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SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

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FORM 10-K  
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(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, 2001

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

33-0525145

(State or other jurisdiction

(I.R.S. Employer

of incorporation or organization)

Identification Number)

10555 Science Center Drive, San Diego, CA

92121

(Address of principal executive office)

(Zip Code)

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

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

registered pursuant to Section 12(g) of the Act: Common Stock, \$0.001 par value

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 [X] 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. [ ]

The aggregate market value of the voting stock held by non-affiliates of the Registrant as of March 15, 2002 totaled approximately \$1,102,649 based on the closing stock price as reported by the Nasdaq National Market. As of March 15, 2002, there were 30,399,620 shares of the Registrant's Common Stock, \$0.001 par value per share, outstanding.

DOCUMENTS INCORPORATED BY REFERENCE

Certain information required by Part III of Form 10-K is incorporated by reference from the Registrant's Proxy Statement for the Annual Meeting of Stockholders to be held on May 23, 2002 (the "Proxy Statement"), which will be filed with the Securities and Exchange Commission within 120 days after the close of the Registrant's fiscal year ended December 31, 2001.

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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, cancer, diabetes and multiple sclerosis. We currently have 15 programs in various stages of research and development, including seven programs in clinical development. Our lead clinical development program is a 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 five of our 15 programs. We currently have active collaborations with GlaxoSmithKline, Wyeth-Ayerst Laboratories (Wyeth-Ayerst), a division of American Home Products and Taisho Pharmaceutical Co., Ltd. (Taisho).

Our Product Pipeline

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

Program	Compound	Targeted Indication	Status	Commercial Rights
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PRODUCTS UNDER DEVELOPMENT:

GABA-A Agonist	NBI-34060	Insomnia	Phase III	Neurocrine
CRF R1 Antagonist	NBI-34041	Anxiety, Depression	Phase I	GlaxoSmithKline/Neurocrine
IL-4 Fusion Toxin	NBI-3001	Malignant Glioma	Phase II	Neurocrine
IL-4 Fusion Toxin	NBI-3001	Additional Cancers (kidney, lung, breast)	Phase I	Neurocrine
Altered Peptide Ligand	NBI-5788	Multiple Sclerosis	Phase II	Neurocrine



GnRH Antagonist	Endometriosis, Prostate Cancer	Phase I	Neurocrine
RESEARCH:			
Excitatory Amino Acid Transporters	Neurodegenerative Diseases	Research	Wyeth-Ayerst/Neurocrine
CRF R1 Antagonist	Gastrointestinal Disorders	Research	GlaxoSmithKline/Neurocrine
CRF R2 Antagonist	Eating Disorders	Research	GlaxoSmithKline/Neurocrine
Urocortin/CRF R2 Agonist	Obesity	Research	Eli Lilly/Neurocrine
Melanocortin Receptor Agonist/Antagonist	Obesity/cachexia	Research	Neurocrine
Melanin Concentrating Hormone Antagonist	Obesity	Research	Neurocrine
Hypocretin Agonist/Antagonist	Sleep Disorders	Research	Neurocrine
CCR7	Immune/Cancer	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 the 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.

"Research" indicates identification and evaluation of compounds in laboratory and pre-clinical models.

"R1 and R2" refer to two CRF receptor subtypes.

## Products under Development

### GABA-A Agonist

Insomnia is a prevalent neurological disorder in the United States, with approximately one-half of the adult population reporting trouble sleeping a few nights per week or more, according to the National Sleep Foundation. Additionally, the National Sleep Foundation reported that approximately 29% of the adult population indicated that they experience insomnia every night or almost every night. It is also estimated that the elderly comprise 13% of the total insomnia population. Despite this widespread prevalence, insomnia remains a disorder with high unmet medical needs, including the ability to maintain 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, or GABA, and the site of action is called the GABA-A receptor.

During the 1980s, a class of drugs that targets the GABA-A receptor, known as benzodiazepines, were used as sedatives to treat insomnia. The most well-known of the benzodiazepines is Valium(copyright). This class of drugs produced several undesirable side effects, including negative interactions with other central nervous system depressants, such as alcohol, the development of tolerance upon repeat dosing, insomnia following discontinuation of dosing, 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 whose cognitive function may already be impaired by the aging process. 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 reduce the side effects associated with benzodiazepines. The most popular of the non-benzodiazepines are marketed in the U.S. as Ambien(copyright) and Sonata(copyright). Ambien(copyright) is the current leader, with approximately \$1.0 billion in worldwide sales in 2001, according Sanofi-Synthelabo.



Our drug candidate for the treatment of insomnia, NBI-34060, a non-benzodiazepine, acts on a specific site on the GABA-A receptor. It is through this mechanism that the currently marketed non-benzodiazepine therapeutics also produce their sleep-promoting effects. However, NBI-34060 is more potent than the currently marketed non-benzodiazepines, including Ambien(copyright) and Sonata(copyright), and is more selective for the specific subtype of receptors within the brain believed to be responsible for promoting sleep. We believe that this improved profile and more selective drug targeting will reduce the side effects characteristic of the currently marketed products. We also believe that receptor binding studies and pre-clinical studies on NBI-34060 indicate that it is a highly potent GABA-A receptor activator, or agonist, that acts very specifically on the receptor subtype we are targeting. In our Phase II clinical studies, NBI-34060 was devoid of next day residual sedation effects, and we expect it to have a considerably reduced amnestic potential. The elderly population, which represents a large portion of the insomnia market, would benefit especially from a novel therapeutic with an improved safety profile, rapidity of onset and decrease in memory impairment.

We are developing two formulations of NBI-34060, 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 NBI-34060, its relatively short half-life, or duration of action of the compound, in the body. Based on our clinical studies, we have determined that the levels of NBI-34060 in the bloodstream reach the highest point approximately 30 minutes after the patient takes the tablet. NBI-34060 is then rapidly removed from the blood stream to the point that it cannot be detected four hours later. This rapid peak of drug results in rapid sleep onset followed by rapid removal of the drug from the body, reducing the risk of next-day effects. We believe that this short duration of action will allow for bedtime dosing for people who have trouble falling asleep and dosing in the middle of the night for people who have trouble staying asleep without causing the side effects and next day residual sedation effects that occurs with the longer acting drugs like Ambien(copyright). This short duration of action has allowed us to formulate the drug in a modified release form that will effectively provide two doses of drug, a bedtime dose and a middle of the night dose, which will both rapidly induce sleep and maintain sleep through the night. If successful, this would represent the first non-benzodiazepine approved by the United States Food and Drug Administration (FDA) for maintaining, rather than simply inducing, sleep.

We have completed 25 Phase I and Phase II clinical trials of NBI-34060

for safety and efficacy involving approximately 1,300 subjects. In our Phase II clinical studies, NBI-34060 has been 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 NBI-34060, 10 mg Ambien(copyright) 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 NBI-34060 does not lead to next day residual sedation effects, while both Ambien(copyright) 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 NBI-34060 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 659 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 NBI-34060 compared to Ambien(copyright) and 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. Based on these results, we have initiated Phase III clinical development to support marketing registration. Our Phase III program will involve approximately 3,300 additional subjects in eight large clinical trials. Our first Phase III clinical trial of NBI-34060, commenced in November 2001, will involve approximately 500 patients to evaluate two doses of an immediate release formulation of NBI-34060 for long-term use in patients with chronic insomnia.

We face the risk that the side effects and efficacy profile of NBI-34060 seen in our Phase I and II trials may not be confirmed in additional clinical trials or that the results of future trials may not warrant further trials.

#### Corticotropin-Releasing Factor

According to the Surgeon General's 1999 Report on Mental Health, 6.5% of the U.S. adult population experiences a major depressive episode each year and 16.4% of the U.S. adult population has an anxiety disorder. Existing anti-depressant and anti-anxiety therapeutics sold in excess of \$11.7 billion worldwide in 2000, 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 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 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 R1 and CRF R2, 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 Prozac(copyright), Zoloft(copyright), Paxil(copyright) and Celexa(copyright) 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. Results from this trial 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 by our collaborator Janssen Pharmaceutica N.V. (Janssen), we continue to be strongly encouraged by these results, which we believe support the hypothesized mechanism of action.

Our initial CRF antagonist clinical studies were conducted pursuant to our two collaborations with Janssen. Our first collaboration was in 1995 and led to the development of NBI-30775. While NBI-30775 appeared to be safe in Janssen's clinical studies (including the Phase IIa proof of concept study described above), reversible increases in liver enzymes occurred in two volunteers in an expanded safety study. As a result, Janssen announced its decision to discontinue development of NBI-30775. While all collaborative work under the Janssen agreement was completed in 1998, because of the positive efficacy results for NBI-30775, Janssen decided to proceed with a back-up compound identified from the collaborative Janssen/Neurocrine patent portfolio and funded certain additional work at Neurocrine to identify additional first generation back-up compounds to NBI-30775 from the same chemical series. This work was completed in February 2001. Our back-up program agreement provides that in August 2001 Neurocrine was to receive either a \$3.5 million milestone payment from Janssen or exclusive rights to the first generation back-up compounds. We agreed to postpone the August event to allow Janssen to complete certain studies with the back-up program compounds. 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. We do not expect any additional payments of any kind under the Janssen agreements.

In 1998, we announced that we had initiated a proprietary CRF R1 antagonist program independent of Janssen. This program led to the discovery of a novel class of second generation CRF R1 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 R1 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. The future development of this product candidate will be directed by a joint steering committee of Neurocrine and GSK and will take into account data from this study.

We face the risk that CRF R1 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 II clinical testing 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. The Surgeon General's 1999 Report on Mental Health estimates that anxiety disorders affect 16.4% of the U.S. adult population. Of the pharmaceutical agents that other companies currently market for the treatment of anxiety disorders, benzodiazepines, such as Valium(copyright) and Xanax(copyright), and the anxiolytic BuSpar(copyright) 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. Despite the undesirable side effects of the benzodiazepines and the delayed time-of-onset of BuSpar(copyright), these market leaders collectively achieved approximately \$1.5 billion worldwide in revenues in the year 2000, according to Med Ad News. In view of significant evidence implicating CRF in anxiety-related disorders, we are developing small molecule CRF R1 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 open label Phase IIa clinical trial for depression described above, Janssen analyzed the anti-anxiety effects of the CRF R1 receptor antagonist NBI-30775 using the Hamilton Anxiety Scores. Janssen observed 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 candidates from our independent CRF R1 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 R1 receptor may be effective in treating anxiety-related disorders. Despite these early results, further clinical studies may fail to demonstrate that CRF R1 antagonists are safe or effective in addressing anxiety.

#### 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, lung and breast 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 cells and subsequently kill 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 National Institutes of Health, or 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 a significant cause of cancer death. Despite current therapeutic options such as surgery, radiation and chemotherapy, according to the American Cancer Society, the median survival rate for malignant glioma, the most common form of malignant brain cancer, is only in the range of nine to twelve months. 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 twelve months. The American Association for Cancer Research has reported that there has been no improvement in survival for malignant brain cancer over the past 25 years.

