a Participant to receive any distribution hereunder shall be an unsecured claim against the general assets of the Company. No Company assets shall in any way be subject to any prior claim by any Participant. The Company shall have no duty whatsoever to set aside or invest any amounts credited to any Deferred Compensation Account, Supplemental Contributions Account or Matching Contributions Account established under the Plan. Nothing in the Plan shall confer upon any Eligible Executive of the Company any right to continued employment by the Company, nor shall it interfere in any way with the right, if any, of the Company to terminate the employment of any Eligible Executive at any time for any reason. A Participant shall have no right, title, or interest whatsoever in or to any specific assets of the Company, nor any investments, if any, which the Company may make to aid it in meeting its obligations hereunder. Nothing contained in this Plan, and no action taken pursuant to its provisions, shall create or be construed to create a trust of any kind, or a fiduciary relationship, between the Company and any Participant or any other person. The Company may enter into a "rabbi" trust agreement to provide for a source of funds out of which all or any portion of the benefits under the Plan may be satisfied.

SECTION 13. RESTRICTIONS ON ALIENATION. No amount deferred or credited to any Account under the Plan shall be subject in any manner to anticipation, alienation, sale, transfer, assignment, pledge, encumbrance, levy or charge. Any attempt to so anticipate, alienate, sell, transfer, assign, pledge, encumber, levy or charge the same shall be void; nor shall any amount be in any manner be subject to any claims for the debts, contracts, liabilities, engagements or torts of the Participant (or the Participant's beneficiary or personal representative) entitled to such benefit. No Participant shall be entitled to borrow at any time any portion of the Participant's Account balances under the Plan.



SECTION 14. WITHHOLDING. There shall be deducted from all payments under the Plan the amount of any taxes required to be withheld by any Federal, state or local government. The Participants, their beneficiaries and personal representatives shall bear any and all Federal, foreign, state, local, income, or other taxes imposed on amounts paid under the Plan.

SECTION 15. PARTICIPANTS BOUND BY TERMS OF THE PLAN. By electing to become a Participant, each Eligible Executive shall be deemed conclusively to have accepted and consented to all terms of the Plan and all actions or decisions made by the Company with regard to the Plan. Such terms and consent shall also apply to and be binding upon the beneficiaries, personal representatives and other successors in interest of each Participant. Each Participant shall receive a copy of the Plan.

SECTION 16. DESIGNATION OF BENEFICIARY (IES). Each Participant under the Plan may designate a beneficiary or beneficiaries to receive any payment which under the terms of the Plan becomes payable on, after or as a result of the Participant's death. At any time, and from time to time, any such designation may be changed or canceled by the Participant without the consent of any such beneficiary. Any such designation, change or cancellation must be on a form provided for that purpose by the Committee and shall not be effective until received by the Committee. If no beneficiary has been designated by a deceased Participant, the beneficiary shall be the Participant's estate. If the Participant designates more than one beneficiary, any payments under the Plan to such beneficiaries shall be made in equal shares unless the Participant has expressly designated otherwise, in which case the payments shall be made in the shares designated by the Participant.

SECTION 17. SEVERABILITY OF PROVISIONS. In the event any provision of the Plan would serve to invalidate the Plan, that provision shall be deemed to be null and void, and the Plan shall be construed as if it did not contain the particular provision that would make it invalid. The Plan shall be binding upon and inure to the benefit of (a) the Company and its respective successors and assigns, and (b) each Participant, his or her designees and estate. Nothing in the Plan shall preclude the Company from consolidating or merging into or with, or transferring all or substantially all of its assets to, another corporation, or engaging in any other corporate transaction.

SECTION 18. GOVERNING LAW AND INTERPRETATION. The Plan shall be construed and enforced in accordance with, and the rights of the parties hereto shall be governed by, the laws of the state of California. This Plan shall not be interpreted as either an employment or trust agreement.

SECTION 19. OTHER COMPANY BENEFIT AND COMPENSATION PROGRAMS. Payments and other benefits received by a Participant under the Plan shall not be deemed a part of a Participant's compensation for purposes of the determination of benefits under any other employee welfare or benefit plans or arrangements, if any, provided by the Company or any affiliate of the Company. The existence of the Plan notwithstanding, the Company may adopt such other compensation plans or programs and additional compensation arrangements as it deems necessary to attract, retain and motivate employees. The Committee is authorized to cause to be established a trust agreement or several trust agreements or similar arrangements from which the Committee may make payments of amounts due or to become due to any Participants under the Plan.

SECTION 20. ARBITRATION. Except as otherwise provided in this Plan, any controversy between the parties arising out of this Plan shall be submitted to the American Arbitration Association for arbitration in San Diego, California. The costs of the arbitration, including any American Arbitration Association administration fee, the arbitrator's fee, and costs for the use of facilities during the hearings, shall be borne equally by the parties to the arbitration. Attorneys' fees may be awarded to the prevailing or most prevailing party at the discretion of the arbitrator. The provisions of Sections 1282.6, 1283, and 1283.05 of the California Code of Civil Procedure shall apply to the arbitration. The arbitrator shall not have any power to alter, amend, modify or change any of the terms of this Plan nor to grant any remedy which is either prohibited by the terms of this Plan, or not available in a court of law.

SECTION 21. EFFECTIVE DATE OF THE PLAN. The Plan shall be restated effective as of February 22, 2000 upon its adoption by the Company.

IN WITNESS WHEREOF, the restated Plan is hereby adopted by the Company on this 22 day of February, 2000.

Neurocrine Biosciences, Inc.

By: /s/ Paul W. Hawran  
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CONSENT OF ERNST & YOUNG LLP, INDEPENDENT AUDITORS

We consent to the incorporation by reference in the Registration Statements (Form S-3 No. 333-73216) and (Form S-8 Nos. 333-101756, 333-92328, 333-65198, 333-57096, 333-44012, 333-87127, 333-57875) of our report dated January 24, 2003, with respect to the financial statements of Neurocrine Biosciences, Inc. included in the Annual Report (Form 10-K) for the year ended December 31, 2002.

/s/ Ernst & Young LLP

San Diego, California  
March 4, 2003