SECURITIES AND EXCHANGE COMMISSION
Washington, D.C. 20549

FORM 10-K

(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, 2000
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 of incorporation or organization)	(I.R.S. Employer 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. [X]

The aggregate market value of the voting stock held by non-affiliates of the Registrant as of March 23, 2001 totaled approximately $344,192,047 million based on the closing stock price as reported by the Nasdaq National Market. As of March 23, 2001, there were 25,428,731 shares of the Registrant's Common Stock, $.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 24, 2001 (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, 2000.

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PART I

Forward-Looking Statements

This Annual Report on Form 10-K and the information incorporated 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. A number of factors could cause results to differ materially from those anticipated by the forward-looking statements, including those discussed under "Risk Factors" and "Management's Discussion and Analysis of Financial Condition and Results of Operations." You should be aware that the occurrence of any of the events discussed under "Risk Factors" and elsewhere in this prospectus 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

Overview

Neurocrine Biosciences, Inc. is a product-based biopharmaceutical company focused on neurologic and endocrine diseases and disorders. Our product candidates address some of the largest pharmaceutical markets in the world including insomnia, anxiety, depression, cancer and diabetes. We currently have 15 programs in various stages of research and development. Of these 15 programs, five programs are in clinical development and three programs are in advanced preclinical development which we expect to progress into human clinical trials in the near future. We believe the other seven research projects will help supply clinical development candidates in the future. While we independently develop the majority of our product candidates, we utilize collaborators in four of our 15 programs, including Janssen Pharmaceutica, a subsidiary of Johnson & Johnson, Wyeth-Ayerst Laboratories, a division of American Home Products, Taisho Pharmaceutical and Eli Lilly. Under these collaborations, we receive funds for product development, in addition to receiving milestone payments and royalties on worldwide product sales.

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 five projects in clinical development, three programs in advanced preclinical development which we expect to progress into the clinic in the near future, and seven 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 utilize a multidisciplinary research approach to identify and validate novel drug targets for internal development or collaboration. For example, corticotropin-releasing factor, 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 orally available 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 150 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 commercial or co-promotional 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. Our current strategic alliances include:

- Janssen, to focus on corticotropin-releasing factor receptor antagonists to treat anxiety and depression;
- Wyeth-Ayerst, to research, develop and commercialize compounds to treat neurodegenerative and psychiatric diseases;
- Taisho, to develop our compound to treat Type 1 Diabetes in which the body does not produce enough insulin; and
- Eli Lilly, to collaborate in the discovery, development and commercialization of 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. In May 1998, we licensed from the National Institutes of Health an interleukin 4 fusion toxin that is currently in clinical trials for recurrent malignant glioma. 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 melanocortin technology and other intellectual property 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 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. These alliances include:

- our alliance with Rigel, Inc. to use Rigel's intellectual property and expertise to discover novel protein targets involved in neural cell and antibody activation;

- our alliance with Arena Pharmaceuticals involving the application of Arena's constitutive activation technology to a family of receptors;

- our alliance with Array Biopharma, Inc. to design and synthesize a focused library of small molecules; and

- our alliance with Caliper Technologies Corp. to utilize Caliper's proprietary microfluidics technology to screen against our targets.

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 preclinical 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 Product Pipeline

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

Program	Compound	Targeted Indication	Status	Commercial Rights
PRODUCTS UNDER DEVELOPMENT:				
GABA-A Agonist	NBI-34060	Insomnia	Phase II	Neurocrine
CRF R1 Antagonist	NBI-37582	Anxiety, Depression	Preclinical	Janssen/ Neurocrine
CRF R1 Antagonist	NBI-34041	Anxiety, Depression	Phase I	Neurocrine
IL-4 Fusion Toxin	NBI-3001	Malignant Glioma	Phase II	Neurocrine
IL-4 Fusion Toxin	NBI-3001	Additional Cancers (kidney, lung)	Preclinical	Neurocrine
Altered Peptide Ligand	NBI-5788	Multiple Sclerosis	Phase II	Neurocrine
Altered Peptide Ligand	NBI-6024	Type 1 Diabetes	Phase I/II	Taisho/Neurocrine
GnRH Antagonist		Endometriosis, Prostate Cancer	Preclinical	Neurocrine
RESEARCH:				
Excitatory Amino Acid Transporters		Neurodegenerative Diseases	Research	Wyeth-Ayerst/ Neurocrine
CRF R1 Antagonist		Gastrointestinal Disorders	Research	Neurocrine
CRF R2 Antagonist		Eating Disorders	Research	Neurocrine
Urocortin/CRF R2 Agonist		Obesity	Research	Eli Lilly
Melanocortin Receptor Agonist		Obesity	Research	Neurocrine
Melanin Concentrating Hormone Antagonist		Obesity	Research	Neurocrine
Hypocretin Agonist/Antagonist		Sleep Disorders	Research	Neurocrine

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

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

"Preclinical" indicates that a drug candidate is being selected, or has been selected, and is undergoing toxicology studies and manufacturing to allow for Phase I clinical trials.

"Development" indicates that lead compounds have been discovered that meet certain laboratory and preclinical criteria. These compounds may undergo structural modification and more extensive evaluation prior to selection for preclinical development.

"Research" indicates identification and evaluation of compounds in laboratory and preclinical models.

Products Under Development

GABA-A Agonist

Insomnia is a prevalent neurological disorder in the United States, with up to 58% of the adult population reporting one or more symptoms of insomnia a few nights per week or more, according to the National Sleep Foundation. 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, was used as sedatives to treat insomnia. The most well-known of the benzodiazepines is Valium(R). 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, hangover effects the next day, 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 as Ambien(R) and Sonata(R). Ambien(R) is the current leader with worldwide sales in 2000 of approximately $840 million.

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 produces their sleep-promoting effects. However, NBI-34060 is more potent than the currently marketed non-benzodiazepines, including Ambien(R) and Sonata(R), and is more selective than the benzodiazepines 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 preclinical 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. NBI-34060 also appears to be devoid of next day hangover effects and we expect it to have a considerably reduced amnesic 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.

Researchers designed the first Phase I clinical trial on NBI-34060 to determine the safety and tolerance of NBI-34060 and provide a preliminary

evaluation of the sedative potential in 42 normal volunteers as reflected in self-ratings of drowsiness, disruption of memory and impairment of coordination. In this trial, subjects tolerated NBI-34060 well, and reported no serious or unexpected adverse side effects. The subjects consistently reported drowsiness, indicating strong potential for the sedative properties of the compound. Subsequently, in the first quarter of 1999, we completed a second Phase I clinical trial in 30 healthy volunteers to further explore the safety and kinetic profile of NBI-34060. As demonstrated in the first Phase I trial, NBI-34060 demonstrated a very good safety profile.

In 1999, we completed a Phase II placebo-controlled multi-center clinical trial evaluating the efficacy of NBI-34060 in 228 subjects with transient insomnia. Transient insomnia means occasional sleeplessness caused by environmental factors, such as jetlag. The trial was conducted in a sleep laboratory employing objective assessments of sleep onset and safety. The results indicated that NBI-34060 is safe and effective in helping subjects with transient insomnia achieve rapid sleep without the next day residual effects associated with most currently marketed sedatives. The results showed that the primary clinical endpoint and the required regulatory endpoint for approval, time to sleep onset, was reached at a statistically significant level. In this trial, those subjects receiving NBI-34060 took a mean time of 16 minutes to progress to sleep onset versus a mean time of 34 minutes in the placebo group. These results were statistically significant at $p < 0.001$. This means that applying widely used statistical methods, the chance that these results could have occurred by accident was less than one in 1,000. In addition, the data indicated that a majority of subjects in the treated group fell asleep within 9.5 minutes as indicated by the median time to sleep onset as compared to 23 minutes in the placebo group.

Results of a Phase II clinical trial comparing NBI-34060, Ambien(R) and zopiclone relative to placebo during middle of the night dosing, demonstrated that NBI-34060 does not lead to next-day hangover effects, while both Ambien(R) and zopiclone exhibited statistically significant measures of next-day adverse side effects of residual sedation. In two clinical trials evaluating the effects of NBI-34060 on the largest target populations for insomnia (the elderly and females), results demonstrated that NBI-34060 showed no significant pharmacokinetic differences in age or gender. In a randomized, double-blind, placebo-controlled clinical study with multiple doses of NBI-34060 conducted in young adults and elderly subjects, results demonstrate that NBI-34060 works as a sedative-hypnotic with no major differences in the pharmacokinetics for maximum plasma levels or total drug exposure between young adults and elderly subjects. Also, there were no changes between these patient populations in the accumulation of NBI-34060 after four consecutive nightly doses. Safety evaluation and subjective measures of next-day residual effect confirmed that the drug was well-tolerated in both groups with the expected sedation during the night, and with no hangover or residual carry over next-day effect.

Based on the results from our Phase II trials, we have moved to expand clinical development of NBI-34060. In 2000 we initiated nine clinical trials involving 503 subjects to evaluate various formulations and patient subgroups. Among other research goals, we intend to determine whether NBI-34060 is effective in treating chronic insomnia, which is sleeplessness not caused by environmental factors. We are developing a formulation of NBI-34060 to treat chronic insomnia. We are also designing a large-scale pivotal Phase III program, from which we expect to determine the approvability of the drug candidate. Currently, we expect to begin this pivotal trial in the second half of 2001.

Another important feature of NBI-34060 is its relatively short half-life, or duration of action of the compound, in the body. The levels of NBI-34060 in the blood stream reach the highest point 30 minutes after the subject takes the tablet. The NBI-34060 is then rapidly removed from the blood stream so 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 of the drug. 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 hangover that occurs with the longer acting drugs like Ambien(R) and the benzodiazepines. We also believe that this short duration of action will allow 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 FDA for maintaining, rather than simply inducing, sleep.

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 approximately $11.1 billion worldwide in 1999, with sales anticipated in excess of $12.6 billion in 2000 according to market analyst reports from Datamonitor. However, there remain significant unmet medical needs. The leading drug class, known as the selective serotonin re-uptake 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. Corticotropin-releasing factor antagonists may provide such an advance in anti-depressant therapy through a specific mechanism for combating the hormonal abnormalities associated with 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. Corticotropin-releasing factor 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 corticotropin-releasing factor, which induces the physical effects that are associated with stress and which can lead to depression or anxiety.

The novelty and specificity of the corticotropin-releasing factor mechanism of action and the prospect of improving upon selective serotonin re-uptake 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 corticotropin-releasing factor, or CRF, field through our intellectual property portfolio and relationship with experts in the neuropsychiatric field. Wylie Vale, Ph.D., our co-founder and Chief Scientific Advisor, is considered to be a leader in this field of research. We have further characterized the CRF receptor system and have identified additional members of the CRF receptor family. We have received patents 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(R), Zoloft(R), Paxil(R) and Celexa(R) 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 anti-depressant therapies is their slow onset of action.

In our CRF R1 antagonist program, our corporate collaborator, Janssen Pharmaceutica, selected a CRF R1 receptor antagonist drug candidate, NBI-30775, for preclinical studies in 1996. Janssen initiated and completed a number of Phase I clinical trials on the compound in late 1998 and initiated a Phase IIa open label trial 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, Janssen administered NBI-30775 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. We were strongly encouraged by these results, which we believe support the hypothesized mechanism of action. While this trial found NBI-30775 to be safe, 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. However, because of the positive efficacy results for NBI-30775, Janssen decided to proceed with a back-up compound identified from its research relationship with us. In 2000, Janssen selected a back-up candidate to develop, NBI-37582. This candidate is currently in late preclinical testing.

In addition to our CRF R1 program with Janssen, we are conducting an independent CRF R1 antagonist program focused on a series of our proprietary chemical compounds. We have selected several lead candidates for this program and entered into Phase I clinical trials in December 2000. This Phase I, randomized, double-blind, placebo-controlled, single-dose trial was conducted in 48 normal healthy volunteers and was designed to evaluate the safety, tolerability, pharmacokinetics, and pharmacodynamics, including endocrine profiles, over a range of six escalating doses. Initial pharmacokinetic evaluation indicates rapid absorption and good dose-proportionality and plasma half lives supportive of a once-a-day dosing schedule. No safety issues were noted which would preclude advancement into the next phase of clinical evaluation. A two week multiple dose, dose-escalating Phase I placebo controlled clinical trial will be initiated to further evaluate the safety and endocrine profiles of this compound to prepare for Phase II efficacy evaluation. We anticipate initiating Phase II clinical trials in the second half of 2001.

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, Janssen or we may decide not to initiate Phase I 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(R) and Xanax(R), 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 these adverse effects, total sales of benzodiazepines were approximately $800 million in 1999. 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.