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. A secondary objective was to document therapeutic effect. We completed this trial in June 2000. We enrolled a total of 31 patients with recurrent gliomas which were unresponsive to surgery and radiotherapy in the trial. Our researchers treated patients with intratumoral infusions of NBI-3001 for up to four days. 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. The researchers did not observe any significant peripheral drug-related toxicities. The researchers reported that, of the 27 patients who completed therapy:

- o 7 patients, or 26%, were evaluated at least once during follow-up as complete remissions, defined as no evidence of viable tumor;
- o 10 patients, or 37%, were evaluated at least once during follow-up as



a partial response, defined as greater than 50% reduction in tumor mass; and

- o 10 patients, or 37%, were evaluated at least once during follow-up as continuing to suffer from stable or progressive disease.

In addition, the six-month median survival data showed trends toward efficacy. In the fourth quarter of 2000, we initiated an additional Phase II trial to better establish a dosing regimen, safety and efficacy for Phase III studies. To date, 30 patients have been enrolled in three dosing groups. These patients will be followed to evaluate 26-week survival, safety, tolerability and optimal clinical dose prior to embarking on the Phase III program. We have selected an acceptable dose for our Phase III program. We have elected to enroll additional patients in our Phase II study to expand our safety database for the selected dose and gain data on product manufactured for the Phase III study.

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.

**Additional 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 investigational new drug, or 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, non-small-cell lung and breast cancers. These three cancers had a combined expected incidence in 2001 of approximately 400,000 people in the United States according to the American Cancer Society.



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.

#### 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, bacteria or other proteins the T cell recognizes as foreign. T cells recognize these antigens 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 between 250,000 and 350,000 cases of multiple sclerosis in the United States and a similar number of patients in Europe. 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 \$1.8 billion in 2000.

Our co-founder, 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 IND with the FDA and received approval in 1996 to commence clinical trials. We subsequently initiated clinical development of our altered peptide ligand for the treatment of multiple sclerosis, NBI-5788, in 1999.

We have completed one Phase I and two Phase II trials of NBI-5788 in patients with a recurring form of multiple sclerosis. One of these 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 was an open label, unblinded, non-placebo-controlled study in eight patients conducted in collaboration with the NIH. While allergic reactions were seen in some 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 efficacy trial to determine the optimal dose and frequency of administration. Our aim for future trials will be to further establish the benefit of low-dose altered peptide ligand therapy in patients with multiple sclerosis. 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 potential products.



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 juvenile-onset diabetes, 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 in North America, afflicting approximately one million patients in 2000. 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.

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. Working with leading diabetologists at the Barbara Davis Center for Childhood Diabetes at the University of Colorado, our scientists have engineered an altered peptide ligand that affects immune cells targeting the pancreas. 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 100 diabetic patients. Data from these trials indicates that NBI-6024 is safe and well tolerated. We and Taisho initiated a Phase IIb clinical program in the fourth quarter of 2001. The first trial in this Phase IIb clinical program is 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 40 medical sites in the United States, Canada, Europe and South America and enroll approximately 400 patients. The United States sites will be initiated following completion of the United States Phase I/II studies.

In 2000, we entered into agreements with Taisho providing them with worldwide rights to NBI-6024. Pursuant to the collaboration agreements, we will receive licensing and option fees, payments for certain development and regulatory milestones, significant reimbursement of worldwide development expenses and payments based on sales.

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, or antagonizes, this transmitter pathway and is clinically useful in treating hormone-dependent diseases such as prostate cancer and endometriosis. Other companies have developed several peptide drugs on this principle, such as Lupron(copyright) and Zoladex(copyright), and according to market analyst reports by Med Ad News, the annual worldwide sales in 2000 for these drugs were approximately \$2.5 billion. These drugs are peptide agonist and must be administered by injection 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 that does not have the tendency to initially exacerbate the patient's condition. We selected a lead clinical candidate in early 2001 and initiated our Phase I clinical program in November 2001. 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.

We plan to focus our clinical efforts on prostate cancer and in the area of women's health, including endometriosis and uterine fibroids. According to the Endometriosis Association, researchers believe that more than five million women in the U.S. and Canada are affected by 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 available peptide agonists may be an alternative to surgery and encourage a higher treatment rate. We also believe our drug will have utility on the treatment of prostate cancer, of which there are expected to be approximately 200,000 new cases in 2001 in the U.S., according to the American Cancer Society.





## Research

### Excitatory Amino Acid Transporters

Some of the most successful central nervous system drugs, including selective serotonin reuptake inhibitors such as Prozac (copyright), selectively target brain amino acid transporters. Similarly, we are targeting a set of proteins generally located in the brain which transport brain chemicals in and out of cells, called excitatory amino acid transporters, to selectively control the levels of a brain chemical called glutamate in order 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 are collaborating with Wyeth-Ayerst to control glutamate transporter function as a novel strategy for the treatment of neurodegenerative and psychiatric disorders. Our collaboration includes 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.

In 2000, we expanded our excitatory amino acid transporter research and initiated a research program focused on retinal cell death associated with damage from low blood flow. 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-Ayerst.

### CRF R1 Antagonist

Recent reports have 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 between 10% to 20% of American adults, according to the International Foundation for Gastrointestinal Disorders. 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. Since researchers believe that CRF is the primary mediator of stress, they have suggested that CRF R1 antagonists may provide a treatment for irritable bowel syndrome. Together with GSK, we are evaluating our proprietary CRF R1 antagonists for treatment of irritable bowel syndrome. We face the risks that pre-clinical studies may not warrant initiating clinical testing of these candidates or that any initial clinical data may not support continuation of the program and additional clinical trials.

#### CRF R2 Antagonist

Our scientists were the first to isolate a second CRF receptor, called CRF R2. We believe the distribution of CRF R2 in the brain suggests that CRF R2 could play a role in some forms of anxiety and some eating disorders. Our researchers have demonstrated that administration of a CRF R2 antagonist reduces measures of anxiety in studies of obsessive compulsive disorder and conditioned fear. We are also evaluating our proprietary CRF R2 antagonist for treatment of a variety of eating disorders. We have screened our small molecule 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.

## Urocortin/CRF R2 Agonist

CRF R2 agonists may represent a therapeutic strategy to elevate CRF and a related neuropeptide called urocortin. Preliminary data indicates that CRF and urocortin may act as central regulators of both appetite and metabolism. We have evaluated CRF R2 agonists in various models of obesity and have observed reduced food intake and weight loss. In 1996, we initiated a collaboration with Eli Lilly which included a three year funded research program to screen and optimize CRF R2 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. To date, researchers have identified a family of five melanocortin receptor subtypes. Recently, researchers discovered that one of the melanocortin receptor subtypes, subtype 4, plays an important role in the mechanism regulating appetite, body weight and insulin secretion. The subtype 4 receptor is activated by melanocyte stimulating hormone (MSH). 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 or diabetes. On the other hand, the subtype 4 receptor is deactivated by AGRP. AGRP has been shown to have the reverse effect of MSH, 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 as well as failure to thrive in infants. For these reasons, we are also studying subtype receptor antagonists and agonists and have discovered novel, potent and selective compounds that are now being evaluated in relevant animal models. 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 regulating eating behavior. Based on these findings, we believe that blocking the effect of melanin concentrating hormone with a small molecule antagonist may represent a novel approach to the treatment of obesity. Neurocrine has initiated a research effort to identify 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.

#### Hypocretin Agonist/Antagonist

Hypocretins are peptides that researchers have linked to a variety of activities, including the control of eating, cardiovascular regulation and water intake. Recent publications have also reported that hypocretins appear to have a critical role as regulators of sleep. Some studies point to a lack of hypocretin as being instrumental in the development of narcolepsy and suggest that a small molecule agonist may be able to offset the lack of hypocretin and provide therapy for narcolepsy. The hypocretin system may also contribute to the regulation of other sleeping disorders such as insomnia, particularly since administration of excess hypocretin into animals promotes wakefulness. We have screened our small molecule library to identify agonists and antagonists for the hypocretin receptors and are in the process of optimizing the compounds that resulted from these screens. We will be using these compounds to further characterize the hypocretin system. We face the risk that our research in this area will not lead to product candidates.

#### CCR7

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 diseases such as rheumatoid arthritis, diabetes, or multiple sclerosis. The chemokine receptor CCR7 has been shown in mice experiments to be critical for developing these immune responses. We have initiated a research effort to identify orally-active compounds which will block CCR7. These compounds may provide a novel therapeutic strategy for treating rheumatoid arthritis, diabetes, or multiple sclerosis.

## Our Discovery Technology

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

Our Multi-Channel Discovery. 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(TM).

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

The power of MCD however, lies not in its application to a single receptor as a drug target but in the database of compounds that are characterized and isolated for the next target from the same class of receptors. Our current focus is on 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 10,000-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 15 programs in various stages of research and development, with seven projects in clinical development and eight 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. Melanocortin and hypocretin modulators are compounds which affect proteins in the brain believed to be involved in many activities of the body. We believe these compounds build upon our franchise and expertise in obesity and sleep disorders. The creativity and productivity of our discovery research group will continue to be a critical component for our continued success. Our team of approximately 105 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 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:

- o GlaxoSmithKline, for second generation corticotropin-releasing factor receptor antagonists to treat anxiety and depression and irritable

bowel syndrome;

- o Wyeth-Ayerst, for compounds to treat neurodegenerative and psychiatric diseases;
- o Taisho, for compounds to treat Type 1 diabetes, in which the body does not produce enough insulin; and
- o 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, lung and other cancers. 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-Ayerst. We also acquired from Northwest NeuroLogic, Inc. intellectual property relating to melanocortin technology and other technologies that we are developing. In June 1998, we licensed exclusive worldwide commercial rights for NBI-34060, our compound for the treatment of insomnia, from DOV Pharmaceuticals, Inc. 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 CRF1 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:

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. The total collaborative value of the GSK collaboration is the largest in Neurocrine's history. As of December 31, 2001, we have recorded revenues of \$667,000 in license fees, \$15.5 million in milestone payments, \$2.7 million in sponsored research and development and \$390,000 in reimbursement of development costs. In addition, we have \$6.9 million of deferred license fees and sponsored research revenues that will be amortized over the life of the agreement and as services are performed, respectively.

Taisho Pharmaceutical Co., Ltd. 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. Together with Taisho, we formed a steering committee to oversee the worldwide development of NBI-6024. We will receive license fees, milestone payments, and reimbursement of 100% of worldwide development expenses. In addition, we will receive payments on product sales for the term of the patents covering NBI-6024, subject to adjustment for payments to third parties. Taisho may terminate the agreement at its discretion upon prior written notice to us. In such event, all product rights would revert to us. As of December 31, 2001, we have recorded revenues of \$2.0 million for the exclusive option, \$1.1 million in license fees, \$9.5 million in milestone payments, \$2.9 million in sponsored research and \$8.3

million in reimbursement of development costs. In addition, we have \$2.9 million of deferred license fees and sponsored research revenues that will be amortized over the life of the agreement and as services are performed, respectively.

Wyeth-Ayerst Laboratories. Effective January 1999, we entered into a collaboration and license agreement with Wyeth-Ayerst 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-Ayerst exclusive and non-exclusive rights to different portions of 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-Ayerst 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. As of December 31, 2001, we have received payments and recognized a total of \$12.4 million under the Wyeth-Ayerst agreement, consisting of \$9.0 million in sponsored research and \$3.4 million in milestone payments.

The three-year term of the sponsored research under the Wyeth-Ayerst agreement was scheduled to terminate January 1, 2002, but in December 2001, we and Wyeth-Ayerst agreed to extend the term of the sponsored research for a period of three months during which time we and Wyeth-Ayerst will discuss a further extension. In connection with the three-month extension, we received \$375,000 of sponsored research funding.

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 R2 agonists for central nervous system diseases and disorders. Under the agreement, we received and recognized three years of sponsored research and development payments totaling \$17.2 million. We also 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 payments under this agreement.

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 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 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. All collaboration products identified under the 1999 agreement are subject to the same terms and conditions as the products arising under the 1995 agreement. This additional research was completed in February 2001. Our 1999 agreement provides that in August 2001 Neurocrine was to receive either a \$3.5 million milestone payment from Janssen or exclusive rights to the first generation back-up compounds. We agreed to postpone the August event to allow Janssen to complete certain studies with the back-up program compounds. 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 R1 antagonist compounds developed thereunder reverted to us. We do not expect any additional payments of any kind under the Janssen agreement.

As of December 31, 2001, we have received and recognized a total of \$21.1 million, including \$14.7 million in sponsored research, \$3.5 million in milestones, \$2.0 million in license fees and \$943,000 for reimbursement of outside costs under these agreements. In connection with the 1995 agreement,

Johnson & Johnson Development Corporation purchased \$5.0 million of our common stock.

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 13 issued U.S. patents, approximately 60 pending U.S. patent applications and another approximately 140 issued and pending foreign patents and applications. We have licensed, from institutions such as The Salk Institute, Stanford University, Oregon Health Sciences University, DOV Pharmaceuticals, Inc. 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. Two of our European patents are subject to opposition proceedings. These proceedings relate to our broad patent covering immune therapeutics in diabetes and multiple sclerosis. If successful, these opposition proceedings could reduce the breadth of some of our proprietary rights, but we believe they would not materially impede our commercialization strategy. 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 European 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 in Europe 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, the hypocretin 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 a U.S. patent relating to IL-4 proteins that is controlled by another entity 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.

NBI-34060, our leading gamma amino-butyrac acid agonist compound for the treatment of insomnia, is covered generically in an issued U.S. patent, which we licensed from DOV Pharmaceuticals, Inc. The term of the U.S. patent is due to expire in June 2003. NBI-34060 is not currently covered by any foreign patents of which we are aware. We intend to seek additional protection of this compound in three ways. First, we have filed nine U.S. and foreign patent applications directed to the synthesis, formulations and various forms of NBI-34060, which could extend patent protection to the year 2020. We face the risk that these patents may not issue, or may subsequently be challenged successfully. Second, patent term extension under the Hatch/Waxman Patent Term Extension Act may add patent life in the U.S. beyond the June 2003 expiration, depending on the length of clinical trials and other factors involved in the filing of a new drug application. Third, in addition to this 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

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.

- o In June 2001, we licensed nonexclusive rights to the BON cell line from the University of Texas Medical Branch.
- o In May 2001, we licensed nonexclusive rights to a murine CCR7 expressing cell line from Public Health Service.
- o In March 2001, we licensed nonexclusive rights to a saoS-2 cell line from The Sloan-Kettering Institute for Cancer Research.
- o In March 2001, we licensed a HERG cell line from Wisconsin Alumni Research Foundation.
- o In October 2000, we licensed nonexclusive rights to several GT1-cell lines from The Salk Institute.
- o In August 2000, we licensed nonexclusive rights to CRF R1 deficient mice from the Research Development Foundation.
- o In July 2000, we licensed exclusive rights to melanocortin subtype 3 receptor knock-out mice from Oregon Health Sciences University.
- o In August 1999, we licensed nonexclusive rights to the human gonadotropin-releasing hormone receptor from Mount Sinai School of Medicine.
- o In January 1999, we licensed exclusive worldwide rights to patents relating to excitatory amino acid transporters and melanocortin from Oregon Health Sciences University.
- o In December 1998, we licensed nonexclusive rights to technology covering melanocortin subtype 4 from the University of Michigan.
- o In June 1998, we licensed exclusive worldwide rights to our sedative compound, NBI-34060, from DOV Pharmaceuticals, Inc.
- o 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.
- o In October 1997, we licensed co-exclusive rights to technology

relating to the prevention of diabetes from University Technology Corporation.



- o In November 1996, we licensed exclusive worldwide rights to technology directed to peptide therapeutics for the treatment of autoimmune disease from the Trustees of Dartmouth College.
  
- o In November 1994, we licensed exclusive worldwide rights to technology relating to treatment of multiple sclerosis using peptide analogs of myelin basic protein from Stanford University.
  
- o In November 1993, we licensed exclusive worldwide rights to CRF R1 from the Salk Institute for Biological Studies.

#### Manufacturing

We currently rely, and will continue to rely for at least the next few years, on contract manufacturers to produce sufficient quantities of our product candidates for use in our pre-clinical and anticipated clinical trials.

Manufacturers of our NBI-34060 clinical trial material include Organichem Corporation, Pharmaceutics International, Inc. and Patheon, Inc. Polypeptide Laboratories, Bachem, Cook Pharmaceutical Solutions, Pyramid Laboratories and Prima Pharm Inc. manufacture our altered peptide ligands NBI-6024 and NBI-5788. Cedarburg Pharmaceuticals, Albany Molecular Research and Pharmaceutics International, Inc. manufacture our CRF antagonist compounds. MediChem and Pharmaceutics International, Inc. manufacture our GnRH antagonist compounds. Manufacturers of our NBI-3001 clinical trial material include Diosynth and Charles River Laboratories.

There is currently a limited supply of some of these components. Furthermore, 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.

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, marketing or distribution capabilities. In

order to commercialize any of our product candidates, we must either internally develop sales, marketing and distribution capabilities or make arrangements with third parties to perform these services. We intend to sell, market and distribute some products directly and intend to rely on relationships with third parties to sell, market and distribute other products. Under our collaboration agreements with GSK, Wyeth-Ayerst, Taisho and Eli Lilly, we may have the opportunity to co-promote some of our products in the United States. To market any of our products directly, we must develop a marketing and sales force with technical expertise and with supporting distribution 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 conducted many of our clinical trials in Europe and South Africa.

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.

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

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:

- o other drug development technologies;
- o methods of preventing or reducing the incidence of disease, including vaccines; and
- o 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 glioma, other forms of cancer, certain women's health disorders, Type 1 diabetes and multiple sclerosis.

We are developing a gamma amino-butyric acid receptor agonist, NBI-34060, for the treatment of insomnia. Ambien(copyright) and Sonata(copyright) are already marketed for the treatment of insomnia by Sanofi-Synthelabo and American Home Products / Elan, respectively.

In the area of anxiety disorders, our product candidates will compete

with well-established products such as Valium(copyright), marketed by Hoffman-La Roche, Xanax(copyright), marketed by Pharmacia, BuSpar(copyright), marketed by Bristol-Myers Squibb, 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(copyright), marketed by Eli Lilly as well as its generic alternatives, Zoloft(copyright), marketed by Pfizer, Paxil(copyright), marketed by GSK, and Celexa(copyright), 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(copyright) is approved in the U.S. and Europe for use in a subset of brain cancers known as recurrent glioblastoma multiforme. Gliadel(copyright) is also under review by the FDA for treatment of primary glioblastoma, and an application has been filed in Europe for this indication. Gliadel(copyright) 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(copyright) is marketed by Chiron for the treatment of kidney cancer, and drug treatments for non-small-cell lung cancer include Taxotere(copyright), marketed by Aventis, Taxol(copyright), marketed by Bristol-Myers Squibb, Navelbine(copyright), marketed by GSK, and Gemzar(copyright), which is marketed by Eli Lilly. Breast cancer agents include Taxotere(copyright), marketed by Aventis, Nolvadex(copyright) and Arimidex(copyright), marketed by AstraZeneca, and Herceptin(copyright), marketed by Genentech.

Products that may compete with NBI-5788, our altered peptide ligand for multiple sclerosis, include Betaseron(copyright) and Avonex(copyright), similar forms of beta-interferon marketed by Berlex BioSciences and Biogen, respectively, and Rebif(copyright) marketed by Ares Serono. Copaxone(copyright), 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.



There are a number of competitors to products in our research pipeline. Lupron Depot (copyright), marketed by Takeda-Abbott Pharmaceuticals, Zoladex (copyright), marketed by AstraZeneca, and Synarel (copyright), marketed by Pharmacia, are gonadotropin-releasing hormone peptide agonists that have been approved for the treatment of prostate cancer, endometriosis, infertility, breast cancer 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 (copyright) from Roche Laboratories and Meridia (copyright) 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:

- o capital resources;
- o research and development resources, including personnel and technology;
- o regulatory experience;
- o pre-clinical study and clinical testing experience;
- o manufacturing and marketing experience; and
- o 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, 2001, we had 222 employees, consisting of 211 full-time and 11 part-time employees. Of the full-time employees, approximately 72 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. We are highly dependent on the principal members of our management and scientific staff. If we were to lose the services of any of these



personnel, we might not be able to achieve 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 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 12 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.

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.

Stephen M. Hedrick, Ph.D., is Professor and Chairman of Cell Biology at the University of California, San Diego. Dr. Hedrick is an expert in T cell immunology and co-discovered the first T cell receptor genes and identified the regions responsible for antigen binding. He is an editor for the Journal of Immunology.

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.

George F. Koob, Ph.D., is a Professor of the Department of Neuropharmacology at The Scripps Research Institute and an Adjunct Professor in the Departments of Psychology and Psychiatry at the University of California, San Diego. Dr. Koob is an internationally recognized behavioral pharmacology expert on the role of peptides in the central nervous system, the neurochemical basis of addiction and in the development of pre-clinical behavioral procedures for the screening of anxiolytic and antidepressant drugs and memory enhancers.

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.

## RISK FACTORS

### Risks Related to the Company

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 \$36.9 million in the year ended December 31, 2001. As a result of ongoing operating losses, we had an accumulated deficit of \$107.4 million as of December 31, 2001. We do not expect to be profitable in 2002. 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:

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

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 twelve 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:

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

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 for the foreseeable future, 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:

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

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

In November 2001, we began enrolling subjects in a Phase III clinical trial for NBI-34060, our insomnia product under development. Since this is our most advanced product program, our business and reputation would be particularly harmed if the product does not prove to be efficacious in our late stage clinical trials or we fail to receive necessary regulatory approvals on a timely basis or achieve market acceptance.

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.

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.

In connection with our clinical trials, we face the risks that:

- o we or the FDA may suspend the trials;



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

- o the results may not replicate the results of earlier, smaller trials;
- o the results may not be statistically significant;
- o patient recruitment may be slower than expected; and
- o 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.