With our corporate collaborator, Janssen, and in our independent CRF R1 antagonist program, we are developing small molecule therapeutics to block the effects of overproduction of CRF in anxiety. As a co-examined variable in the Janssen 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 preclinical 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, Janssen or we may decide not to initiate clinical testing of CRF R1 antagonist compounds for anxiety. Even if those trials are conducted, the data may not support continuation of the program and additional clinical trials.

IL-4 Fusion Toxin

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

In 1998, we exclusively licensed from the National Institutes of Health 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 bacterial 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. The most common form of malignant brain cancer is malignant glioma. These tumors arise within the brain and generally remain confined to the brain. According to the American Cancer Society, despite surgical, radiation and chemotherapy treatments, the median survival rate for malignant glioma is only in the range of 9 to 12 months. The clinical course of malignant glioma is characterized by relentless loss of vital neurological functions and death within approximately 12 months.

In 1999 we initiated a Phase I/II trial of NBI-3001 in patients with malignant glioma in which the primary endpoints were safety and tumor regression. 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:

- seven patients, or 26%, experienced complete remissions, defined as no evidence of viable tumor;
- 10 patients, or 37%, experienced a partial response, defined as greater than 50% reduction in tumor mass; and
- 10 patients, or 37%, continued to suffer from stable or progressive disease.

In addition, the six-month median survival data showed trends toward efficacy. We initiated an additional confirmatory Phase II trial to further establish dosing regiment, safety and efficacy in the fourth quarter of 2000. We also plan to initiate a Phase III trial in the second half of 2001.

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 are conducting preclinical 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 preclinical models. We plan to initiate a Phase I clinical trial in the second quarter of 2001 to first investigate the safety and efficacy of NBI-3001 against kidney and non-small-cell lung cancers. 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 preclinical 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 Ligands

The American Autoimmune Related Diseases Association estimates that over 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, bacterias 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 an estimated 350,000 cases of multiple sclerosis in the United States and a similar number of patients in Europe with approximately 17,000 new cases diagnosed worldwide each year. 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.

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 know as myelin basic protein. We designed a novel altered peptide ligand based on myelin basic protein that would target the autoreactive T cells that cause neurological damage in multiple sclerosis. Together with Novartis Pharmaceuticals Corporation, our former collaborative partner for this program, we filed an investigational new drug application with the FDA and received approval in 1996 to commence clinical trials. We subsequently completed Phase I clinical trials, and initiated two Phase II clinical trials of our altered peptide ligand for the treatment of multiple sclerosis, NBI-5788, in 1999.

The first Phase II trial was a multi-center, placebo controlled, randomized parallel group design involving three doses of the altered peptide ligand in 5, 20, and 50 mg weekly doses for four months in 13 centers in North America and Europe. In July 1999 while the Phase II trials were underway, Novartis exercised its right to terminate the collaboration effective January 2000. Subsequently, the Data and Safety Monitoring Board for the trial recommended, and we agreed, that administration of the trial drug be discontinued based on reports of adverse allergic reactions. We continued to evaluate all of the enrolled patients in the study through December 1999 in accordance with the study protocol. We reacquired all rights to the program from Novartis on January 7, 2000 and initiated data analysis. The final data analysis from the multi-center trial showed no increases in either clinical relapses or in new lesions in all patients, even those with allergic reactions. Of the patients completing the double-blind phase of the study, the total volume of enhancing lesions was reduced in the 5 mg dose group compared to the placebo-control patents ($p<0.029$ Mann Whitney for two treatments). We could not conduct this same secondary analysis in the 20 mg or 50 mg groups, since there were not enough patients with positive scans for us to evaluate their magnetic resonance imaging changes. Moreover, 57% of the patients in the 5 mg group experienced reductions in the volume of new enhancing lesions compared to 25% in the placebo group. Because of these factors, we believe that for this compound, optimal dosing may be at lower levels, and we are currently planning a Phase IIb trial to establish the efficacy profile and optimum dosing regiment for NBI-5788.

The second Phase II trial, which we conducted in collaboration with the National Institutes of Health, involved an open-label, unblinded, non-placebo control trial in eight patients, seven of whom received multiple injections of 50 mg weekly while the final subject received 5 mg. In this trial, published in Nature Medicine, the authors observed a higher incidence of new brain lesions in two patients who received 50 mg doses and the one patient who received 5 mg doses. As a result, the trial was stopped. However, the authors did not provide direct evidence that NBI-5788 triggered the lesions.

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. Type 1 diabetes is one of the most prevalent chronic childhood conditions in North America, afflicting approximately one million patients in 1999. 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 pre-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 preclinical 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 2 Phase I safety and dose escalating clinical program in diabetic patients. These trials included 50 Type 1 diabetic patients. Data from this trial indicates that NBI-6024 is safe and well tolerated. We are enrolling patients for an additional Phase I multi-dose trial and expect to initiate the first Phase II trial in early 2001 to assess the safety and biological activity of multiple doses of NBI-6024 in adult, adolescent and pediatric patients with Type 1 diabetes and a Phase II/III trial in the third quarter of 2001.

In January 2000, we entered into an agreement with Taisho Pharmaceutical Co., Ltd. providing Taisho with an exclusive option to obtain European, Asian and North American rights to NBI-6024. In July 2000, Taisho exercised the option as to European and Asian rights, and we granted Taisho exclusive rights to NBI-6024 in those regions. Under the collaboration agreement, 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 upon commercialization. In November, 2000 we expanded our collaboration with Taisho, granting Taisho the exclusive rights to develop and commercialize NBI-6024 in North America and other countries outside of Europe and Asia. The worldwide collaboration is valued at up to $100 million, including all potential licensing fees, purchase fees, milestones and development expenses.

We face the risk that large-scale studies of our drug in Type 1 diabetes patients may show different results than our preclinical studies in animals and in cells derived from Type 1 diabetes patients or our Phase I trials.

Gonadotropin-Releasing Hormone Receptor

Gonadotropin-releasing hormone, or GnRH, is a brain peptide that stimulates the secretion of the pituitary hormones that are responsible for sex steroid production and normal reproductive function. Researchers have found that chronic administration of GnRH agonists reversibly shuts down this transmitter pathway and is clinically useful in treating hormone-dependent diseases such as prostate cancer and endometriosis. Other companies have developed several peptide drugs on this principle, such as Lupron(R) and Zoladex(R), and according to market analyst reports by Euromonitor and Epicom Business Intelligence, these drugs now have an estimated market size in excess of $2.0 billion annually worldwide. However, since these drugs are peptides, they must be injected rather

than taken orally. These types of agonists take up to several weeks to exert their effect, a factor not seen with direct gonadotropin-releasing hormone antagonists. Until these drugs exert their effects, they have shown a tendency to exacerbate the condition.

We believe that there is a large market potential for an orally delivered gonadotropin-releasing hormone antagonist that does not have the tendency to initially exacerbate the patient's condition. We have screened our small molecule library and conducted structure activity studies to produce small molecule orally-active gonadotropin-releasing hormone antagonists. We have identified several series of small molecule compounds and are conducting additional studies to select a final clinical candidate. We intend to select a lead clinical candidate in the first half of 2001 and expect to initiate Phase I clinical trials in the second half of 2001. We believe that the results of these Phase I studies will be predictive of efficacy in many potential indications. We face the risk that our work in this area may not lead to clinical candidates or that, even if we select a candidate, clinical trials may show it is not safe and effective.

We plan to focus our clinical efforts on prostate cancer and in the area of women's health, including endometriosis, uterine fibroids and infertility. According to a 1993 article in Contemporary OB/GYN, researchers believe that more than five million women in the U.S. alone are affected by chronic endometriosis, representing approximately 10% prevalence in reproductive age women. Of those afflicted, approximately 200,000 patients are treated in a hospital setting, and an additional 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 in the treatment of prostate cancer, which has over 180,000 new cases per year 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(R), 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 Laboratories, a division of American Home Products Corporation, 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 preclinical 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 National Institutes of Health 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 Peripheral Uses

Recent reports have suggested that corticotropin-releasing factor, or 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 up to 15% of American adults, mostly women, 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. We are evaluating our proprietary CRF R1 antagonists for treatment of irritable bowel syndrome. We face the risks that preclinical 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 Antagonists

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.

CRF R2 Agonists/Urocortin Agonist

CRF R2 agonists may represent a therapeutic strategy to elevate CRF and a related neuropeptide called urocortin. Preliminary data indicate 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 three-year research collaboration with Eli Lilly to screen and optimize CRF R2 agonists. In October 1999, the funded research portion of the program was completed as scheduled and Eli Lilly 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 Agonists/Antagonists

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. When melanocyte stimulating hormone is injected, 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. We hope to identify an orally active subtype 4 agonist compound. However, we may fail to do so and we face the risk that our melanocortin research will not lead to product candidates.

Melanin Concentrating Hormone Antagonists

Recent studies suggest that melanin concentrating hormone 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. Thus, we have identified the melanin concentrating hormone receptor as a compelling drug target that may

be complementary to other obesity/anorexia drug targets in our drug discovery pipeline. We face the risk that our research in this area will not lead to product candidates.

Hypocretin

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. It is possible that the hypocretin system also contributes 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.

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.

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 (NBI-VL) containing over 108 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 (GPCR's). 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 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:

Janssen Pharmaceutica, N.V. In January 1995, we entered into the first of two research and development agreements with Janssen Pharmaceutica, N.V., an indirect wholly-owned subsidiary of Johnson & Johnson, to collaborate in the discovery, development and commercialization of small molecule CRF R1 antagonists for the treatment of anxiety, depression and substance abuse. These collaborations utilize our expertise in cloning and characterizing CRF R1 subtypes, CRF pharmacology and medicinal chemistry. 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 term of the licenses are for the term of the patents licensed under the agreement. Pursuant to this agreement, we have received $2.0 million in up-front license payments and are eligible to receive royalties on product sales for the term of the patents covering the compounds subject to reduction for payments to third parties. We may also receive royalties for products not covered by issued patents and agreed minimum annual royalties. In addition, we have the option of co-promoting the first marketed product from the collaboration in North America for five years. The 1995 agreement will terminate upon the expiration of the patents covering the collaboration products but may also be terminated for failure by either party to meet its obligations, bankruptcy, or in some circumstances, upon assignment of the agreement by Janssen or us. In 1996 Janssen selected a clinical candidate from the compounds discovered in connection with the first Janssen agreement and commenced clinical trials in Europe. 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 will receive 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.

Under the Janssen agreements, we are entitled to receive up to $39.2 million for sponsored research, milestones and license fees, plus additional amounts for potential royalties and reimbursement of outside costs. The amount we are entitled to receive includes $14.7 million for sponsored research and $2.0 million in license fees, plus up to $22.5 million in milestone payments for the indications of anxiety, depression and substance abuse, in each case upon achievement of development and regulatory goals. As of December 31, 2000, we have received a total of $20.6 million, including $14.3 million in sponsored research, $3.5 million in milestones, $2.0 million in license fees and $755,000 for reimbursement of outside costs. Janssen is responsible for funding all clinical development and marketing activities, including reimbursement to us for our promotional efforts, if any. In connection with the 1995 agreement, Johnson & Johnson Development Corporation purchased $5.0 million of our common stock.

Taisho Pharmaceutical Co., Ltd. In December 1999, we entered into an agreement with Taisho Pharmaceutical Co., Ltd. providing to Taisho 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 this option, we a received $2.0 million option fee. In June 2000, Taisho exercised its option as to Europe and Asia, and a steering committee, comprised of delegates from both companies, was formed to oversee the development of NBI-6024. Pursuant to that agreement, we will receive license fees, milestone payments and reimbursement of development expenses. In addition, if the compound is ultimately commercialized, we will receive payments on product sales in Europe and Japan for the term of the patents covering NBI-6024 subject to adjustment for payments to third parties. In November 2000, we expanded our collaboration with Taisho, granting Taisho the exclusive rights to develop and commercialize NBI-6024 in North America and other countries outside of Europe and Asia. The worldwide collaboration is valued at up to $100 million, including all potential licensing fees, purchase fees, milestones and development expenses. As of December 31, 2000, we have received a total of $4.0 million in license fees, $4.0 million in milestone payments, and $829,000 in reimbursements of development costs. The license fees were deferred and are being recognized as revenues over the life of the agreement at $319,000 in 2000, $818,000 in each of the years 2001 through 2004 and $409,000 in 2005.

Wyeth-Ayerst Laboratories. Effective January 1999, we entered into a Collaboration and License Agreement with Wyeth-Ayerst Laboratories, a division of American Home Products Corporation, relating to the research, development and commercialization of compounds that control excitatory amino acid transporters for the treatment of neurodegenerative and psychiatric diseases. Pursuant to the agreement, we are entitled to receive up to $80.3 million for sponsored research and milestones, plus additional amounts for potential royalties. The amount we are entitled to receive consists of $11.0 million for sponsored research over a three-year period, plus up to $69.3 million in milestone payments upon achievement of certain research, development and regulatory events. We have granted Wyeth-Ayerst exclusive and non-exclusive rights to our excitatory amino acid transporters technology as well as exclusive rights to any products developed during the collaboration. These licenses are for the term of the patents licensed. We will receive royalties on product sales for the terms of the patents covering the collaboration products, subject to adjustments for royalties payable to other parties. We will also receive royalties for products that are not the subject of issued patents. We also have 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 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, 2000, we have received $6.0 million in sponsored research payments, $3.0 million for the achievement of four milestones and $50,000 in license fees, which are being deferred and recognized over the life of the agreement.

Eli Lilly and Company. In October 1996, we entered into a research and license agreement with Eli Lilly and Company 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 were entitled to receive three years of funded research payments. 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. Through October 1999, we received a total of $17.2 million in research and development payments under the agreement. We have granted Eli Lilly an exclusive worldwide license to manufacture and market CRF binding protein ligand antagonists and CRF R2 agonist products. The licenses granted under the agreement are for the term of the patents licensed and we are entitled to receive a royalty on product sales for the term of those patents. We have the option to co-promote products for the treatment of dementia in the United States and to receive a portion of the profits resulting from sales, subject to our obligation to pay a portion of the development costs for such product rather than royalties. The agreement may be terminated for failure by either party to meet its obligations or if blocking patents prevent the development of products.

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 preclinical 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 additional 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 five issued U.S. patents, approximately 60 pending U.S. patent applications and another approximately 105 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 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 the CRF R2 patent and our broad patent covering immune therapeutics in diabetes. 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 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 two U.S. patents relating to IL-4 proteins that are controlled by other entities which, if construed very broadly, and if valid as so construed, could prevent us from commercializing our IL-4 fusion toxin products in the United States unless we obtain a license, which may not be available to us on commercially reasonable terms, or at all. We do not believe that our research and development activities as currently conducted infringe any valid issued patents.

NBI-34060, our leading gamma amino-butyric acid agonist compound for the treatment of insomnia, is covered generically in an issued U.S. patent, which we licensed from DOV Pharmaceuticals. It is not currently covered by any foreign patents of which we are aware. The term of the U.S. patent is due to expire in June 2003. We intend to seek additional protection of this compound in three ways. First, we have filed eight U.S. and foreign patent applications on 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 10 years in the European Union, measured from the date of FDA, or corresponding foreign, approval.

In-Licensed Technology

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

- In October 2000, we licensed nonexclusive rights to GT1-1 cell line from The Salk Institute.
- In August 2000, we licensed nonexclusive rights to CRF R1 deficient mice from the Research Development Foundation.
- In July 2000, we licensed exclusive rights to melanocortin subtype 3 receptor knock-out mice from Oregon Health Sciences University.

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

- In January 1999, we licensed exclusive worldwide rights to patents relating to excitatory amino acid transporters and melanocortin 1-5 from Oregon Health Sciences University.

- In December 1998, we licensed nonexclusive rights to technology covering melanocortin subtype 4 receptor from the University of Michigan.

- In June 1998, we licensed exclusive worldwide rights to our sedative compound, NBI-34060, from DOV Pharmaceuticals, Inc.

- In May 1998, we licensed exclusive worldwide rights to patents covering NBI-3001, our IL-4 fusion toxin, from the National Institutes of Health and inventors Ira Pastan and David Fitzgerald.

- In November 1996, we licensed exclusive worldwide rights to technology directed to peptide therapeutics for the treatment of autoimmune disease from Trustees of Dartmouth College.

- In October 1997, we licensed co-exclusive rights to technology relating to the prevention of diabetes from University Technology Corporation.

- 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.

- 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 preclinical and anticipated clinical trials. Manufacturers of our NBI-34060 and CRF antagonist compounds clinical trial material include Albany Molecular Research, Cedarburg Pharmaceuticals, Organichem Corporation and Pharmaceutics International. Cook Pharmaceuticals, Covance Biotechnology Services, Polypeptide Laboratories, Primedica and Pyramid Laboratories manufacture our altered peptide ligands, NBI-6024 and NBI-5788 and our recombinant protein NBI-3001. We also rely, and intend to continue to rely, on third parties to provide the components of these product candidates, such as proteins, peptides, phospholipids, small molecules and bulk chemical materials.

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 Janssen, Wyeth-Ayerst and Eli Lilly, we may have the opportunity

to co-promote 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 preclinical studies and clinical trials and other approval procedures of the FDA and similar regulatory authorities in foreign countries. Various federal and state statutes and regulations also govern or influence testing, manufacturing, safety, labeling, storage and record-keeping related to such products and their marketing. The process of obtaining these approvals and the subsequent substantial compliance with appropriate federal and state statutes and regulations require the expenditure of substantial time and financial resources.

Preclinical studies are generally conducted in laboratory animals to evaluate the potential safety and the efficacy of a product. Drug developers submit the results of preclinical studies to the FDA as a part of an investigative 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 preclinical 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 with in countries outside the United States.

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

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

Orphan Drug Designation

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

Approvals Outside the United States

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

Fast Track Designation

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

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:

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

Developments by others may render our product candidates or technologies obsolete or noncompetitive. We are performing research on or developing products for the treatment of several disorders including anxiety, depression, insomnia, malignant glioma, other forms of cancer and multiple sclerosis.

In the area of anxiety disorders, our product candidates will compete with well-established products such as Valium(R), marketed by Hoffman-La Roche, Xanax(R), marketed by Pharmacia Upjohn, Buspar(R), marketed by Bristol-Myers-Squibb, and others.

We are also developing products for depression, which will compete with well-established products in the antidepressant class, including Prozac(R), marketed by Eli Lilly, Zoloft(R) marketed by Pfizer, and Paxil(R), marketed by GlaxoSmith Kline. Certain technologies under development by other pharmaceutical companies could result in additional commercial treatments for depression and anxiety. In addition, a number of companies are also conducting research on molecules to block CRF, which is the same mechanism of action employed by our compounds.

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

Guilford Pharmaceuticals' Gliadel(R), approved for use in a type of brain cancers known as recurrent glioblastoma multiforme, would 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 only for recurrent glioblastoma multiforme, where it 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(R) is marketed by Chiron for the treatment of kidney cancer, and drug treatments for non-small-cell lung cancer include Platinol(R) and Taxol(R), which are marketed by Bristol-Myers-Squibb, and Gemzar(R), which is marketed by Eli Lilly.

Products that may compete with NBI-5788, our altered peptide ligand for multiple sclerosis, include Betaseron(R) and Avonex(R), similar forms of beta-interferon marketed by Berlex BioSciences and Biogen, respectively. Copaxone(R), 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(R), marketed by Takeda-Abbott Pharmaceuticals, Zoladex(R), marketed by AstraZeneca, and Synarel(R), marketed by Pharmacia Upjohn, are gonadotropin-releasing hormone peptide agonists that have been approved for the treatment of prostate cancer, endometriosis, infertility, breast cancer and central precocious puberty. In addition, peptide antagonists, including Abarelix(R) and Antagon Injection(R), are under development by Amgen and Organon, respectively, for these indications. These drugs may compete with any small molecule gonadotropin-releasing hormone antagonists we develop for these indications.

Anti-obesity therapeutics currently available include Xenical(R) from Roche Laboratories and Meridia(R) from Knoll Pharmaceuticals. 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:

- capital resources;
- research and development resources, including personnel and technology;
- regulatory experience;
- preclinical study and clinical testing experience;
- 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 impact our stock price.

Insurance

The Company maintains product liability insurance for clinical trials. The Company intends to expand its 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 the Company will be able to maintain insurance coverage at a reasonable cost or in sufficient amounts to protect the Company against losses due to liability. There can also be no assurance that the Company will be able to obtain commercially reasonable product liability insurance for any products approved for marketing. A successful product liability claim or series of claims brought against the Company could have a material adverse effect on its business, financial condition and results of operations.

Employees

As of December 31, 2000, we had 188 employees, consisting of 179 full-time and 9 part-time employees. Of the full-time employees, approximately 63 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.

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 or maintain profitability. Since our inception, we have incurred significant net losses, including net losses of $28.8 million in the period from January 1, 2000 through December 31, 2000. As a result of ongoing operating losses, we had an accumulated deficit of $70.5 million as of December 31, 2000. We are not currently profitable. Even if we succeed in developing and commercializing one or more of our drugs, we expect to incur substantial losses for the foreseeable future and may never become profitable. 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.

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

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

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

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

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:

- be found ineffective or cause harmful side effects during preclinical studies or clinical trials;
- fail to receive necessary regulatory approvals;

- be precluded from commercialization by proprietary rights of third parties;

- be difficult to manufacture on a large scale; or

- be uneconomical or fail to achieve market acceptance.

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

We may not receive regulatory approvals for our product candidates. 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 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. 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 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.

In particular, human therapeutic products are subject to rigorous preclinical testing and clinical trials and other approval procedures of the FDA and similar regulatory authorities in foreign countries. Various federal and state statutes and regulations also govern or influence testing, manufacturing, safety, labeling, storage and record-keeping related to these products and their marketing. Any delay in, or suspension of, our clinical trials will delay the filing of our new drug applications with the FDA and, ultimately, our ability to commercialize our drugs and generate product revenues.

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

- we or the FDA may suspend the trials;

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

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

- the results may not be statistically significant;

- patient recruitment may be slower than expected; and

- patients may drop out of the trials.

In addition, we depend on independent clinical investigators to conduct our clinical trials under their agreements with us. These 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. These investigators may also have relationships with other commercial entities, some of which may compete with us. If independent investigators assist our competitors at our expense, it could harm our competitive position.

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

We depend on continuing our current strategic alliances and developing additional strategic alliances to develop and commercialize our compounds. We depend upon our corporate collaborators to provide adequate funding for a number of our programs. Under these arrangements, our corporate collaborators are responsible for:

- selecting compounds for subsequent development as drug candidates;

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

- manufacturing and commercializing any resulting drugs.

Our strategy for developing and commercializing our products is dependent upon maintaining our current arrangements and establishing new arrangements with research collaborators, corporate collaborators and others. We currently have collaborations with Janssen Pharmaceutica, Wyeth-Ayerst, Taisho Pharmaceutical and Eli Lilly. Because we rely heavily on our corporate collaborators, our development of our projects would be substantially delayed if our collaborators:

- fail to select a compound we have discovered for subsequent development into marketable products;

- fail to gain the requisite regulatory approvals of these products;

- do not successfully commercialize products that we originate;

- do not conduct their collaborative activities in a timely manner;

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

- terminate their alliances with us;

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

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

- merge with a third party that may wish to terminate the collaboration.

These issues and possible disagreements with our corporate collaborators could lead to delays in the collaborative research, development or commercialization of many of our product candidates. Furthermore, disagreements with these parties could require or result in litigation or arbitration, which would be time-consuming and expensive. If any of these issues arise, it may delay the filing of our 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 may not comply with FDA regulations relating to manufacturing our products for clinical trials and commercial purposes or other regulatory requirements now or in the future. Our reliance on contract manufacturers also exposes us to the following risks:

- Contract manufacturers may encounter difficulties in achieving volume production, quality control and quality assurance, and also may experience shortages in qualified personnel. As a result, our contract manufacturers might not be able to meet our clinical schedules.

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

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

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

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 discontinue their 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 payers may subject our products to sales and pharmaceutical pricing controls that could limit our product revenues and delay profitability. The continuing efforts of government and third-party payers to contain or reduce the costs of health care through various means may reduce our potential revenues. These payers' 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 payers 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:

- the timing of receipt of marketing approvals;

- the safety and efficacy of the products;

- the emergence of equivalent or superior products; and

- the cost-effectiveness of the products.

If the medical community and patients do not ultimately accept our products as being safe and effective, we may not recover our investment.

Risks Related to Our Industry

We face intense competition and if we are unable to compete effectively, the demand for our products, if any, may be reduced. The biotechnology and pharmaceutical industries are subject to rapid and intense technological change. We face, and will continue to face, competition in the development and marketing of our product candidates from academic institutions, government agencies, research institutions and biotechnology and pharmaceutical companies. Competition may also arise from, among other things:

- other drug development technologies;

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

- new small molecule or other classes of therapeutic agents.