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

We depend on independent clinical investigators and contract research organizations, or CROs, to conduct our clinical trials under their agreements with us. The investigators are not our employees and we cannot control the amount or timing of resources that they devote to our programs. If independent investigators fail to devote sufficient time and resources to our drug development programs, or if their performance is substandard, it 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 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:

- o selecting compounds for subsequent development as drug candidates;
- o conducting pre-clinical studies and clinical trials and obtaining required regulatory approvals for these drug candidates; and
- o 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 GlaxoSmithKline, Wyeth-Ayerst and Taisho. Because we rely heavily on our corporate collaborators, the development of our projects would be substantially delayed if our collaborators:

- o fail to select a compound we have discovered for subsequent development into marketable products;
- o fail to gain the requisite regulatory approvals of these products;
- o do not successfully commercialize products that we originate;
- o do not conduct their collaborative activities in a timely manner;
- o do not devote sufficient time and resources to our partnered programs or potential products;
- o terminate their alliances with us;
- o develop, either alone or with others, products that may compete with our products;
- o dispute our respective allocations of rights to any products or technology developed during our collaborations; or
- o 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 arises, it may delay the filing of our new drug applications and, ultimately, our generation of product revenues.



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:

- o 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;
- o 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;
- o 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 and distribute our products; and
- o 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.

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.

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 and we do not have a marketing and sales staff or distribution capabilities. 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.

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.

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

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

- o 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:

- o other drug development technologies;
- o methods of preventing or reducing the incidence of disease, including vaccines; and
- o 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 anxiety, depression, insomnia, malignant glioma, other forms of cancer and multiple sclerosis, and there are a number of competitors to products in our research pipeline. If one or more of these 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:





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

Any of these competitive factors could reduce demand for our products. For more specific information about the competition we face, please review the information under the subheading "Competition" earlier in this report.

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:

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

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

We also rely upon unpatented trade secrets and improvements, unpatented know-how and continuing technological innovation to develop and maintain our competitive position, which we seek to protect, in part, 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. Two of our European patents are subject to opposition proceedings which, if successful, could reduce the breadth of some of our proprietary rights. These proceedings relate to our broad patent covering immune therapeutics in diabetes and multiple sclerosis. In addition, 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. For more information about our intellectual property, please review the information under the subheading "Intellectual Property" earlier in this report.

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 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 sublet approximately 10,500 square feet of this building to one tenant through March 31, 2002.

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
	----	---
Year Ended December 31, 2000		
1st Quarter .....	\$47.50	\$20.75
2nd Quarter .....	39.75	13.94
3rd Quarter .....	46.00	29.13
4th Quarter .....	44.88	25.50
Year Ended December 31, 2001		
1st Quarter .....	\$36.50	\$14.25
2nd Quarter .....	39.99	16.75
3rd Quarter .....	40.71	27.93
4th Quarter .....	54.26	30.36

As of February 28, 2002, there were approximately 111 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.

2001            2000            1999 (2)    1998 (1)(2)    1997  
 -----  
 (in thousands, except for earnings/(loss) per share data)

STATEMENT OF OPERATIONS DATA

Revenues

Sponsored research and development .....	\$ 16,880	\$ 6,881	\$ 12,662	\$ 12,361	\$ 14,985
Milestones and license fees .....	22,937	6,345	3,000	2,500	10,250
Grant income and other revenues .....	1,425	1,362	1,129	1,176	909
	-----	-----	-----	-----	-----
Total revenues .....	41,242	14,588	16,791	16,037	26,144

Operating expenses

Research and development .....	74,267	40,227	29,169	21,803	18,758
General and administrative .....	10,857	9,962	7,476	6,594	5,664
Write-off of acquired in-process research and development and licenses .....	--	--	--	4,910	--
	-----	-----	-----	-----	-----
Total operating expenses .....	85,124	50,189	36,645	33,307	24,422

Income (loss) from operations .....	(43,882)	(35,601)	(19,854)	(17,270)	1,722
Interest income, net .....	6,662	6,048	2,851	4,000	3,931
Other income .....	430	1,047	1,066	504	818
Equity in NPI losses and other adjustments, net .....	--	--	(885)	(7,188)	(1,130)
	-----	-----	-----	-----	-----
Net income (loss) before income taxes ....	(36,790)	(28,506)	(16,822)	(19,954)	5,341
Income taxes .....	120	302	--	1	214



Net income (loss) .....	\$ (36,910)	\$ (28,808)	\$ (16,822)	\$ (19,955)	\$ 5,127
Earnings (loss) per share					
Basic .....	\$ (1.42)	\$ (1.30)	\$ (0.88)	\$ (1.10)	\$ 0.30
Diluted .....	\$ (1.42)	\$ (1.30)	\$ (0.88)	\$ (1.10)	\$ 0.28
Shares used in calculation of earnings (loss) per share					
Basic .....	26,028	22,124	19,072	18,141	16,930
Diluted .....	26,028	22,124	19,072	18,141	18,184

#### BALANCE SHEET DATA

Cash, cash equivalents and short-term investments .....					
	\$319,982	\$164,670	\$ 91,098	\$ 62,670	\$ 75,092
Working capital .....	306,754	157,446	86,168	60,064	69,362
Total assets .....	346,350	185,962	109,222	80,529	91,903
Long-term debt and capital lease obligations .....					
	3,600	2,283	2,139	2,247	722
Accumulated deficit .....	(107,390)	(70,480)	(41,672)	(24,850)	(4,895)
Total stockholders' equity .....	310,393	163,208	96,354	71,958	83,152

(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 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 which involve risks and uncertainties, pertaining generally 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 factors, including those set forth in this Annual Report on Form 10-K.

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, cancer, multiple sclerosis and diabetes. 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, 2001, we have incurred a cumulative deficit of \$107.4 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, which 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 period earned. Milestone payments are recognized as revenue upon achievement of pre-defined scientific events. Revenues from government grants are recognized based on a percentage-of-completion basis as the related costs are incurred. We recognize revenue only on payments that are nonrefundable and when the work is performed.

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, which are generally cancelable. We review and accrue clinical trials expenses based on work performed, which relies on estimates of total hours incurred and completion of certain 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 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 represent at-risk equity. 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.

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, 2001, 2000 and 1999

Our revenues for the year ended December 31, 2001 were \$41.2 million compared with \$14.6 million in 2000, and \$16.8 million in 1999. 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 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 the Janssen agreement. These activities concluded, as scheduled, in February 2001. Under the Janssen agreement, we recognized \$525,000 during 2001 and \$3.0 million during 2000.

The decline in revenues from 1999 to 2000 resulted primarily from the conclusion of a collaboration with Novartis in January 2000 and the sponsored research portion of a collaboration with Eli Lilly in October 1999. During 1999, we received \$6.8 million in revenues under these agreements, in addition to \$3.0 million in milestones under the agreement with Wyeth-Ayerst. The absence of these revenues during 2000 was partially offset by \$7.1 million in revenues from Taisho. In addition, revenues recognized from Janssen were \$3.0 million in 2000 compared to \$2.4 million recognized in 1999.

Research and development expenses increased to \$74.3 million during 2001 compared with \$40.2 million during 2000 and \$29.2 million in 1999. Increased expenses reflect advancement of our drug candidates through progressive clinical development phases. We expect to incur significant increases 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 \$10.9 million during 2001 compared with \$10.0 million during 2000 and \$7.5 million during 1999. The increase in administrative 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. The increase in expenses from 1999 to 2000 resulted primarily from approximately \$1.0 million in business development consulting primarily relating to the Taisho agreement and \$1.1 million of non-cash stock compensation charges relating to the employee stock purchase program and consultant stock options.

Interest income increased to \$7.0 million during 2001 compared with \$6.3 million during 2000 and \$3.1 million during 1999. The increase in 2001, compared with 2000 and 1999, primarily resulted from higher investment balances achieved through public and private offerings of our common stock. 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. And, in December 1999, we sold 2.3 million shares of our common stock in a private placement resulting in net proceeds of \$39.5 million.

In December 1999, we sold our investment in NPI and recorded a gain of \$526,000. Our proportionate share of NPI operating losses during 1999 was \$764,000. In addition, we recorded a write-down in the investment value of \$646,000 during 1999 relating to the decline in cash redemption value of the NPI preferred shares.

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 to support company growth. During 2002, we expect sublease income to decrease significantly as increases in personnel will require us to use more office and laboratory space.

Our net loss for 2001 was \$36.9 million, or \$1.42 per share, compared with \$28.8 million, or \$1.30 per share, in 2000 and \$16.8 million, or \$0.88 per share, in 1999. The increase in net loss primarily resulted from an increase in scientific personnel and expanded clinical development activities. 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, 2001, our cash, cash equivalents, and short-term investments totaled \$320.0 million compared with \$164.7 million at December 31, 2000. The increase in cash balances from December 31, 2000 to December 31, 2001 resulted from the sale of 4.0 million shares of our common stock in a public offering, which generated net cash proceeds of \$175.6 million. The increase in cash was offset by net cash used in operating activities during 2001.

Net cash used in operating activities during fiscal year 2001 was \$21.9

million compared with \$18.6 million in 2000 and \$10.3 million during 1999. The increase in cash used in operations for 2001 compared to the prior periods resulted primarily from the increase in clinical development activities and the addition of scientific and clinical development personnel.

Net cash used in investing activities during fiscal year 2001 was \$16.6 million compared to \$75.7 million during 2000 and \$21.2 million in 1999. 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 2001, 2000 and 1999 were \$3.8 million, \$2.4 million and \$2.1 million, respectively, and were financed primarily through capital leasing arrangements. Capital equipment purchases for 2002 also will be financed primarily through leasing agreements and are expected to be approximately \$6.9 million.

Net cash provided by financing activities during fiscal year 2001 was \$181.3 million compared with \$94.1 million in 2000 and \$41.0 million during 1999. Cash provided during 2001, 2000 and 1999 includes net proceeds from public and private offerings of our common stock of \$175.6 million, \$90.4 million and \$39.5 million, respectively.

Factors that may affect future financial condition and liquidity

We anticipate significant increases in expenditures as we continue to expand our research and development activities. Because of our limited financial resources, our strategies to develop some of our programs include collaborative agreements with major pharmaceutical companies and sales of our common stock in both public and private offerings. Our collaborative agreements typically include a partial recovery of our research costs through license fees, contract research funding and milestone revenues. Our collaborators are also financially and managerially responsible for clinical development and commercialization. In these cases, the estimated completion date would largely be under the control of

the collaborator. We 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, 2001 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 \$13.8 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.

Contractual Obligations	Total	Less than	1 - 3	After
		1 year	years	3 years
(in thousands)				
Long-term debt .....	\$ 149	\$ 149	\$ --	\$ --
Capital lease obligations .....	6,216	2,277	3,253	686
Operating lease .....	38,078	2,626	5,572	29,880
License & research agreements .....	1,724	884	770	70
Clinical development agreements .....	48,107	26,330	21,777	--
<b>Total contractual obligations ....</b>	<b>\$94,247</b>	<b>\$32,239</b>	<b>\$31,372</b>	<b>\$30,636</b>

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, 2001, 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:

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

For each of our programs, we periodically assess the scientific

progress and merits of the programs to determine if continued research and development is economically viable. Certain of our programs have been terminated due to the lack of scientific progress and lack of prospects for ultimate commercialization. Because of the uncertainties associated with research and

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

Our product candidates have not yet achieved FDA regulatory approval, which is required before we can market them as therapeutic products. In 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:

- o continued scientific progress in our research and development programs;
- o the magnitude of our research and development programs;
- o progress with pre-clinical testing and clinical trials;
- o the time and costs involved in obtaining regulatory approvals;
- o the costs involved in filing and pursuing patent applications and enforcing patent claims;

- o competing technological and market developments;
  
- o the establishment of additional strategic alliances;
  
- o the cost of manufacturing facilities and of commercialization activities and arrangements; and
  
- o 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 twelve months. However, we cannot guarantee that these capital resources and payments will be sufficient to conduct 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, potentially including off-balance sheet financing. 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, 2001, 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 June 2001, the Financial Accounting Standards Board (FASB) issued SFAS No. 141, "Business Combinations," and SFAS No. 142, "Goodwill and Other Intangible Assets." SFAS No. 141 supercedes Accounting Principles Board (APB) Opinion No. 16, "Business Combinations," and SFAS No. 38, "Accounting for

Preacquisition Contingencies of Purchased Enterprises," and requires that all business combinations be accounted for by a single method -- the purchase method. SFAS No. 141 also provides guidance on the recognition of intangible assets identified in a business combination and requires enhanced financial statement disclosures. SFAS No. 142 adopts a more aggregate view of goodwill and bases the accounting for goodwill on the units of the combined entity into which an acquired entity is integrated. In addition, SFAS No. 142 concludes that goodwill and intangible assets that have indefinite useful lives will not be amortized but rather will be tested at least annually for impairment. Intangible assets that have finite lives will continue to be amortized over their useful lives. SFAS No. 141 is effective for all business combinations initiated after June 30, 2001. The adoption of SFAS No. 142 is required for fiscal years beginning after December 15, 2001, except for the nonamortization and amortization provisions, which are required for goodwill and intangible assets acquired after June 30, 2001. The adoption of SFAS No. 141 had no impact on our financial position or results of operations. We will adopt SFAS No. 142 in the first quarter of 2002 and believe that the adoption will not have a material impact on our financial position or results of operations.

In October 2001, the FASB issued SFAS No. 144, "Accounting for the Impairment or Disposal of Long-Lived Assets," which establishes one accounting model to be used for long-lived assets to be disposed of by sale and broadens the presentation of discontinued operations to include more disposal transactions. SFAS No. 144 supercedes SFAS No. 121, "Accounting for the Impairment of Long-Lived Assets and for Long-Lived Assets to Be Disposed Of," and the accounting and reporting provisions of APB Opinion No. 30. SFAS No. 144 is effective for fiscal years beginning after December 15, 2001. We will adopt SFAS No. 144 in the first quarter of 2002 and believe that the adoption will not have a material impact on our financial position or results of operations.

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 14 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 2002 Annual Meeting of Stockholders, to be filed pursuant to Regulation 14A with the Securities and Exchange Commission within 120 days of December 31, 2001. 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 2002 Annual Meeting of Stockholders, to be filed pursuant to Regulation 14A with the Securities and Exchange Commission within 120 days of December 31, 2001. 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 2002 Annual Meeting of Stockholders, to be filed pursuant to Regulation 14A with the Securities and Exchange Commission within 120 days of December 31, 2001. 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 2002 Annual Meeting of Stockholders, to be filed pursuant to Regulation 14A, with the Securities and Exchange Commission within 120 days of December 31, 2001. Such information is incorporated herein by reference.

PART IV

ITEM 14. 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, 2001 and 2000

Statements of Operations for the years ended December 31, 2001, 2000 and 1999

Statements of Stockholders' Equity for the years ended December 31, 2001, 2000 and 1999

Statements of Cash Flows for the years ended December 31, 2001, 2000 and 1999

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 Forms 8-K dated November 16, 2001, November 27, 2001, December 3, 2001 and December 4, 2001.

1. The Registrant filed a Current Report on Form 8-K dated November 16, 2001 to report, pursuant to Item 5 (Other Events) and Item 7 (Final Statements, Pro Forma Financial Information and Exhibits), its announcement of the first pivotal Phase III clinical trial of

2. The Registrant filed a Current Report on Form 8-K dated November 27, 2001 to report, pursuant to Item 5 (Other Events) and Item 7 (Final Statements, Pro Forma Financial Information and Exhibits), its announcement of the dosing of seven subjects in the initiation of a Phase I clinical trial with the Company's proprietary, orally active, gonadotropin-releasing hormone antagonist.
3. The Registrant filed a Current Report on Form 8-K dated November 27, 2001 to report, pursuant to Item 5 (Other Events) and Item 7 (Final Statements, Pro Forma Financial Information and Exhibits), the Company's intent to file a preliminary prospectus supplement to its \$200 million universal shelf registration statement with the Securities and Exchange Commission relating to the proposed underwritten public offering of 3,250,000 shares of its common stock.
4. The Registrant filed a Current Report on Form 8-K dated December 3, 2001 to report, pursuant to Item 5 (Other Events) and Item 7 (Final Statements, Pro Forma Financial Information and Exhibits), the Company's filing of the form of Underwriting Agreement by and among the Company and Deutsche Banc Alex. Brown Inc. and Credit Suisse First Boston Corporation, as representatives of the several underwriters, to be used in connection with the proposed public offering.
5. The Registrant filed a Current Report on Form 8-K dated December 4, 2001 to report, pursuant to Item 5 (Other Events) and Item 7 (Final Statements, Pro Forma Financial Information and Exhibits), its announcement of the pricing of the public offering of 3,500,000 shares of common stock (plus an optional 525,000 shares for over-allotments) at a price of \$46.75 per share.

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

Exhibit

Number Description

-----  
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)
- 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, M.D. (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 Pharmaceuticals, Inc. and the Registrant (6)
- 10.24\* Warrant Agreement dated June 30, 1998, between DOV Pharmaceuticals, 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-Ayerst 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, M.D., Ph.D. (18)
- 21.1 Subsidiaries of the Company
- 23.1 Consent of Ernst & Young LLP, Independent Auditors
- 24.1 Power of Attorney

- -----

- (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 Report on Form 8-K filed on December 15, 2000
  
- (14) Incorporated by reference to the Company's Report on Form S-8 filed on 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 Report on Form 8-K filed on January 14, 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 14 (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

By: /s/ Gary A. Lyons

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Gary A. Lyons

President and Chief Executive Officer

Date: March 26, 2002

POWER OF ATTORNEY

KNOW ALL PERSONS BY THESE PRESENTS, that each person whose signature appears below constitutes and appoints Gary A. Lyons and Paul Hawran, jointly and severally his attorneys-in-fact, each with the power of substitution, for him in any and all capacities, to sign any amendment to this Report on Form 10-K, and to file the same, with exhibits thereto and other documents in connection therewith, with the Securities and Exchange Commission, hereby ratifying and confirming all that each of said attorneys-in-fact, or his substitute or substitutes, may or cause to be done by virtue hereof.

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:

Signature	Title	Date
- -----	-----	----
/s/ Gary A. Lyons ----- Gary A. Lyons	President, Chief Executive Officer and Director (Principal Executive Officer)	March 26 2002
/s/ Paul W. Hawran ----- Paul W. Hawran	Chief Financial Officer (Principal Financial and Accounting Officer)	March 26, 2002
/s/ Joseph A. Mollica ----- Joseph A. Mollica.	Chairman of the Board of Directors	March 26, 2002
/s/ Richard F. Pops ----- Richard F. Pops	Director	March 26, 2002
/s/ Stephen A. Sherwin -----	Director	March 26, 2002

Stephen A. Sherwin

/s/ Lawrence Steinman

Director

March 26, 2002

- -----

Lawrence Steinman

/s/ Wylie W. Vale

Director

March 26, 2002

- -----

Wylie W. Vale

NEUROCRINE BIOSCIENCES, INC.  
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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, 2001 and 2000, and the related statements of operations, stockholders' equity, and cash flows for each of the three years in the period ended December 31, 2001. 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, 2001 and 2000, and the results of its operations and its cash flows for each of the three years in the period ended December 31, 2001, in conformity with accounting principles generally accepted in the United States.

/s/ ERNST & YOUNG LLP

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ERNST & YOUNG LLP





NEUROCRINE BIOSCIENCES, INC

Balance Sheets

(in thousands, except for par value and share totals)

	December 31,	
	-----	-----
	2001	2000
	-----	-----
ASSETS		
Current assets:		
Cash and cash equivalents .....	\$ 163,888	\$ 21,078
Short-term investments, available-for-sale .....	156,094	143,592
Receivables under collaborative agreements .....	9,949	5,974
Other current assets .....	1,584	1,761
	-----	-----
Total current assets .....	331,515	172,405
Property and equipment, net .....	12,088	11,300
Licensed technology and patent applications costs, net ...	188	362
Other non-current assets .....	2,559	1,895
	-----	-----
Total assets .....	\$ 346,350	\$ 185,962
	=====	=====
LIABILITIES AND STOCKHOLDERS' EQUITY		
Current liabilities:		
Accounts payable .....	\$ 1,539	\$ 1,065
Accrued liabilities .....	15,753	11,135
Deferred revenues .....	5,382	1,172
Current portion of long-term debt .....	149	149
Current portion of capital lease obligations .....	1,938	1,438
	-----	-----
Total current liabilities .....	24,761	14,959
Long-term debt, net of current portion .....	--	162
Capital lease obligations, net of current portion ....	3,600	2,121
Deferred rent .....	2,196	1,646

Deferred revenues .....	4,417	2,890
Other liabilities .....	983	976
	-----	-----
Total liabilities .....	35,957	22,754
Commitments and contingencies (See Note 6) .....	--	--
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 30,347,744 in 2001 and 25,314,470 in 2000 .....	30	25
Additional paid-in capital .....	420,018	233,565
Deferred compensation .....	(1,815)	(59)
Notes receivable from stockholders .....	(381)	(104)
Accumulated other comprehensive loss .....	(69)	261
Accumulated deficit .....	(107,390)	(70,480)
	-----	-----
Total stockholders' equity .....	310,393	163,208
	-----	-----
Total liabilities and stockholders' equity .....	\$ 346,350	\$ 185,962
	=====	=====

See accompanying notes.

NEUROCRINE BIOSCIENCES, INC.

Statements of Operations

(in thousands, except loss per share data)

	Years Ended December 31,		
	2001	2000	1999 (1)
Revenues:			
Sponsored research and development .....	\$ 16,880	\$ 6,881	\$ 12,662
Milestones and license fees .....	22,937	6,345	3,000
Grant income and other revenues .....	1,425	1,362	1,129
	-----	-----	-----
Total revenues .....	41,242	14,588	16,791
Operating expenses:			
Research and development .....	74,267	40,227	29,169
General and administrative .....	10,857	9,962	7,476
	-----	-----	-----
Total operating expenses .....	85,124	50,189	36,645
Loss from operations .....	(43,882)	(35,601)	(19,854)
Other income and expenses:			
Interest income .....	6,978	6,276	3,082
Interest expense .....	(316)	(228)	(231)
Equity in NPI losses and other adjustments, net .....	-	-	(885)
Other income .....	430	1,047	1,066
	-----	-----	-----
Loss before taxes .....	(36,790)	(28,506)	(16,822)
Income taxes .....	120	302	-
	-----	-----	-----
Net loss .....	\$ (36,910)	\$ (28,808)	\$ (16,822)
	=====	=====	=====
Loss per common share:			
Basic and diluted .....	\$ (1.42)	\$ (1.30)	\$ (0.88)

	=====	=====	=====
Shares used in the calculation of loss			
per common share - basic and diluted.....	26,028	22,124	19,072
	=====	=====	=====

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(1) Sponsored research and development includes \$491 in revenue from a related party for the year ended December 31, 1999.