Developments by others may render our product candidates or technologies obsolete or noncompetitive. We are performing research on or developing products for the treatment of several disorders including 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:

- capital resources;

- research and development resources, including personnel and technology;

- regulatory experience;

- preclinical study and clinical testing experience;

- manufacturing and marketing experience; and

- production facilities.

Any of these competitive factors could reduce demand for our products. For more specific information about the competition we face, please see the section "Business" under the subheading "Competition".

If we are unable to protect our intellectual property, our competitors could develop and market products based on our discoveries, which may reduce demand for our products. Our success will depend on our ability to, among other things:

- obtain patent protection for our products;

- preserve our trade secrets;

- prevent third parties from infringing upon our proprietary rights; and

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

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

We also rely upon unpatented trade secrets and improvements, unpatented know-how and continuing technological innovation to develop and maintain our competitive position, which we seek to protect, in part, 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.

We may not be able to adequately enforce any of our patents to protect our proprietary technology and compounds. Litigation may be necessary to defend against or assert infringement claims to enforce our issued patents and to protect our trade secrets or know-how, or to determine the scope and validity of the proprietary rights of others. 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 corticotropin-releasing factor receptor patent and our broad patent covering immune therapeutics in diabetes. 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.

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. 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. If we do not obtain those licenses, we could encounter delays in product introductions while we attempt to design around those patents, or we could find that we are unable to develop, manufacture or sell products requiring those licenses. We are aware of pending and issued patent claims to certain uses of some of the types of compounds we are developing.

If we are unable to resolve third-party disputes regarding the validity of our patents or our alleged infringement of other third parties' patents, we may not be able to sell some or all of our products. For more information about our intellectual property, please see the section "Business" under the subheading "Intellectual Property".

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 $5 million per occurrence and $5 million in the aggregate. However, insurance coverage is becoming increasingly expensive, and we may not be able to maintain insurance coverage at a reasonable cost or in sufficient amounts to protect us against losses due to liability. 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.

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 members meet at least yearly to advise us in the selection, implementation and prioritization of our research programs. Some members meet more frequently to advise us with regard to our specific 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, 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.

Floyd E. Bloom, M.D., is Chairman of the Department of Neuropharmacology at The Scripps Research Institute. Dr. Bloom is an internationally recognized expert in the fields of neuropharmacology and neurobiology.

Michael Brownstein, M.D., Ph.D., is Chief of the Laboratory of Cell Biology at the National Institute of Mental Health. 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 is an editor of the journal Endocrinology.

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 Member 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 preclinical 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 Chief Scientific Advisor, Neuroimmunology and a member of our Founding Board of Scientific and Medical Advisors and our Executive Committee.

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

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 Neurocrine. A change in these regulations or policies could adversely affect our relationship with any of our Scientific Advisory Board members.

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. Our lease payments are $208,000 per month with annual increases of 4% on September 1st of each year. We have sublet approximately 14,500 square feet of this building to two separate tenants through July 31, 2001 and September 30, 2001, respectively.

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, 1999		
1st Quarter	$ 7.50	$ 4.88
2nd Quarter	5.88	4.00
3rd Quarter	5.94	3.75
4th Quarter	29.63	5.38
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

As of February 28, 2001, there were approximately 134 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 consolidated financial data have been derived from our audited consolidated 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 consolidated financial statements and notes thereto appearing elsewhere in this Form 10-K.

	2000	1999	1998 (1)	1997	1996
	(in thousands, except for earnings/(loss) per share data)				
STATEMENT OF OPERATIONS DATA					
Revenues					
Sponsored research and development	$ 6,881	$ 12,171	$ 8,751	$14,985	$9,092
Sponsored research and development from related party	-	491	3,610	-	-
Milestones and license fees	6,345	3,000	2,500	10,250	9,000
Grant income and other revenues	1,362	1,129	1,176	909	1,124
Total revenues	14,588	16,791	16,037	26,144	19,216
Operating expenses					
Research and development	40,227	29,169	21,803	18,758	12,569
General and administrative	9,962	7,476	6,594	5,664	3,697
Write-off of acquired in-process research and development and licenses	-	-	4,910	-	-
Total operating expenses	50,189	36,645	33,307	24,422	16,266
Income (loss) from operations	(35,601)	(19,854)	(17,270)	1,722	2,950
Interest income, net	6,048	2,851	4,000	3,931	2,598
Other income (expense)	1,047	1,066	504	818	574
Equity in NPI net losses and other adjustments, net	-	(885)	(7,188)	(1,130)	-
Net income (loss) before income taxes	(28,506)	(16,822)	(19,954)	5,341	6,122
Income taxes	302	-	1	214	248
Net income (loss)	$(28,808)	$(16,822)	$(19,955)	$ 5,127	$5,874
Earnings (loss) per share					
Basic	$ (1.30)	$ (0.88)	$ (1.10)	$ 0.30	$ 0.39
Diluted	(1.30)	(0.88)	(1.10)	0.28	0.36
Shares used in calculation of earnings (loss) per share					
Basic	22,124	19,072	18,141	16,930	14,971
Diluted	22,124	19,072	18,141	18,184	16,127
BALANCE SHEET DATA					
Cash, cash equivalents and short-term investments	164,670	91,098	62,670	75,092	69,920
Working capital	154,556	86,168	60,064	69,362	68,023
Total assets	185,962	109,222	80,529	91,903	77,957
Long-term debt and capital lease obligations	2,283	2,139	2,247	722	847
Accumulated deficit	(70,480)	(41,672)	(24,850)	(4,895)	(10,022)
Total stockholders' equity	163,208	96,354	71,958	83,152	72,767

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(1) Includes results of operations and financial position of Northwest NeuroLogic, Inc. from May 28, 1998, the date of acquisition (See Note 8 of the Notes to the Financial Statements).

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, preclinical 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 and 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 below and those outlined in the "Business" section included in Item 1.

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. Our product candidates address some of the largest pharmaceutical markets in the world including insomnia, anxiety, depression, cancer 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 in anticipation of significant increases in operating expenses as products are advanced through the various stages of clinical development. As of December 31, 2000, we have incurred a cumulative deficit of $70.5 million and expect to incur operating losses in the future, which may be greater than losses in prior years.

Results of Operations

Our revenues for the year ended December 31, 2000 were $14.6 million compared with $16.8 million in 1999, and $16.0 million in 1998. The decline in revenues from 1999 to 2000 resulted primarily from the conclusion of the Novartis collaboration in January 2000 and the sponsored research portion of the Eli Lilly & Company ("Eli Lilly") collaboration 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 Wyeth-Ayerst Laboratories ("Wyeth-Ayerst") agreement. The absence of these revenues during 2000 was partially offset by $7.1 million in revenues received from Taisho Pharmaceuticals Co., Ltd. ("Taisho"). In addition, revenues received from Janssen Pharmaceutica, N.V. ("Janssen") were $3.0 million in 2000 compared to $2.4 million received in 1999.

Revenues for 1999 and 1998 were similar in total but had different compositions resulting from several significant events. During 1999, we entered into a collaborative agreement with Wyeth-Ayerst and agreed to a two-year extension of our 1995 collaboration with Janssen. The new agreements generated revenues of $8.4 million during 1999. Non-recurring revenues recorded in 1998 included $4.7 million in sponsored development and $2.3 million in milestones received under the Novartis and Neuroscience Pharma, Inc. ("NPI") agreements. In addition, due to the conclusion of the sponsored research portion of the Eli Lilly agreement in October 1999, revenues received from Eli Lilly during 1999 were $3.2 million compared to $4.1 million received in 1998.

Research and development expenses increased to $40.2 million during 2000 compared with $29.2 million during 1999 and $21.8 million in 1998. 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 $10.0 million during 2000 compared with $7.5 million during 1999 and $6.6 million in 1998. Increased expenses from 1999 to 2000 resulted primarily from $1.1 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. Increased expenses from 1998 to 1999 resulted primarily from the addition of personnel required to support expanding research and development activities. We expect these expenses to continue to rise in 2001 as we expand clinical studies.

During 1998, we wrote-off acquired in-process research and development costs of $4.9 million. This amount included the acquisition of Northwest NeuroLogic, Inc. ("NNL") and the in-licensing of drug candidates for our insomnia and malignant glioma programs. Both of the in-licensed programs are currently under clinical development.

Interest income increased to $6.3 million during 2000 compared with $3.1 million during 1999 and $4.2 million for 1998. The increase in 2000, compared with 1999 and 1998, primarily resulted from higher investment balances achieved through offerings of our common stock. We completed a private placement of 2.3 million shares in December 1999, resulting in net proceeds of $39.5 million. In December 2000, we sold 3.2 million shares in a public offering, which resulted in net proceeds of $90.4 million. Due to the increase in cash reserves generated from these transactions, we anticipate an increase in interest income during 2001.

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 and 1998 were $764,000 and $3.4 million, respectively. In addition, we recorded a write-down in the investment value of $646,000 during 1999 and $3.8 million during 1998 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 2001, we expect sublease income to decrease significantly as increases in personnel will require more office and laboratory space.

Net loss for 2000 was $28.8 million, or $1.30 per share, compared with $16.8 million, or $0.88 per share, and $20.0 million, or $1.10 per share, for 1999 and 1998, respectively. 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.

To date, our revenues have come principally from funded research and achievements of milestones under corporate collaborations. The nature and amount of these revenues from period to period may lead to substantial fluctuations in the results of year-to-year revenues and earnings. Accordingly, results and earnings of one period are not predictive of future periods.

Liquidity and Capital Resources

At December 31, 2000, our cash, cash equivalents, and short-term investments totaled $164.7 million compared with $91.1 million at December 31, 1999. The increase in cash balances at December 31, 2000 resulted from the public offering of our common stock, which generated net cash proceeds of $90.4 million.

Net cash used by operating activities during fiscal year 2000 was $18.6 million compared with $10.3 million during 1999 and $10.7 million during 1998. The increase in cash used in operations during 2000 compared with 1999 and 1998 resulted primarily from the increase in clinical development activities and the addition of scientific personnel.

Net cash used by investing activities during fiscal year 2000 was $75.7 million compared to $21.2 million in 1999 and net cash provided by investing activities of $4.7 million in 1998. The fluctuations in cash used and provided resulted primarily from the timing differences in the 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 are expected to be approximately $4.0 million and will be financed primarily through leasing arrangements.

Net cash provided by financing activities during fiscal year 2000 was $94.1 million compared with $41.0 million and $1.9 million during 1999 and 1998, respectively. Cash provided during 2000 includes $90.4 million of net proceeds from the public offering of our common stock. Cash provided during 1999 includes

$39.5 million of net proceeds received from the private sale of our common stock. Cash provided during 1998 resulted primarily from capital lease financings.

In July 2000, we licensed to Taisho the exclusive rights to develop and commercialize NBI-6024 in Europe and Asia. In December 2000, we expanded our collaboration with Taisho, providing Taisho the exclusive rights to develop and commercialize our altered peptide ligand (APL) for diabetes in North America and other countries outside of Europe and Asia. With the expanded agreement, we will collaborate in the worldwide clinical development of NBI-6024 and we will receive funding for activities we conduct on behalf of the collaboration. The worldwide collaboration is valued at up to $100 million, including all potential licensing fees, purchase fees, milestones and development expenses. In addition, we will receive payments based on any future sales of NBI-6024. NBI-6024 is currently in Phase I/II clinical trials, with Phase II trials planned for 2001. As of December 31, 2000, we have received $2.0 million in option fees, $4.0 million in license fees, $4.0 million in milestones, and $829,000 in reimbursements of third-party costs. The license fees were deferred and are being recognized as revenues over the life of the agreement at $319,000 in 2000, 818,000 in each of the years 2001 through 2004 and $409,000 in 2005.

In September 1999, we signed an amendment to our 1995 agreement with Janssen. The amendment provides for a new sponsored research period designed to identify new corticotropin-releasing factor receptor antagonists, which will be subject to the terms of the original agreement signed in 1995. The term of the amendment is from April 1999 through February 2001. Under the agreement, we will receive $5.0 million in sponsored research funding, up to $3.5 million in milestone achievements and reimbursement of all outside and third-party costs associated with the project. As of December 31, 2000, we have received $4.6 million in sponsored research and $755,000 in reimbursements of third-party costs.

In January 1999, we entered into an agreement with Wyeth-Ayerst, the pharmaceutical division of American Home Products, on the research, development and commercialization of compounds, which modulate excitatory amino acid transporters for the treatment of neurodegenerative and psychiatric diseases.