See accompanying notes.

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

	Common stock		Additional	Deferred compensation
	Shares	Amount	paid-in capital	
BALANCE AT DECEMBER 31, 1998 .....	18,931	\$19	\$ 97,064	\$ (187)
Net loss .....	-	-	-	-
Unrealized loss on short-term investments .....	-	-	-	-
Comprehensive loss .....	-	-	-	-
Issuance of common stock from option exercises .....	307	-	1,507	-
Issuance of common stock pursuant to the Employee Stock Purchase Plan .....	42	-	213	-
Issuance of common stock, net of offering costs .....	2,328	3	39,293	-
Amortization of deferred compensation, net .....	-	-	721	(224)
BALANCE AT DECEMBER 31, 1999 .....	21,608	22	138,798	(411)
Net loss .....	-	-	-	-
Unrealized gain on short-term investments .....	-	-	-	-
Comprehensive loss .....	-	-	-	-
Issuance of common stock from exercise of warrants .....	23	-	-	-
Issuance of common stock for notes .....	6	-	1	-
Issuance of common stock from option exercises .....	354	-	2,328	-
Issuance of common stock pursuant to the Employee Stock Purchase Plan .....	98	-	1,339	-
Issuance of common stock, net of offering costs .....	3,225	3	90,353	-
Payments received on stockholder notes .....	-	-	-	-
Reversal of accrued 12/99 private placement costs .....	-	-	182	-
Amortization of deferred compensation, net .....	-	-	564	352
BALANCE AT DECEMBER 31, 2000 .....	25,314	25	233,565	(59)
Net loss .....	-	-	-	-

Unrealized loss on short-term investments .....	-	-	-	-
Comprehensive loss .....	-	-	-	-
Issuance of common stock from exercise of warrants .....	43	-	1,902	-
Issuance of common stock for notes .....	7	-	277	-
Issuance of common stock from option exercises .....	781	1	2,436	-
Issuance of common stock pursuant to the Employee Stock Purchase Plan .....	178	-	3,382	-
Issuance of common stock, net of offering costs .....	4,025	4	175,558	-
Amortization of deferred compensation, net .....	-	-	2,898	(1,756)
-----				
BALANCE AT DECEMBER 31, 2001 .....	30,348	\$30	\$420,018	\$(1,815)
=====				

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

	Notes receivable from stockholders	Accumulated other comprehensive income (Loss)	Accumulated deficit	Total stockholders' equity
BALANCE AT DECEMBER 31, 1998	\$(119)	\$ 31	\$ (24,850)	\$ 71,958
Net loss	-	-	(16,822)	(16,822)
Unrealized loss on short-term investments	-	(295)	-	(295)
Comprehensive loss	-	-	-	(17,117)
Issuance of common stock from option exercises	-	-	-	1,507
Issuance of common stock pursuant to the Employee Stock Purchase Plan	-	-	-	213
Issuance of common stock, net of offering costs	-	-	-	39,296
Amortization of deferred compensation, net	-	-	-	497
BALANCE AT DECEMBER 31, 1999	(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	-	-	-	
Issuance of common stock for notes	-	-	-	1
Issuance of common stock from option exercises	-	-	-	2,328
Issuance of common stock pursuant to the Employee Stock Purchase Plan	-	-	-	1,339
Issuance of common stock, net of offering costs	-	-	-	90,356
Payments received on stockholder notes	15	-	-	15
Reversal of accrued 12/99 private placement costs	-	-	-	182
Amortization of deferred compensation, net	-	-	-	916

BALANCE AT DECEMBER 31, 2000	(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	-	-	-	1,902
Issuance of common stock for notes	(277)	-	-	-
Issuance of common stock from option exercises	-	-	-	2,437
Issuance of common stock pursuant to the Employee				
Stock Purchase Plan	-	-	-	3,382
Issuance of common stock, net of offering costs	-	-	-	175,562
Amortization of deferred compensation, net	-	-	-	1,142
				-----
BALANCE AT DECEMBER 31, 2001	\$ (381)	\$ (69)	\$ (107,390)	\$310,393
				=====

See accompanying notes.



NEUROCRINE BIOSCIENCES, INC.

Statements of Cash Flows

(in thousands)

	Years Ended December 31,		
	2001	2000	1999
<b>CASH FLOW FROM OPERATING ACTIVITIES</b>			
Net loss .....	\$ (36,910)	\$ (28,808)	\$ (16,822)
Adjustments to reconcile net loss to net cash used in operating activities:			
Equity in NPI losses and other adjustments, net .....	-	-	885
Depreciation and amortization .....	2,651	2,198	2,066
Loss on abandonment of assets .....	198	80	133
Deferred revenues .....	5,737	3,907	(14)
Deferred rent .....	597	868	748
Non-cash compensation expense .....	4,024	2,677	497
Change in operating assets and liabilities:			
Accounts receivable and other current assets .....	(3,798)	(4,020)	(752)
Other non-current assets .....	(322)	1,014	(357)
Accounts payable and accrued liabilities .....	5,967	3,439	3,360
Net cash used in operating activities .....	(21,856)	(18,645)	(10,256)
<b>CASH FLOW FROM INVESTING ACTIVITIES</b>			
Purchases of short-term investments .....	(175,886)	(151,582)	(87,728)
Sales/maturities of short-term investments .....	163,054	78,348	68,562
Purchases of property and equipment, net .....	(3,805)	(2,440)	(2,061)
Net cash used in investing activities .....	(16,637)	(75,674)	(21,227)
<b>CASH FLOW FROM FINANCING ACTIVITIES</b>			
Issuance of common stock .....	179,486	93,360	41,016
Proceeds received from long-term obligations .....	3,483	1,741	981
Principal payments on long-term obligations .....	(1,666)	(984)	(957)
Payments received on notes receivable from stockholders .....	-	15	-

Net cash provided by financing activities .....	181,303	94,132	41,040
Net increase (decrease) in cash and cash equivalents .....	142,810	(187)	9,557
Cash and cash equivalents at beginning of the year .....	21,078	21,265	11,708
Cash and cash equivalents at end of the year .....	\$ 163,888	\$ 21,078	\$ 21,265

SUPPLEMENTAL DISCLOSURES

Supplemental disclosures of cash flow information:

Interest paid .....	\$ 312	\$ 228	\$ 231
Taxes paid .....	\$ 120	\$ 302	\$ -

See accompanying notes.

NEUROCRINE BIOSCIENCES, INC.

NOTES TO THE FINANCIAL STATEMENTS

December 31, 2001

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, cancer, multiple sclerosis and diabetes.

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. 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, 2001, 2000 and 1999, the Company had collaborative research agreements that accounted for 97%, 91% and 93%, 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 seven to eleven 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. Assets written-off during 2001 had a net book value of \$19,000. Accumulated amortization at December 31, 2001 and 2000 was \$841,000 and \$753,000, respectively.

Impairment of Long-Lived Assets. In accordance with Statement of Financial Accounting Standards (SFAS) No. 121, "Accounting for the Impairment of Long-Lived Assets and for Long-Lived Assets to Be Disposed Of," 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 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, 2001.

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, 2001, 2000 and 1999.

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 period earned. Milestone payments are recognized as revenue upon achievement of pre-defined scientific events. Revenues from government grants are recognized based on a percentage-of-completion basis as the related costs are incurred. The Company recognizes revenue only on payments that are nonrefundable and when the work is performed.

In December 1999, the Securities and Exchange Commission (SEC) issued Staff Accounting Bulletin (SAB) No. 101, "Revenue Recognition in Financial Statements." SAB 101 provides guidance in applying generally accepted accounting principles to revenue recognition in financial statements, including the recognition of nonrefundable up-front fees received in conjunction with a research and development arrangement. The adoption of this pronouncement was required effective with the fourth quarter of 2000.

As required by the adoption of SAB 101, the Company reviewed all up-front payments, license fees and milestones received in the current and prior years. 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 remote and unpredictable at the onset of the collaboration and

are based on the success of scientific efforts.

Based on that review, the Company determined that \$4.2 million of license fees received during 2000 were subject to the adoption of SAB No. 101. All other fees received relate to agreements under which the research portion of the collaboration has been completed or the agreements have been terminated entirely. In accordance with Accounting Principles Board (APB) Opinion No. 20, the adoption of SAB No. 101 was recognized by including the cumulative effect of the change in accounting principle in the net loss for the fourth quarter of 2000. The otherwise reported net loss for the year ended December 31, 2000 was increased by approximately \$3.8 million. These license fee revenues were deferred and will be amortized as income through 2005.

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 providing services under collaborative research agreements and grants. Research and development expenses relating to collaborative agreements and grants were approximately \$24.9 million, \$10.1 million and \$7.2 million during 2001, 2000 and 1999, respectively.

Stock-Based Compensation. As permitted by SFAS No. 123, "Accounting for Stock-Based Compensation," the Company has elected to follow 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.

In March 2000, the Financial Accounting Standards Board (FASB) issued Interpretation No. 44 (FIN 44), "Accounting for Certain Transactions Involving Stock Compensation - An Interpretation of APB Opinion No. 25". This interpretation clarifies the definition of employee for purposes of applying APB Opinion No. 25, the criteria for determining whether a plan qualifies as a non-compensatory plan, the accounting consequence of various modifications to the terms of a previously fixed stock option or award, and the accounting for an exchange of stock compensation awards in a business combination. FIN 44 was effective and the Company adopted the interpretation on July 1, 2000. The adoption did not have a material impact on the Company's results of operations.

Deferred charges for options granted to non-employees has 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 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. Deferred charges for options granted to non-employees are periodically remeasured as the underlying options vest and are included in deferred compensation in the financial statements.

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 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 2.0 million, 2.6 million and 642,000 for the years ended December 31, 2001, 2000 and 1999, 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.

Reclassifications. Certain reclassifications have been made to prior year amounts to conform to the presentation for the year ended December 31, 2001.

Impact of Recently Issued Accounting Standards. In June 2001, the FASB issued SFAS No. 141, "Business Combinations," and SFAS No. 142, "Goodwill and Other Intangible Assets." SFAS No. 141 supercedes APB No. 16, "Business Combinations," and SFAS No. 38, "Accounting for Preacquisition Contingencies of Purchased Enterprises," and requires that all business combinations be accounted for by a single method -- the purchase method. SFAS No. 141 also provides guidance on the recognition of intangible assets identified in a business combination and requires enhanced financial statement disclosures. SFAS No. 142 adopts a more aggregate view of goodwill and bases the accounting for goodwill on the units of the combined entity into which an acquired entity is integrated. In addition, SFAS No. 142 concludes that goodwill and intangible assets that have indefinite useful lives will not be amortized but rather will be tested at least annually for impairment. Intangible assets that have finite lives will continue to be amortized over their useful lives. SFAS No. 141 is effective for all business combinations initiated after June 30, 2001. The adoption of SFAS No. 142 is required for fiscal years beginning after December 15, 2001, except



for the nonamortization and amortization provisions, which are required for goodwill and intangible assets acquired after June 30, 2001. The adoption of SFAS No. 141 had no impact on the Company's financial position or results of operations. The Company will adopt SFAS No. 142 in the first quarter of 2002 and believes that the adoption will not have a material impact on its financial position or results of operations.

In October 2001, the FASB issued SFAS No. 144, "Accounting for the Impairment or Disposal of Long-Lived Assets," which establishes one accounting model to be used for long-lived assets to be disposed of by sale and broadens the presentation of discontinued operations to include more disposal transactions. SFAS No. 144 supercedes SFAS No. 121, "Accounting for the Impairment of Long-Lived Assets and for Long-Lived Assets to Be Disposed Of," and the accounting and reporting provisions of APB Opinion No. 30. SFAS No. 144 is effective for fiscal years beginning after December 15, 2001. The Company will adopt SFAS No. 144 in the first quarter of 2002 and believes that the adoption will not have a material impact on its financial position or results of operations.

Note 2. SHORT-TERM INVESTMENTS

Cash, cash equivalents, and short-term investments totaled \$320.0 million and \$164.7 million as of December 31, 2001 and 2000, 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
December 31, 2001				
US Government securities .....	\$ 6,000	\$ 17	\$ --	\$ 6,017
Corporate debt securities ....	150,163	--	(86)	150,077
Total securities ....	\$156,163	\$ 17	\$ (86)	\$156,094

December 31, 2000

US Government securities .....	\$ 2,000	\$ --	\$ (3)	\$ 1,997
Corporate debt securities ....	141,331	264	--	141,595
	-----	-----	-----	-----
Total securities ....	\$143,331	\$ 264	\$ (3)	\$143,592
	=====	=====	=====	=====

The amortized cost and estimated fair value of debt securities by contractual maturity at December 31, 2001 are shown below (in thousands):

	Amortized Cost	Estimated Fair Value
	-----	-----
Due in 12 months or less .....	\$113,597	\$113,618
Due between 12 months and 44 months .....	42,566	42,476
	-----	-----
	\$156,163	\$156,094
	=====	=====

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

	Years Ended December 31,		
	2001	2000	1999
	-----	-----	-----
Proceeds from sales .....	\$163,054	\$ 78,348	\$ 68,562
Gross realized gains on sales .....	\$ 583	\$ 304	\$ 4
Gross realized losses on sales .....	\$ (870)	\$ (32)	\$ (150)

NOTE 3. PROPERTY AND EQUIPMENT

Property and equipment at December 31, 2001 and 2000 consist of the following (in thousands):

	-----	-----
	2001	2000
	-----	-----
Land .....	\$ 4,661	\$ 5,003
Furniture and fixtures .....	1,583	2,051
Equipment .....	12,734	11,179
Leasehold improvements .....	1,238	1,113
	-----	-----
	20,216	19,346
Less accumulated depreciation ...	(8,128)	(8,046)
	-----	-----
Property and equipment, net .....	\$ 12,088	\$ 11,300
	=====	=====

Furniture and equipment under capital leases were \$10.3 million and \$8.5 million at December 31, 2001 and 2000, respectively. Accumulated depreciation of furniture and equipment under capital leases totaled \$5.0 million and \$5.0 million at December 31, 2001 and 2000, respectively. The Company entered into \$3.5 million of additional capital leases during 2001 and \$1.8 million during 2000.

NOTE 4. ACCRUED LIABILITIES

Accrued liabilities at December 31, 2001 and 2000 consist of the following (in thousands):

	-----	-----
	2001	2000
	-----	-----
Accrued employee benefits .....	\$ 2,438	\$ 2,992

Accrued professional fees .....	1,300	1,229
Accrued development costs .....	11,150	6,199
Other accrued liabilities .....	865	715
	-----	-----
	\$ 15,753	\$ 11,135
	=====	=====

NOTE 5. DEBT

During 1997, the Company partially financed the purchase of land under a five-year note payable for approximately \$747,000, which bears interest at a floating rate of prime plus one quarter percent (5.00% and 9.75% at December 31, 2001 and 2000, respectively). The note is repayable in equal monthly installments beginning February 1998. At December 31, 2001, the balance of the note was \$149,000, which is scheduled for repayment in the year 2002.

NOTE 6. COMMITMENTS AND CONTINGENCIES

Capital Lease Obligations. The Company has financed certain equipment under capital lease obligations, which expire on various dates through the year 2005 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 \$2.2 million and \$1.6 million at December 31, 2001 and 2000, respectively. Rent expense was \$1.7 million, \$2.5 million and \$2.7 million for

the years ended December 31, 2001, 2000 and 1999, respectively. Sublease income was \$698,000, \$1.2 million and \$1.2 million for the years ended December 31, 2001, 2000 and 1999, respectively.

The Company subleases a portion of the space to an unrelated party. The sublease will expire in March 2002. Future minimum sublease income to be received under non-cancelable subleases at December 31, 2001 will be approximately \$90,000 for the year ending December 31, 2002.

**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 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 \$13.8 million over the lives of these agreements, in addition to sales royalties ranging from 1% - 6%. 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, 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, 2001 are as follows (in thousands):

			Licenses &	
	Capital	Operating	Research	Development
	Leases	Leases	Agreements	Agreements
	-----			
Fiscal Year:				
2002 .....	\$ 2,277	\$ 2,626	\$ 884	\$ 26,330
2003 .....	1,749	2,731	507	17,422
2004 ....	1,504	2,841	263	4,355
2005 .....	686	2,954	20	-
2006 .....	-	3,072	10	-
Thereafter .....	-	23,854	40	-
	-----			
Total minimum payments .....	\$ 6,216	\$38,078	\$ 1,724	\$ 48,107
Less: amounts representing				
interest .....	(678)			
	-----			
Future minimum payments .....	5,538			
Less: current portion .....	(1,938)			
	-----			
Future payments on capital				
lease obligations .....	\$ 3,600			
	=====			

NOTE 7. SCIENCE PARK CENTER, LLC

In May 1997, the Company along with two unrelated parties formed a limited liability company in order to construct an office and laboratory facility. Science Park Center LLC (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 an LLC and leases the facility to a lessee. At least 3% of the third party funds represent at-risk equity and must remain at-risk to qualify as an operating lease. A synthetic lease is treated as an operating lease for accounting purposes and a financing lease for tax purposes. The Company selected the synthetic lease for financing advantages. The Company 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 is included in land and interest payments from the LLC and offset rent expenses recorded by the Company. The amount included in land at December 31, 2001 and 2000 was \$3.2 million and \$3.5 million, respectively. The interest income from the LLC note offset the Company's facilities expenses by approximately \$298,000, \$304,000 and \$331,000 for the years ended December 31, 2001, 2000 and 1999, respectively.

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 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,	
	-----	-----
	2001	2000
	-----	-----
Current assets .....	\$ 240	\$ 230
Building, net .....	14,038	14,564
Land .....	3,485	3,485
Deferred rent .....	2,196	1,646
	-----	-----
Total assets .....	\$19,959	\$19,925
	=====	=====
Current liabilities .....	\$ 112	\$ 5
Notes payable to Neurocrine .....	3,161	3,502
Building loan .....	14,280	14,444
Distribution payable .....	1,695	991
	-----	-----
Total liabilities .....	19,248	18,942
Retained earnings .....	711	983
	-----	-----
Total liabilities and shareholders' equity .....	\$19,959	\$19,925
	=====	=====



Science Park Center, LLC

Statements of Income

(unaudited, in thousands)

	Years Ended December 31,		
	-----	-----	-----
	2001	2000	1999
	-----	-----	-----
Rental income .....	\$3,076	\$3,076	\$3,087
Operating expenses .....	632	635	622
Interest expense, net .....	1,366	1,293	1,329
Income taxes .....	10	5	7
	-----	-----	-----
Net income .....	\$1,068	\$1,143	\$1,129
	=====	=====	=====

The Company receives disbursements from the LLC from retained earnings above and beyond the at-risk equity of the unrelated parties. The LLC accrues the disbursements payable to Neurocrine on a monthly basis and periodically makes cash payments to reduce those payables. The disbursements due Neurocrine are offset against rent expense recorded by the Company. Disbursements recorded by the Company for the years ended December 31, 2001, 2000 and 1999 were \$1.1 million, \$723,000 and \$855,000, respectively.

Note 8. 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 8.0 million shares of common stock for issuance upon exercise of options or stock purchase rights granted under the

1992 Incentive Stock Option Plan, 1996 Director Option Plan, 1997 NNL Stock Option 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 and may be designated as incentive stock options or nonstatutory stock options under the plans. Of the shares available for future issuance under the Option Plans, 3.9 million are outstanding grants and 909,000 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):

	2001		2000		1999	
	Weighted Average Exercise Options	Price	Weighted Average Exercise Options	Price	Weighted Average Exercise Options	Price
Outstanding at January 1 .....	3,911	\$12.75	3,158	\$ 5.91	2,793	\$6.02
Granted .....	980	31.17	1,136	29.66	1,142	6.03
Exercised .....	(850)	6.14	(354)	6.56	(412)	4.79
Canceled .....	(158)	19.09	(29)	11.69	(365)	6.52
Outstanding at December 31 ...	3,883	\$18.59	3,911	\$12.75	3,158	\$5.91

A summary of options outstanding as of December 31, 2001 follows (in thousands, except for weighted average remaining contractual life and weighted average exercise price data):

Options Outstanding			Options Exercisable		
Range of Exercise Prices	Outstanding as of 12/31/01	Weighted	Weighted Average Exercise Price	Exercisable As of 12/31/01	Weighted
		Average Remaining Contractual Life			Average Exercise Price
\$ 0.02 to \$ 4.88	642	4.2	\$ 3.42	540	\$ 3.29
\$ 4.94 to \$ 7.00	615	6.5	5.94	445	6.08
\$ 7.01 to \$10.25	602	5.6	8.21	565	8.13
\$11.19 to \$27.00	640	8.4	21.05	156	19.47
\$27.60 to \$34.50	698	9.0	32.22	166	33.69
\$34.98 to \$52.83	686	9.1	37.06	131	37.15
\$ 0.02 to \$52.83	3,883	7.2	\$18.59	2,003	\$11.27

The weighted average fair values (computed using Black-Scholes) of the options granted during 2001, 2000 and 1999 were \$20.54, \$20.51 and \$3.75, 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 2001, 2000 and 1999, respectively: risk-free interest rates of 4.4%, 5.0% and 6.4%; a dividend yield of 0.0% (for all years); volatility factors of the expected market price of the Company's common stock of .80, .81 and .74; 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 2001, 2000 and 1999 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, 2001, 2000 and 1999 follows (in thousands, except for loss per share data):

	2001	2000	1999
	-----	-----	-----
Net loss as reported .....	\$(36,910)	\$(28,808)	\$(16,822)
Loss per share			
(basic and diluted) .....	\$ (1.42)	\$ (1.30)	\$ (0.88)
Pro forma net loss .....	\$(44,188)	\$(31,057)	\$(18,303)
Pro forma loss per share			
(basic and diluted) .....	\$ (1.70)	\$ (1.40)	\$ (0.96)

Employee Stock Purchase Plan. The Company has reserved 525,000 shares of common stock for issuance under the 1996 Employee Stock Purchase Plan, as amended on May 24, 2001 (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, 2001, 369,000 shares have been issued pursuant to the Purchase Plan.