The Wyeth-Ayerst agreement provides for sharing proprietary technologies, funding for research, payments for milestones reached, plus royalties on sales from products resulting from the collaboration. Under the terms of the agreement, we expect to receive three to five years of funding for research and development as well as worldwide royalties on commercial sales of products that result from the collaboration. Wyeth-Ayerst will also provide us with access to chemical libraries for screening within the collaborative field. As of December 31, 2000, we have received $6.0 million in sponsored research payments, $3.0 million for the achievement of four milestones and $50,000 in license fees, which are being deferred and recognized over the life of the agreement.

During 1998, we expensed acquired in-process research and development of $4.9 million. These charges consisted of $4.2 million for the acquisition of Northwest NeuroLogic, through which we received licenses to the melanocortin receptor and excitatory amino acid transporters programs, and $710,000 for licenses to insomnia and brain cancer compounds. We performed scientific due diligence related to the acquired projects and because they were based on narrow scientific hypotheses, we concluded that none of these programs had alternative future uses.

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

Because of our limited financial resources, our strategy to develop some of our programs is to enter into collaborative agreements with major pharmaceutical companies. Through these collaborations, we could partially recover our research costs through contract research and milestone revenues. The collaborators would then be financially responsible for all clinical development and commercialization costs.

In May 1998, when we acquired the in-process research and development programs from NNL, we estimated the costs to identify a clinical candidate and provide minimal research support during the clinical development stages for the melanocortin receptor program to be $15.4 million over an 8-year period. Costs to identify a clinical candidate and provide minimal research support during the

clinical development stages of the excitatory amino acid transporters program were estimated at $22.4 million. Estimated revenues from the collaborative arrangements were anticipated to reduce our net costs. The clinical development and commercialization costs were to be completely funded by the collaborator.

During fiscal year 2001, we anticipate that our gross costs for continued research on these programs will approximate $5 million. Our research efforts may not result in clinical candidates for either compound. We intend to collaborate on the melanocortin receptor technology. We would expect the collaborator to then be responsible for the clinical development, commercialization and funding. Our excitatory amino acid transporters program is currently under a collaborative agreement with Wyeth-Ayerst. Consequently, we cannot estimate the time or resources they will commit to the development of this program.

Our insomnia and brain cancer compounds are both in the early stages of clinical testing. During 2001, we expect to spend approximately $35 million on additional clinical testing of the brain cancer and insomnia compounds. We expect the clinical testing of both compounds to continue for at least the next two years, but our efforts may not result in commercially viable products. If our efforts were completely successful and we did not collaborate on these compounds, we estimate that each compound could cost an additional $50-$150 million and take up to five years to reach commercial viability.

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.

We believe that our existing capital resources, together with interest income and future payments due under our strategic alliances, will be sufficient to satisfy our current and projected funding requirements for at least the next 12 months. However, we cannot guarantee that these capital resources and payments will be sufficient to conduct 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 will require additional funding to continue our research and product development programs, to conduct preclinical studies and clinical trials, for operating expenses, to pursue regulatory approvals for our product candidates, for the costs involved in filing and prosecuting patent applications and enforcing or defending patent claims, if any, 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, preclinical 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 and on our long-term debt. 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 with maturities of less than 44 months. If a 10% change in interest rates were to have occurred on December 31, 2000, 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.

Interest risk exposure on long-term debt relates to our note payable, which bears a floating interest rate of prime plus one quarter percent (9.75% at December 31, 2000, 8.75% at December 31, 1999 and 8.00% at December 31, 1998). At December 31, 2000, 1999 and 1998, the note balance was $311,000, $461,000 and $610,000, respectively. This note is payable in equal monthly installments through January 2003. Based on the balance of our long-term debt, 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 and 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 "Risk Factors" included in Part I of this report.

New Accounting Pronouncements

In December 1999, the SEC issued Staff Accounting Bulletin No. 101, "Revenue Recognition in Financial Statements" (SAB 101). 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, we 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 our 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, we determined that $4.2 million of license fees received during 2000 were subject to the adoption of SAB 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 101 was recognized by including the cumulative effect of the change in accounting principle in the net loss for the fourth quarter of 2000. Our 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 at $915,000 in 2001, $835,000 in 2002, $828,000 in 2003, $818,000 in 2004 and $409,000 in 2005.

In March 2000, the Financial Accounting Standards Board, or FASB, released Interpretation No. 44, "Accounting for Certain Transactions involving Stock Compensation, an interpretation of APB Opinion No. 25," (FIN 44) which provides clarification of Opinion 25 for certain issues such as the determination of who is an employee, 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. We believe that our practices are in conformity with this guidance, and therefore FIN 44 had no impact on our financial statements.

In June 1998, the FASB issued Statement of Financial Accounting Standards (SFAS) No. 133,"Accounting for Derivative Instruments and Hedging Activities." We expect to adopt the new Statement effective January 1, 2001. This statement requires the recognition of all derivative instruments as either assets or liabilities in the statement of financial position and the measurement of those instruments at fair value. The Company does not expect the adoption of this statement to have a material impact on its results of operations or financial position.

In September 2000, the FASB issued SFAS No. 140, "Accounting for Transfers and Servicing of Financial Assets and Extinguishments of Liabilities." SFAS 140 provides accounting and reporting standards for transfers and servicing of financial assets and extinguishments of liabilities and is effective for transfers and servicing of financial assets and extinguishments of liabilities occurring after March 31, 2001. The adoption of SFAS 140 is not expected to have a material impact on our financial statements.

ITEM 7A. QUANTITATIVE AND QUALITATIVE DISCLOSURES ABOUT MARKET RISK

Quantitative and Qualitative Disclosures about Market Risk is contained in Item 7, Management Discussion and Analysis--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 the Company's Notice of 2001 Annual Meeting of Stockholders and Proxy Statement, pursuant to Regulation 14A, to be filed with the Securities and Exchange Commission within 120 days of December 31, 2000. Such information is incorporated herein by reference.

ITEM 11. EXECUTIVE COMPENSATION

Information required by this item will be contained in the Company's Notice of 2001 Annual Meeting of Stockholders and Proxy Statement, pursuant to Regulation 14A, to be filed with the Securities and Exchange Commission within 120 days of December 31, 2000. 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 the Company's Notice of 2001 Annual Meeting of Stockholders and Proxy Statement, pursuant to Regulation 14A, to be filed with the Securities and Exchange Commission within 120 days of December 31, 2000. Such information is incorporated herein by reference.

ITEM 13. CERTAIN RELATIONSHIPS AND RELATED TRANSACTIONS

Information required by this item will be contained in the Company's Notice of 2001 Annual Meeting of Stockholders and Proxy Statement, pursuant to Regulation 14A, to be filed with the Securities and Exchange Commission within 120 days of December 31, 2000. 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 Consolidated Balance Sheet as of December 31, 2000 and 1999 Consolidated Statement of Operations for the years ended December 31, 2000, 1999 and 1998 Consolidated Statement of Stockholders' Equity for the years ended December 31, 2000, 1999 and 1998 Consolidated Statement of Cash Flows for the years ended December 31, 2000, 1999 and 1998 Notes to the Consolidated Financial Statements (includes unaudited Selected Quarterly Financial Data)

2. List of all Financial Statement schedules. All schedules are omitted because they are not applicable or the required information is shown in the Consolidated 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 December 14, 2000 and December 15, 2000.

1. The Registrant filed a Current Report on Form 8-K dated April 6, 2000 to report pursuant to Item 5 (Other Events) and Item 7 (Final Statements, Pro Forma Financial Information and Exhibits) announcing Janssen Pharmaceutica's replacement of R121919 with a back-up compound

2. The Registrant filed a Current Report on Form *-K dated December 14, 2000 to report pursuant to Item 5 (Other Events) and Item 7 (Final Statements, Pro Forma Financial Information and Exhibits) the incorporation by reference of its final prospectus dated December 5, 2000. 3. The Registrant filed a Current Report on Form 8-K dated December 15, 2000 to report pursuant to Item 5 (Other Events) the expansion of its collaboration with Taisho Pharmaceuticals Co., LTD.

(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 (7)
2.2	Form of Warrant pursuant to the Agreement and Plan of Reorganization dated May 1, 1998 (7)
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 (7)
4.5	Amended and Restated Rights Agreement by and between the Registrant and American Stock Transfer & Trust Company, as Rights Agent, dated as of July 19, 1999 (9)
4.6	Stock Purchase Agreement dated December 20 through 23, 1999, between Neurocrine Biosciences, Inc. and each of the Purchasers named therein (11)
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 (10)
10.3	1996 Employee Stock Purchase Plan (1)
10.4	1996 Director Stock Option Plan and form of stock option agreement (1)
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) (13)
10.7	Employment Agreement dated March 1, 1997, between the Registrant and Paul W. Hawran, as amended May 24, 2000 (4) (13)
10.8	Consulting Agreement dated September 25, 1992, between the Registrant and Wylie A. Vale, Ph.D. (1)
10.9	Consulting Agreement effective January 1, 1992, between the Registrant and Lawrence J. Steinman, MD (1)
10.10	License Agreement dated July 17, 1992, by and between The Salk Institute for Biological Studies and the Registrant (1)

10.11 License Agreement dated November 16, 1993, by and between The Salk Institute for Biological Studies and the Registrant (1)

10.12 License Agreement dated October 19, 1992, by and between the Board of Trustees of the Leland Stanford Junior University and the Registrant (1)

10.13 Agreement dated January 1, 1995, by and between the Registrant and Janssen Pharmaceutica, N.V. (1)

10.14* Research and License Agreement dated October 15, 1996, between the Registrant and Eli Lilly and Company (2)

10.15* Lease between Science Park Center LLC and the Registrant dated July 31, 1997 (5)

10.16* Option Agreement between Science Park Center LLC (Optionor) and the Registrant dated July 31, 1997 (Optionee) (5)

10.17* Construction Loan Agreement Science Park Center LLC and the Registrant dated July 31, 1997 (5)

10.18 Secured Promissory Note Science Park Center LLC and the Registrant dated July 31, 1997 (5)

10.19* Operating Agreement for Science Park Center LLC between Nexus Properties, Inc. and the Registrant dated July 31, 1997 (5)

10.20 Form of incentive stock option agreement and nonstatutory stock option agreement for use in connection with 1992 Incentive Stock Plan (1)

10.21* Patent License Agreement dated May 7, 1998, between the US Public Health Service and the Registrant (7)

10.22* Patent License Agreement dated April 28, 1998, between and among Ira Pastan, David Fitzgerald and the Registrant (7)

10.23* Sub-License and Development Agreement dated June 30, 1998, by and between DOV Pharmaceutical, Inc. and the Registrant (7)

10.24* Warrant Agreement dated June 30, 1998, between DOV Pharmaceutical, Inc. and the Registrant (7)

10.25* Warrant Agreement dated June 30, 1998, between Jeff Margolis and the Registrant (7)

10.26* Warrant Agreement dated June 30, 1998, between Stephen Ross and the Registrant (7)

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 (8)

10.28* Employment Agreement dated January 1, 1999, between the Registrant and Margaret Valeur-Jensen, as amended May 24, 2000 (8) (13)

10.29* Employment Agreement dated February 9, 1998, between the Registrant and Bruce Campbell, as amended May 24, 2000 (8) (13)

10.30 Amended 1992 Incentive Stock Plan, as amended May 27, 1997, May 27, 1998 and May 21, 1999 (8)

10.31* Agreement by and among Dupont Pharmaceuticals Company, Janssen Pharmaceutica, N.V. and Neurocrine Biosciences, Inc. dated September 28, 1999 (10)

10.32* Amendment Number One to the Agreement between Neurocrine Biosciences, Inc. and Janssen Pharmaceutica, N.V. dated September 24, 1999 (10)

10.33* License Agreement between the Registrant and Taisho Pharmaceutical Co., Ltd. dated July 21, 2000 (13)

10.34** Amendment No. 1 dated November 30, 2000 to the License Agreement between the Registrant and Taisho Pharmaceutical Co., Ltd. dated July 21, 2000

10.35 2001 Stock Option Plan (14)

21.1 Subsidiaries of the Company

23.1 Consent of Ernst & Young LLP, Independent Auditors

24.1 Power of Attorney (see page 34)

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(1) Incorporated by reference to the Company's Registration Statement on Form S-1 (Registration No. 333-03172)

(2) Incorporated by reference to the Company's Report on Form 10-K for the fiscal year ended December 31, 1996

(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 Report on Form 8-K filed on March 13, 1998

(7) Incorporated by reference to the Company's Quarterly Report on Form 10-Q filed on November 16, 1998

(8) Incorporated by reference to the Company's Report on Form 10-K for the fiscal year ended December 31, 1998

(9) Incorporated by reference to the Company's Quarterly Report on Form 10-Q filed on August 11, 1999

(10) Incorporated by reference to the Company's Quarterly Report on Form 10-Q filed on November 12, 1999

(11) Incorporated by reference to the Company's Report on Form S-3 filed on January 20, 2000

(12) Incorporated by reference to the Company's Report on Proxy filed on April 27, 2000

(13) Incorporated by reference to the Company's Quarterly Report on Form 10-Q filed on August 11, 2000

(14) Incorporated by reference to the Company's Registration Statement on Form S-8 filed March 15, 2001 * 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

Gary A. Lyons
President and Chief Executive Officer

Date: March 29, 2001

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 29, 2001
/s/ Paul W. Hawran Paul W. Hawran	Chief Financial Officer (Principal Financial and Accounting Officer)	March 29, 2001
/s/ Joseph A. Mollica Joseph A. Mollica.	Chairman of the Board of Directors	March 29, 2001
/s/ Richard F. Pops Richard F. Pops	Director	March 29, 2001
/s/ Stephen A. Sherwin Stephen A. Sherwin	Director	March 29, 2001
/s/ Lawrence J. Steinman Lawrence J. Steinman	Director	March 29, 2001
/s/ Wylie W. Vale Wylie W. Vale	Director	March 29, 2001

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 consolidated balance sheet of Neurocrine Biosciences, Inc. as of December 31, 2000 and 1999, and the related consolidated statements of operations, stockholders' equity, and cash flows for each of the three years in the period ended December 31, 2000. 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 consolidated financial position of Neurocrine Biosciences, Inc. at December 31, 2000 and 1999, and the consolidated results of its operations and its cash flows for each of the three years in the period ended December 31, 2000, in conformity with accounting principles generally accepted in the United States.