Warrants. The Company has outstanding warrants to purchase 376,000 shares of common stock at the following exercise prices. At December 31, 2001, all outstanding warrants were exercisable.

Warrants Outstanding at

Exercise Prices	December 31, 2001	Expiration
-----------------	-------------------	------------

\$ 8.04	15,000	11/2006
---------	--------	---------

\$10.50	301,000	03/2006
---------	---------	---------

\$41.41	60,000	11/2006
---------	--------	---------

-----

376,000

=====

The following shares of common stock are reserved for future issuance at December 31, 2001 (in thousands):

Stock option plans .....	4,792
Employee stock purchase plan .....	156
Warrants .....	376
	-----
Total .....	5,324
	=====

Note 9. SIGNIFICANT COLLABORATIVE RESEARCH AND DEVELOPMENT AGREEMENTS

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. The total collaborative value of the GSK collaboration is the largest in Neurocrine's history. For the year ended December 31, 2001, the Company recognized \$19.2 million in revenue under the GSK agreement. At December 31, 2001, the Company had \$6.9 million of deferred license fees and sponsored research revenues that will be amortized over the life of the agreement and as services are performed, respectively.

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. Together with Taisho, the Company formed a steering committee to oversee the worldwide development of NBI-6024. The Company will receive license fees, milestone

payments, and reimbursement of 100% of worldwide development expenses. In addition, the Company will receive payments on product sales for the term of the patents covering NBI-6024, subject to adjustment for payments to third parties. Taisho may terminate the agreement at its discretion upon prior written notice to us. In such event, all product rights would revert to the Company. For the years ended December 31, 2001 and 2000, the Company recognized \$16.6 million and \$7.1 million, respectively, in revenue under the Taisho agreement. No revenue was recognized in 1999. As of December 31, 2001, the Company had \$2.9 million of deferred license fees and sponsored research revenues that will be amortized over the life of the agreement and as services are performed, respectively.

Wyeth-Ayerst Laboratories. Effective January 1999, the Company entered into a collaboration and license agreement with Wyeth-Ayerst Laboratories (Wyeth-Ayerst) 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-Ayerst exclusive and non-exclusive rights to different portions of 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-Ayerst may terminate the agreement if they decide that the research is not successful, if they decide 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. For the years ended December 31, 2001, 2000 and 1999, the Company recognized \$3.4 million, \$3.0 million and \$6.0 million, respectively, in revenues under the Wyeth-Ayerst agreement.

The three-year term of the sponsored research under the Wyeth-Ayerst agreement was scheduled to terminate January 1, 2002. However, in December 2001, the Company and Wyeth-Ayerst agreed to extend the term of the sponsored research for a period of three months during which time Neurocrine and Wyeth-Ayerst will discuss a further extension. In connection with the three-month extension, the Company received \$375,000 of sponsored research funding.

Eli Lilly and Company. In October 1996, the Company entered into a research and license agreement with Eli Lilly and Company (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 R2 agonists for central nervous system diseases and disorders. Under the agreement, the Company received and recognized three years of sponsored research and development payments totaling \$17.2 million. The Company also is entitled to milestone payments for certain development and regulatory accomplishments. The Company 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. The Company 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. The Company believes Eli Lilly is not planning any specific future development efforts. Therefore, no further payments are anticipated under this agreement. For the year ended December 31, 1999, the Company recognized \$3.2 million in revenue under the Eli Lilly agreement. No revenues were recognized for the years ended December 31, 2001 and 2000.

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 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. All collaboration products identified under the 1999 agreement are subject to the same terms and conditions as the products arising under the 1995 agreement. This additional research was completed in February 2001. The 1999 agreement provides that in August 2001 Neurocrine was to receive either a \$3.5 million milestone payment from Janssen or exclusive rights to the first generation back-up compounds. The Company agreed to postpone the August event to allow Janssen to complete certain studies with the back-up program compounds. 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 R1 antagonist compounds developed thereunder reverted to Neurocrine. We do not expect additional payments of any kind under the Janssen agreement.

For the years ended December 31, 2001, 2000 and 1999, the Company recognized \$525,000, \$3.0 million and \$2.4 million, respectively, in revenues under terms of the Janssen agreements.

Novartis. In January 1996, the Company entered into an agreement with Novartis under which Novartis paid the Company \$5.0 million in up-front license fees and was obligated to provide the Company with \$7.0 million in research and development funding during the first two years of the agreement. For the years ended December 31, 2000 and 1999, the Company recognized \$90,000 and \$3.6 million in revenue under the Novartis agreement.

On July 7, 1999, Novartis exercised its right to terminate the agreement, effective January 7, 2000. As a result, the Company reacquired the worldwide rights to its multiple sclerosis compound.

Note 10. Related Party Transactions

Neuroscience Pharma, Inc. In March 1996, the Company along with a group of Canadian institutional investors (the Canadian Investors) established Neuroscience Pharma, Inc. (NPI). The Company's contribution was to license certain technology and Canadian marketing rights to NPI. The Canadian Investors contributed approximately \$9.5 million in cash in exchange for shares of NPI preferred stock (the Preferred Shares), which was convertible into shares of the Company's common stock at the option of the Canadian Investors. In addition, the Canadian Investors received warrants exercisable for 383,875 shares of the Company's common stock at an exercise price of \$10.50 per share and may be eligible to receive additional warrants upon the attainment of certain additional funding. As of December 31, 2001, 82,691 warrants have been exercised.

During 1997 and 1998, the Canadian Investors converted their Preferred Shares to shares of the Company's Common Stock. As a result, the Company recorded an investment in NPI equal to the market value of Common Stock issued in exchange for the Preferred Shares and has recognized its proportionate share of the NPI net losses in accordance with the equity method of accounting. Equity in NPI losses totaled \$764,000 in 1999.

During 1996, the Company entered into a sponsored research agreement with NPI. The terms of the agreement called for NPI to fund additional research efforts on technologies licensed to NPI by the Company. Associated with the costs of research on those certain programs, the Company recognized revenues of \$491,000 during 1999.

The Preferred Shares were redeemable for cash at the Company's option. The redemption feature of the Preferred Shares limited their value to the balance of cash and cash equivalents maintained by NPI. Consequently, the Company reduced the value of its NPI investment by \$647,000 during 1999. The balance of the Company's investment in NPI was \$0 at December 31, 1999.

In December 1999, the Company sold its investment in NPI in exchange for cash, receivables and potential royalties on worldwide sales resulting from

certain of NPI's future products. The Company recorded a gain of \$526,000 on the sale of this investment. The gain was calculated using the total consideration of cash and receivables, less the carrying value of the NPI investment. No value was assigned to potential royalties on future product sales due to the uncertainty of this event. This transaction, as well as those discussed above, is included in "Equity in NPI losses and other adjustments, net" reported on the Statements of Operations.

Note 11. Income Taxes

At December 31, 2001, the Company had Federal and California income tax net operating loss carry-forwards of approximately \$76.0 million and \$23.8 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 \$1.3 million and \$5.7 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, 2001 and 2000 are shown below. A valuation allowance of \$45.7 million and \$27.2 million at December 31, 2001 and 2000, 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:

	2001	2000
	-----	-----
Deferred tax assets:		
Net operating loss carry-forwards .....	\$ 27,975	\$ 16,487
Tax credit carry-forwards .....	13,283	8,140
Capitalized research and development .....	3,733	2,098
Other, net .....	729	479
	-----	-----
Total deferred tax assets .....	45,720	27,204
Valuation allowance .....	(45,720)	(27,204)
	-----	-----
Net deferred tax assets .....	\$ -	\$ -
	=====	=====

The provision for income taxes on earnings subject to income taxes differs from the statutory Federal rate at December 31, 2001, 2000 and 1999, due to the following:

	2001	2000	1999
	-----	-----	-----
Federal income taxes at 34% .....	\$(12,582)	\$(9,692)	\$(5,719)
State income tax, net of Federal benefit ...	(1,736)	-	-
Tax effect on non-deductible expenses .....	(4,202)	335	932
Increase in valuation allowance .....	18,520	9,357	4,787
	-----	-----	-----

\$ - \$ - \$ -  
 =====

NOTE 12. 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 \$359,000 for the year ended December 31, 2001. No employer contributions were made in 2000 and 1999.

NOTE 13. SELECTED QUARTERLY FINANCIAL DATA (UNAUDITED)

The following is a summary of the quarterly results of operations for the years ended December 31, 2001 and 2000 (unaudited, in thousands, except for earnings (loss) per share data):

	Quarters Ended				Year Ended
	Mar 31	Jun 30	Sep 30	Dec 31	Dec 31
Fiscal Year Ended 2001					
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



	Quarters Ended					Year Ended
	Mar 31	Jun 30	Sep 30	Sep 30	Dec 31	Dec 31
			As Reported	Restated (1)		
Fiscal Year Ended 2000						
Revenues .....	\$ 2,778	\$ 2,942	\$ 5,323	\$ 2,426	\$ 6,442	\$ 14,588
Operating expenses .....	10,004	10,322	15,008	15,008	14,855	50,189
Net Loss .....	(6,047)	(5,192)	(8,135)	(11,032)	(6,537)	(28,808)
Loss per share -						
Basic and Diluted .....	\$ (0.28)	\$ (0.24)	\$ (0.37)	\$ (0.50)	\$ (0.29)	\$ (1.30)
Shares used in the calculation of						
loss per share:						
Basic and Diluted .....	21,771	21,897	22,032	22,032	22,789	22,124

(1) During the fourth quarter of 2000, the Company adopted SAB 101, Revenue Recognition in Financial Statements. SAB 101 provides, among other revenue items, guidance in the recognition of nonrefundable, up-front fees received in conjunction with a research and development arrangement. The result of the adoption of SAB 101 was to reduce recognition of license fee revenues reported during the third quarter of 2000 by \$2.9 million. These revenues were deferred and will be recognized as income, ratably over the estimated lives of the respective agreements. The adoption of SAB 101 did not require an adjustment for revenues recorded prior to December 31, 1999.





CONSENT OF ERNST & YOUNG LLP, INDEPENDENT AUDITORS

We consent to the incorporation by reference in the Registration Statements (Form S-3 Nos. 333-73216, 333-47252, 333-95005) and (Form S-8 Nos. 333-65198, 333-57096, 333-44012, 333-57875) of our report dated January 25, 2002, with respect to the financial statements of Neurocrine Biosciences, Inc. included in the Annual Report (Form 10-K) for the year ended December 31, 2001.

/s/ Ernst & Young LLP

Ernst & Young LLP

San Diego, California

March 26, 2002