As discussed in Note 1 to the consolidated financial statements, in 2000, the Company changed its method of revenue recognition.

/s/ ERNST & YOUNG LLP

ERNST & YOUNG LLP

San Diego, California
January 29, 2001

NEUROCRINE BIOSCIENCES, INC.
Consolidated Balance Sheet
(in thousands)

	December 31, 2000	December 31, 1999
ASSETS		
Current assets:		
Cash and cash equivalents	$ 21,078	$ 21,265
Short-term investments, available-for-sale	143,592	69,833
Receivables under collaborative agreements	5,974	1,458
Other current assets	1,761	2,257
Total current assets	172,405	94,813
Property and equipment, net	11,300	11,181
Licensed technology and patent applications costs, net	362	615
Other assets	1,895	2,613
Total assets	$185,962	$109,222
LIABILITIES AND STOCKHOLDERS' EQUITY		
Current liabilities:		
Accounts payable	$ 1,065	$ 2,447
Accrued liabilities	11,135	5,069
Deferred revenues	1,172	155
Current portion of long-term debt	149	149
Current portion of capital lease obligations	1,438	825
Total current liabilities	14,959	8,645
Long-term debt, net of current portion	162	312
Capital lease obligations, net of current portion	2,121	1,827
Deferred rent	1,646	1,005
Deferred revenues	2,890	-
Other liabilities	976	1,079
Total liabilities	22,754	12,868
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 25,314,470 in 2000 and 21,608,011 in 1999	25	22
Additional paid in capital	233,565	138,798
Deferred compensation	(59)	(411)
Stockholder notes	(104)	(119)
Accumulated other comprehensive (loss) income	261	(264)
Accumulated deficit	(70,480)	(41,672)
Total stockholders' equity	163,208	96,354
Total liabilities and stockholders' equity	$185,962	$109,222

See accompanying notes.

NEUROCRINE BIOSCIENCES, INC.
Consolidated Statement of Operations
(in thousands)

	Year-ended December 31,		
	2000	1999	1998
Revenues:			
Sponsored research and development	$ 6,881	$ 12,171	$ 8,751
Sponsored research and development from related party	-	491	3,610
Milestones and license fees	6,345	3,000	2,500
Grant income and other revenues	1,362	1,129	1,176
Total revenues	14,588	16,791	16,037
Operating expenses:			
Research and development	40,227	29,169	21,803
General and administrative	9,962	7,476	6,594
Write-off of acquired in-process research and development and licenses	-	-	4,910
Total operating expenses	50,189	36,645	33,307
Income (loss) from operations	(35,601)	(19,854)	(17,270)
Other income and expenses:			
Interest income	6,276	3,082	4,151
Interest expense	(228)	(231)	(151)
Equity in NPI losses and other adjustments, net	-	(885)	(7,188)
Other income	1,047	1,066	504
Income (loss) before taxes	(28,506)	(16,822)	(19,954)
Income taxes	302	-	1
Net income (loss)	$(28,808)	$(16,822)	$(19,955)
Earnings (loss) per common share:			
Basic and diluted	$ (1.30)	$ (0.88)	$ (1.10)
Shares used in the calculation of earnings (loss) per common share:			
Basic and diluted	22,124	19,072	18,141

See accompanying notes.

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

	Common Stock		Additional Paid In	Unearned	Notes Receivable from
	Shares	Amount	Capital	Compensation	Stockholders
BALANCE AT DECEMBER 31, 1997	17,687	$18	$ 88,586	$ (439)	$(120)
Net loss	-	-	-	-	-
Unrealized gain on short-term investments	-	-	-	-	-
Comprehensive loss	-	-	-	-	-
Issuance of common stock for warrants	60	-	142	-	-
Issuance of common stock for option exercises	81	-	286	-	-
Issuance of common stock pursuant to the Employee Stock Purchase Plan	30	-	205	-	-
Issuance of common stock in exchange for NPI Preferred Stock	679	1	3,854	-	-
Issuance of common stock for NNL Acquisition	392	-	4,032	-	-
Issuance of common stock for milestone achievement	2	-	17	-	-
Payments received on stockholder notes	-	-	-	-	1
Amortization of deferred compensation, net	-	-	(58)	252	-
BALANCE AT DECEMBER 31, 1998	18,931	19	97,064	(187)	(119)
Net loss	-	-	-	-	-
Unrealized gain on short-term investments	-	-	-	-	-
Comprehensive loss	-	-	-	-	-
Issuance of common stock for 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)	(119)
Net loss	-	-	-	-	-
Unrealized gain on short-term investments	-	-	-	-	-
Comprehensive loss	-	-	-	-	-
Issuance of common stock for warrants	23		-	-	-
Issuance of common stock for stock purchase agreement	6	-	1	-	-
Issuance of common stock for 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	-	-	-	-	15
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)	$(104)

NEUROCRINE BIOSCIENCES, INC.
Consolidated Statement of Stockholders' Equity
(in thousands, continued)

	Accumulated Other Comprehensive Income (Loss)	Accumulated Deficit	Total Stockholders' Equity
BALANCE AT DECEMBER 31, 1997	$ 2	$ (4,895)	$ 83,152
Net loss	-	(19,955)	(19,955)
Unrealized gain on short-term investments	29	-	29
Comprehensive loss	-	-	(19,926)
Issuance of common stock for warrants	-	-	142
Issuance of common stock for option exercises	-	-	286
Issuance of common stock pursuant to the Employee Stock Purchase Plan	-	-	205
Issuance of common stock in exchange for NPI Preferred Stock	-	-	3,855
Issuance of common stock for NNL Acquisition	-	-	4,032
Issuance of common stock for milestone achievement	-	-	17
Payments received on stockholder notes	-	-	1
Amortization of deferred compensation, net	-	-	194
BALANCE AT DECEMBER 31, 1998	31	(24,850)	71,958
Net loss	-	(16,822)	(16,822)
Unrealized gain on short-term investments	(295)	-	(295)
Comprehensive loss	-	-	(17,117)
Issuance of common stock for 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	(264)	(41,672)	96,354
Net loss	-	(28,808)	(28,808)
Unrealized gain on short-term investments	525	-	525
Comprehensive loss	-	-	68,071
Issuance of common stock for warrants	-	-	
Issuance of common stock for stock purchase agreement	-	-	1
Issuance of common stock for 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
Reversal of accrued 12/99 private placement costs	-	-	182
Amortization of deferred compensation, net	-	-	916
BALANCE AT DECEMBER 31, 2000	$ 261	$(70,480)	$163,208

See accompanying notes.

NEUROCRINE BIOSCIENCES, INC.
Consolidated Statement of Cash Flows
(in thousands)

	Twelve Months Ended December 31,		
	2000	1999	1998
CASH FLOW FROM OPERATING ACTIVITIES			
Net (loss) income	$(28,808)	$(16,822)	$(19,955)
Adjustments to reconcile net income (loss) to net cash Provided by (used in) operating activities:			
Acquisition of Northwest NeuroLogic for Common Stock	-	-	4,200
Equity in NPI losses and other adjustments, net	-	885	7,188
Depreciation and amortization	2,198	2,066	1,720
Loss on abandonment of assets	80	133	460
Gain on sale of equipment	-	-	(15)
Deferred revenues	3,907	(14)	(1,750)
Deferred rent	868	748	(402)
Compensation expenses recognized for stock options	2,677	497	194
Change in operating assets and liabilities, net of acquired business:			
Accounts receivable and other current assets	(4,020)	(752)	(2,898)
Other non-current assets	1,014	(357)	291
Accounts payable and accrued liabilities	3,439	3,360	271
Net used in operating activities	(18,645)	(10,256)	(10,696)
CASH FLOW FROM INVESTING ACTIVITIES			
Purchases of short-term investments	(151,582)	(87,728)	(41,618)
Sales/maturities of short-term investments	78,348	68,562	50,006
Purchases of property and equipment, net	(2,440)	(2,061)	(3,683)
Net cash flows (used in) provided by investing activities	(75,674)	(21,227)	4,705
CASH FLOW FROM FINANCING ACTIVITIES			
Issuance of Common Stock	93,360	41,016	433
Proceeds received from long-term obligations	1,741	981	2,500
Principal payments on long-term obligations	(984)	(957)	(1,006)
Payments received on notes receivable from stockholders	15	-	1
Net cash flows provided by financing activities	94,132	41,040	1,928
Net (decrease) increase in cash and cash equivalents	(187)	9,557	(4,063)
Cash and cash equivalents at beginning of the period	21,265	11,708	15,771
Cash and cash equivalents at end of the period	$ 21,078	$ 21,265	$ 11,708
SUPPLEMENTAL DISCLOSURES			
Supplemental disclosures of cash flow information:			
Interest paid	$ 228	$ 231	$ 150
Taxes paid	302	-	1
Schedule of noncash investing and financing activities:			
Conversion of note receivable to investment in NPI	-	-	$ 1,401
Conversion of NPI Preferred Stock to investment in NPI	-	-	3,855

See accompanying notes.

NEUROCRINE BIOSCIENCES, INC.
NOTES TO THE CONSOLIDATED FINANCIAL STATEMENTS
December 31, 2000

NOTE 1. ORGANIZATION AND SUMMARY OF SIGNIFICANT ACCOUNTING POLICIES

Business Activities. Neurocrine Biosciences, Inc. (the "Company" or "Neurocrine") was incorporated in California on January 17, 1992 and was reincorporated in Delaware in March 1996. Neurocrine is a leading neuroscience company focused on the discovery and development of novel therapeutics for neuropsychiatric, neuroinflammatory and neurodegenerative diseases and disorders. The Company's neuroscience, endocrine and immunology disciplines provide a unique biological understanding of the molecular interaction between central nervous, immune and endocrine systems for the development of therapeutic interventions for anxiety, depression, insomnia, stroke, malignant brain tumors, multiple sclerosis, obesity and diabetes.

Principles of Consolidation. The consolidated financial statements include the accounts of the Company and its wholly owned subsidiary, Northwest NeuroLogic, Inc. ("NNL"). Significant intercompany accounts and transactions have been eliminated in consolidation. In December 1999, NNL was merged with and into the Company.

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

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

Short-Term Investments Available-for-Sale. In accordance with Statement of Financial Accounting Standards (SFAS) No. 115, "Accounting for Certain Debt and Equity Securities," short-term investments are classified as available-for-sale. Available-for-sale securities are carried at fair value, with the unrealized gains and losses reported in comprehensive income. The amortized cost of debt securities in this category is adjusted for amortization of premiums and accretion of discounts to maturity. Such amortization is included in investment 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 investment income or loss. 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.

The Company invests its excess cash primarily in investment grade debt instruments, marketable debt securities of U.S. government agencies, and high-grade commercial paper. Management has established guidelines relative to diversification and maturities that maintain safety and liquidity.

Property and Equipment. Property and equipment are carried at cost. Depreciation and amortization are provided over the estimated useful lives of the assets, ranging from three to ten years, using the straight-line method.

Licensed Technology and Patent Application Costs. Licensed technology consists of worldwide licenses to patents related to the Company's platform technology, which are capitalized at cost and amortized over periods of 7 to 11 years. These costs are regularly reviewed to determine that they include costs for patent applications the Company is pursuing. Costs related to applications that are not being actively pursued are evaluated under Accounting Principles Board (APB) Statement 17 "Intangible Assets" and are adjusted to an appropriate amortization period, which generally results in immediate write-off. Assets written-off during 2000 had a net book value of $80,000. Accumulated amortization at December 31, 2000 and 1999 was $753,000 and $685,000, respectively.

Impairment of long-lived assets. In accordance with SFAS 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, 2000.

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.

Research and Development Revenue and Expenses. 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. Research and development costs are expensed as incurred. Such costs include proprietary research and development activities and expenses associated with collaborative research agreements. Research and development expenses relating to collaborative agreements and grants were approximately $10.1 million, $7.2 million and $12.0 million during 2000, 1999 and 1998, respectively.

Stock-Based Compensation. As permitted by SFAS 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 25". This interpretation clarifies the definition of employee for purposes of applying APB 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 consolidated results of operations.

Deferred charges for options granted to non-employees has been determined in accordance with SFAS 123 and EITF 96-18 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 Per Share. Basic and diluted earnings per share are calculated in accordance with SFAS 128, "Earnings per Share." All earnings per share amounts for all periods have been presented, and where appropriate, were restated to conform to the requirements of SFAS 128.

Comprehensive Income. Comprehensive income is calculated in accordance with SFAS 130, "Comprehensive Income." The Statement 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 consolidated statement of stockholders' equity.

Reclassifications. Certain reclassifications have been made to prior year amounts to conform to the presentation for the year ended December 31, 2000.

Impact of Recently Issued Accounting Standards. In December 1999, the 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, 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 our 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 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 APB 20, the adoption of SAB 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 at $915,000 in 2001, $835,000 in 2002, $828,000 in 2003, $818,000 in 2004 and $409,000 in 2005.

In June 1998, the FASB issued SFAS 133,"Accounting for Derivative Instruments and Hedging Activities." The Company expects to adopt the new Statement effective January 1, 2001. This statement requires the recognition of all derivative instruments as either assets or liabilities in the statement of financial position and the measurement of those instruments at fair value. The Company does not expect the adoption of this statement to have a material impact on its results of operations or financial position.

In September 2000, the FASB issued SFAS No. 140, "Accounting for Transfers and Servicing of Financial Assets and Extinguishments of Liabilities." SFAS 140 provides accounting and reporting standards for transfers and servicing of financial assets and extinguishments of liabilities and is effective for transfers and servicing of financial assets and extinguishments of liabilities occurring after March 31, 2001. The adoption of SFAS 140 is not expected to have a material impact on the Company's financial statements.

Note 2. Short-Term Investments

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, 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

December 31, 1999				
US Government securities	$ 1,997	$ -	$ (24)	$ 1,973
Corporate debt securities	68,100	7	(247)	67,860
Total securities	$ 70,097	$ 7	$ (271)	$ 69,833

Gross realized gains and losses were not material for any of the reported periods. The amortized cost and estimated fair value of debt securities by contractual maturity at December 31, 2000 are shown below (in thousands).

	Amortized Cost	Estimated Fair Value
Due in one year or less	$ 48,000	$ 48,000
Due after one year through four years	95,331	95,592
	$ 143,331	$ 143,592

NOTE 3. PROPERTY AND EQUIPMENT

Property and equipment at December 31, 2000 and 1999 consist of the following (in thousands):

	2000	1999
Land	$ 5,003	$ 5,299
Furniture and fixtures	2,051	1,982
Equipment	11,179	9,046
Leasehold improvements	1,113	875
	19,346	17,202
Less accumulated depreciation	(8,046)	(6,021)
Net property and equipment	$ 11,300	$ 11,181

Furniture and equipment under capital leases were $8.5 million and $6.7 million at December 31, 2000 and 1999, respectively. Accumulated depreciation of furniture and equipment under capital leases totaled $5.0 million and $4.0 million at December 31, 2000 and 1999, respectively. The Company entered into $1.8 million of additional capital leases during 2000 and $981,000 during 1999.

NOTE 4. ACCRUED LIABILITIES

Accrued liabilities at December 31, 2000 and 1999 consist of the following (in thousands):

	2000	1999
Accrued employee benefits	$ 2,992	$ 1,331
Accrued professional fees	1,229	270
Accrued offering expenses	277	1,222
Accrued development costs	6,199	1,828
Taxes payable	26	27
Other accrued liabilities	412	391
	$ 11,135	$ 5,069

NOTE 5. LONG-TERM DEBT

During 1997, the Company partially financed the purchase of land under a 5 year note payable for approximately $747,000, which bears interest at a floating rate of prime plus one quarter percent (9.75% and 8.75% at December 31, 2000 and 1999, respectively). The note is repayable in equal monthly installments beginning February 1998.

At December 31, 2000, the balance of the note was $311,000. The repayment schedule for the note is $149,000 for each year 2001 through 2002 and $13,000 in the year 2003.

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 May 1997, the Company purchased two adjacent parcels of land in San Diego for $5.0 million. In August 1997, the Company sold one parcel to Science Park Center LLC, a California limited liability company (the "LLC"), of which the Company owns a nominal minority interest, in exchange for a note receivable in the amount of $3.5 million plus interest of 8.25%. However, for accounting purposes, this transaction does not qualify as a sale under SFAS No. 98 and therefore, the entire amount of the note receivable is included in land. The amount included in land at December 31, 2000 and 1999 was $3.5 and $3.8 million, respectively. The second parcel of land will be held until such time as additional facilities are required.

During 1998, the LLC constructed an expanded laboratory and office complex, which was leased by the Company under a 15-year operating lease, commencing September 1998. The Company has the option to purchase the facility at any time during the term of the lease at a predetermined price. The lease contains a 4% per year escalation in base rent fees, effective with each anniversary. The Company subleases a portion of the space to two unrelated parties. In August 2001, the first sublease will revert to a month-to-month lease. The second sublease will expire in September 2001.

Repayment schedules for the capital lease obligations and operating lease commitments at December 31, 2000 are as follows (in thousands):

Fiscal Year:	Capital Leases	Operating Leases
2001	$ 1,662	$ 2,525
2002	1,073	2,626
2003	672	2,731
2004	480	2,841
2005	112	2,954
Thereafter	-	26,926
Total minimum payments	$ 3,999	$ 40,603
Less: amounts representing interest	(440)	
Future minimum payments	3,559	
Less: current portion	(1,438)	
Future payments on capital lease obligations	$ 2,121	

Rent expense was $2.5 million, $2.7 million and $2.4 million for the years ended December 31, 2000, 1999 and 1998, respectively. Sublease income was $1.2 million, $1.2 million and $837,000 for the years ended December 31, 2000, 1999, and 1998, respectively.

Future minimum sublease income to be received under non-cancelable subleases at December 31, 2000 will be $297,000 for the year ending December 31, 2001.

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 30-180 days written notice. Under the terms of these agreements, the Company has received licenses to technology, or technology claimed, in certain patents or patent applications. The Company is required to pay 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 make payments upon the achievement of specified milestones. 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.

Note 7. Stockholders' Equity

Common Stock Issuances. From inception through 1996, the Company has issued Common Stock in various private and public offerings, as well as to corporate collaborators, at prices between $5.00 and $30.00 per share resulting in aggregate net proceeds of approximately $201.9 million. This total includes a December 2000 public offering, in which the Company sold 3.2 million shares of its Common Stock at $30 per share. The net proceeds generated from this transaction were $90.4 million.

Options. The Company has authorized 6.5 million shares of its Common Stock for issuance upon exercise of options or stock purchase rights granted under the 1992 Incentive Stock Option Plan, 1996 Director Option Plan and the 1997 NNL Stock Option Plan. These 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 these 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.

A summary of the Company's stock option activity, and related information for the years ended December 31 follows:

	2000		1999		1998	
	Options (in thousands)	Weighted Average Exercise Price	Options (in thousands)	Weighted Average Exercise Price	Options (in thousands)	Weighted Average Exercise Price
Outstanding at January 1, ...	3,158	$ 5.91	2,793	$6.02	2,653	$5.84
Granted	1,136	29.66	1,142	6.03	677	6.26
Exercised	(354)	6.56	(412)	4.79	(81)	3.64
Canceled	(29)	11.69	(365)	6.52	(456)	5.76
Outstanding at December 31, .	3,911	$12.75	3,158	$5.91	2,793	$6.02

A summary of options outstanding as of December 31, 2000 follows:

	Options Outstanding			Options Exercisable	
Range of Exercise Prices	Outstanding as of 12/31/00	Weighted Average Remaining Contractual Life	Weighted Average Exercise Price	Exercisable As of 12/31/00	Weighted Average Exercise Price
$0.02 to $4.19	510	3.6	$ 2.47	447	$2.47
4.25 to 4.94	544	5.7	4.47	416	4.35
5.00 to 6.50	599	7.9	5.52	275	5.57
6.56 to 7.38	498	6.7	7.17	398	7.22
7.75 to 10.25	598	6.4	8.47	476	8.43
11.19 to 34.44	589	9.3	22.70	58	19.35
34.50 to 43.44	573	9.4	36.39	70	35.01
	3,911	7.1	$12.75	2,140	$6.96

The weighted average fair values of the options granted during 2000, 1999 and 1998 were $20.51, $3.75 and $5.59, respectively.

Pro forma information regarding net income (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 2000, 1999 and 1998, respectively: risk-free interest rates of 5.0%, 6.4% and 5.5%; a dividend yield of 0.0% (for all years), volatility factors of the expected market price of the Company's common stock of .81, .74 and .88; 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 2000, 1999 and 1998 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 pro forma information for the years ended December 31, 2000, 1999, and 1998 follows (in thousands, except for per share data):

	2000	1999	1998
Net income (loss) as reported	$(28,808)	$(16,822)	$(19,955)
Earnings (loss) per share (diluted)	(1.30)	(0.88)	(1.10)
Pro forma net income (loss)	(31,057)	(18,303)	(20,758)
Pro forma earnings (loss) per share (diluted)	(1.40)	(0.96)	(1.14)

Employee Stock Purchase Plan. The Company has reserved 425,000 shares of Common Stock for issuance under the 1996 Employee Stock Purchase Plan, as amended on May 24, 2000 (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, 2000, 267,000 shares have been issued pursuant to the Purchase Plan.

Warrants. The Company has outstanding warrants to purchase 356,000 shares of Common Stock at an exercise price of $10.50 per share. These warrants generally expire in 2007. At December 31, 2000, all outstanding warrants were exercisable.

The following shares of Common Stock are reserved for future issuance at December 31, 2000 (in thousands):

Stock option plans	4,142
Employee stock purchase plan	158
Warrants	356
Total	4,656

Of the shares available for future issuance under the Plan, 3.9 million are outstanding grants and 231,000 remain available for future grant.

NOTE 8. ACQUIRED IN-PROCESS RESEARCH AND DEVELOPMENT AND LICENSES

Northwest NeuroLogic, Inc. In May 1998, the Company acquired the assets and liabilities of NNL in exchange for shares of the Company's Common Stock and stock options valued at $4.2 million. Since the acquisition, the operations of NNL have been included in the Company's consolidated statements of operations. The acquisition was accounted for as a purchase and, accordingly, the purchase price was allocated to the assets acquired and the liabilities assumed based on the estimated fair market values. Substantially all of the purchase price was allocated to the in-process research and development. The value allocated to the technology was then expensed because it had not reached technological feasibility and had no future alternative uses. The Company performed scientific due diligence related to the acquired projects, and because they were based on narrow scientific hypotheses, the Company concluded that neither program had alternative future uses.

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

Because of limited financial resources, the Company's strategy to develop some of its programs is to enter into collaborative agreements with major pharmaceutical companies. Through these collaborations, the Company could partially recover its research costs through contract research and milestone revenues. The collaborators would then be financially responsible for all clinical development and commercialization costs.

In May 1998, when the Company acquired the in-process research and development programs from NNL, it estimated the costs to identify a clinical candidate and provide minimal research support during the clinical development stages for the melanocortin receptor program to be $15.4 million over an 8-year period. Costs to identify a clinical candidate and provide minimal research support during the clinical development stages of the excitatory amino acid transporters program were estimated at $22.4 million. Estimated revenues from the collaborative arrangements were anticipated to reduce the Company's net costs. The clinical development and commercialization costs were to be completely funded by the collaborator.

During fiscal year 2001, the Company anticipates that its gross costs for continued research on these programs will approximate $5.0 million. The Company cannot be certain that its research efforts will result in clinical candidates for either compound. The Company intends to collaborate on the

melanocortin receptor technology. The Company would expect the collaborator to then be responsible for the clinical development, commercialization and funding. The excitatory amino acid transporters program is currently under a collaborative agreement with Wyeth-Ayerst. Consequently, the Company cannot estimate the time or resources Wyeth-Ayerst will commit to the development of this program.

The following are pro forma unaudited results of operations for the year ended December 31, 1998 (in thousands, except per share data) had the purchase of NNL been consummated as of January 1, 1998. This pro forma information is not necessarily indicative of the actual results that would have been achieved nor is it necessarily indicative of future results.

Revenues	$16,325
Net loss	(20,013)
Loss per share basic and diluted	$ (1.09)

Other. During 1998, the Company purchased licenses for technologies relating to insomnia and brain cancer in the amount of $710,000. These projects were in the early stages of development, have not reached technological feasibility and have no known alternative uses. Consequently, the costs of these licenses were expensed.

The insomnia and brain cancer compounds are both in the early stages of clinical testing. During 2001, the Company expects to spend approximately $35 million on additional clinical testing of the brain cancer and insomnia compounds. The Company expects the clinical testing of both compounds to continue for at least the next two years, but its efforts may not result in commercially viable products. If the Company's efforts were completely successful and it did not collaborate on these compounds, it is estimated that each compound could cost an additional $50 - $150 million and take up to five years to reach commercial viability.

Note 9. Collaborative Research and Development Agreements

Taisho Pharmaceuticals Co., Ltd. In December 1999, the Company entered into an agreement with Taisho Pharmaceutical Co., Ltd. (Taisho) providing an exclusive option to obtain European, Asian and North American development and commercialization rights for our altered peptide ligand product (APL), NBI-6024, for Type 1 Diabetes. In June 2000, Taisho exercised its option as to Europe and Asia. In November 2000, the agreement was amended to include worldwide development and commercialization rights. Taisho and the Company formed a steering committee to oversee the worldwide development of NBI-6024. Under this agreement, the Company is entitled to receive license fees, milestone payments, and after the November amendment, sponsored research funding and reimbursement of 100% of worldwide development expenses. In addition, the Company will receive payments on product sales in Europe and Japan for the term of the patents covering NBI-6024 subject to adjustment for payments to third parties. The Company is also entitled to receive up to $43.0 million for milestones, plus additional amounts for research funding and reimbursement of development costs and potential sublicense fees. As of December 31, 2000, the Company has received $2.0 million for the exclusive negotiating option, $3.0 million in license fees for the European and Asian commercialization rights, $1.0 million in license fees for the remaining worldwide rights, $4.0 million in milestone payments and $829,000 in reimbursement of development costs. The license fees were deferred and are being recognized as revenues over the life of the agreement at $319,000 in 2000, $818,000 in each of the years 2001 through 2004 and $409,000 in 2005.

Wyeth-Ayerst Laboratories. In January 1999, the Company entered into an agreement with Wyeth-Ayerst Laboratories (Wyeth-Ayerst), the pharmaceutical division of American Home Products Corporation, on the research, development and commercialization of compounds which modulate excitatory amino acid transporters (EAATs) for the treatment of neurodegenerative and psychiatric diseases. EAATs are part of the family of neurotransmitter transporters and play a key role in regulating the actions of neurotransmitters and brain function.

The agreement, valued at up to $80.3 million if a product is commercialized, includes: sharing proprietary technologies, funding for

research, payments for milestones reached, plus royalties on sales from products resulting from the collaboration. Under the terms of the agreement, Neurocrine expects to receive three to five years of funding for research and development as well as worldwide royalties on commercial sales of products that result from the collaboration. Wyeth-Ayerst will also provide Neurocrine with access to chemical libraries for screening within the collaborative field. As of December 31, 2000, the Company received $6.0 million in sponsored research payments, $3.0 million for the achievement of four milestones and $50,000 in license fees, which are being deferred and recognized over the life of the agreement.

Eli Lilly and Company. In October 1996, the Company entered into an agreement with Eli Lilly and Company (Eli Lilly) under which Neurocrine received three years of sponsored research payments totaling $17.2 million. The Company is also 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.

The collaborative research portion of the agreement was completed as scheduled in 1999. The Company will continue to receive milestone payments and royalties upon the successful continuation of the development portion of the agreement, if any.

Janssen Pharmaceutica, N.V. In January 1995, the Company entered into a research and development agreement with Janssen Pharmaceutica, N.V. (Janssen). Under the Janssen agreement, the Company is entitled to receive up to $10.0 million in milestone payments for the indications of anxiety, depression and substance abuse, and up to $9.0 million in additional milestone payments for other indications. The Company has granted Janssen an exclusive worldwide license to manufacture and market products. In exchange, the Company is entitled to receive royalties on worldwide product sales and has certain rights to co-promote such products in North America. Janssen is responsible for funding all clinical development and marketing activities, including reimbursements to Neurocrine for its promotional efforts, if any. As of December 31, 1998, the Company has received $2.0 million in up-front license fees, $9.7 million for three years of sponsored research and $3.5 million in milestone payments. The collaborative research portion of the agreement was completed as scheduled in 1997 with the selection of a clinical candidate and the commencement of clinical trials in Europe. There were no additional revenues received under this agreement in 1999 or 2000.

In September 1999, the Company signed an amendment to its 1995 agreement with Janssen to identify new corticotropin-releasing factor receptor antagonist compounds. The amendment provides for a new sponsored research period to begin April 1999 and conclude in February 2001. All other terms of the agreement will be governed by the original agreement signed in 1995. Under the amendment, the Company will receive $5.0 million in sponsored research funding, up to $3.5 million in milestone achievements and reimbursement of all outside and third party costs associated with the project. As of December 31, 2000, the Company has received $4.6 million in sponsored research and $755,000 in reimbursements of third party costs.

In April 2000, Janssen discontinued development of the compound licensed under the 1995 agreement and replaced it with a back-up compound, which resulted from research under the 1999 amendment. Since the new compound is subject to the terms of the original agreement, the Company will continue to receive milestone payments and royalties upon the successful continuation of the development portion of the agreement. Janssen has the right to terminate the Agreement upon six months notice. However, in the event of termination, other than termination by Janssen for cause or as a result of the acquisition of Neurocrine, all product and technology rights become the exclusive property of Neurocrine

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 Neurocrine with $7.0 million in research and development funding during the first two years of the agreement. In addition, the Company was eligible to receive up to $15.5 million in further research and development funding thereafter. As of December 31, 1999, the Company has

received $18.8 million in sponsored research and development payments and $9.1 million of milestone payments.

On July 7, 1999, Novartis exercised its right to terminate the agreement, effective January 7, 2000. As a result, Neurocrine reacquired the worldwide rights to its multiple sclerosis compound, MSP771.

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 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, 2000, 29,625 warrants have been exercised.

During 1997 and 1998, the 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 and $3.4 million in 1999 and 1998, respectively.

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 and $3.6 million during 1999 and 1998, respectively.

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 and $3.8 million during 1998. The balance of the Company's investment in NPI was $0 at December 31, 1999, and $1.4 million at December 31, 1998.

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 Consolidated Statement of Operations.

Note 11. Earnings per Share

The following data show the amounts used in computing earnings per share and the effect on income and the weighted-average number of shares of dilutive potential common stock (in thousands, except for earning per share data):

	Year Ended December 31,		
	2000	1999	1998
Numerator:			
Net income (loss)	$(28,808)	$(16,822)	$(19,955)
Effect of dilutive securities	-	-	-
Numerator for earnings (loss) per share	$(28,808)	$(16,822)	$(19,955)
Denominator:			
Denominator for basic earnings (loss) per share	22,124	19,072	18,141
Effect of dilutive securities:			
Employee stock options	**	**	**
Convertible preferred stock	**	**	**
Warrants	**	**	**
Dilutive potential of common shares	**	**	**
Demoninator for diluted earnings (loss) per share	22,124	19,072	18,141
Basic earnings (loss) per share	$ (1.30)	$ (0.88)	$ (1.10)
Diluted earnings (loss) per share	$ (1.30)	$ (0.88)	$ (1.10)

**Antidilutive

Note 12. Income Taxes

At December 31, 2000, the Company had Federal and California income tax net operating loss carry-forwards of approximately $43.1 million and $24.3 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 $6.0 million and $2.9 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%, which occurred during 1992 and 1993. 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, 2000 and 1999 are shown below. A valuation allowance of $27.2 million and $13.5 million at December 31, 2000 and 1999, 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:

	2000	1999
Deferred tax assets:		
Net operating loss carry-forwards	$ 16,487	$ 7,400
Tax credit carry-forwards	8,140	4,649
Capitalized research and development	2,098	935
Other, net	479	520
Total deferred tax assets	27,204	13,504
Valuation allowance	(27,204)	(13,504)
Net deferred tax assets	$ -	$ -

The provision for income taxes on earnings subject to income taxes differs from the statutory federal rate at December 31, 2000, 1999 and 1998, due to the following:

	2000	1999	1998
Federal income taxes at 34%	$(9,692)	$(5,719)	$(6,785)
State income tax, net of federal benefit	-	-	1
Tax effect on non-deductible expenses	335	932	4,213
Increase in valuation allowance	9,357	4,787	2,572
	$ -	$ -	$ 1

NOTE 13. SELECTED QUARTERLY FINANCIAL DATA (UNAUDITED)

The following is a summary of the quarterly results of operations for the years ended December 31, 2000 and 1999 (unaudited, in thousands, except for earnings per share data):

	Quarter Ended					Year Ended
	Mar 31	Jun 30	Sep 30 As Reported	Sep 30 Restated (1)	Dec 31	Dec 31
Fiscal Year End 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)
Earnings per share - Diluted	$ (0.28)	$ (0.24)	$ (0.37)	$ (0.50)	$ (0.29)	$ (1.30)
Shares used in the calculation of earnings per share - Diluted	21,771	21,897	22,032	22,032	22,789	22,124

	Quarters Ended				Year Ended
	Mar 31	Jun 30	Sep 30	Dec 31	Dec 31
Fiscal Year End 1999					
Revenues	$ 3,551	$ 3,810	$ 5,231	$ 4,199	$ 16,791
Operating expenses	8,077	9,190	10,213	9,165	36,645
Net Loss	(4,089)	(4,637)	(4,407)	(3,689)	(16,822)
Earnings per share - Diluted	$ (0.22)	$ (0.24)	$ (0.23)	$ (0.19)	$ (0.88)
Shares used in the calculation of earnings per share - Diluted	18,955	18,961	19,006	19,361	19,072

(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.

Exhibit 10.34

AMENDMENT NUMBER ONE

DATED

November 30, 2000

To the

LICENSE AGREEMENT

DATED

July 21, 2000

BETWEEN

TAISHO PHARMACEUTICAL CO., LTD.

AND

NEUROCRINE BIOSCIENCES, INC.

AMENDMENT NUMBER ONE TO THE LICENSE AGREEMENT

AMENDMENT NUMBER ONE (this "Amendment") dated November 30, 2000 to the LICENSE AGREEMENT (the "License Agreement") dated July 21, 2000 by and between Taisho Pharmaceutical Co., Ltd., a Corporation organized under the laws of Japan with principal offices located at 24-1, Takata 3-Chome, Toshima-ku, Tokyo 170-8633, Japan ("Taisho") and Neurocrine Biosciences, Inc., a Delaware Corporation with principal offices located at 10555 Science Center Drive, San Diego, California 92121 ("Neurocrine").

WITNESSETH:

WHEREAS, Taisho and Neurocrine entered into the License Agreement pursuant to which Neurocrine licensed to Taisho exclusive rights to Neurocrine's proprietary altered peptide ligand, NBI-6024, in the Field of Use in Asian and European countries (each as defined in the License Agreement).

WHEREAS, Taisho and Neurocrine now wish to amend the License Agreement to provide for collaboration between Neurocrine and Taisho in the development of NBI-6024 and to provide to Taisho exclusive commercialization rights to NBI-6024 in the Neurocrine Territory (as defined in the License Agreement) as an additional option set forth in Section 3.5 of the License Agreement.

NOW THEREFORE, in consideration of the foregoing and the covenants and promises contained in this Amendment, the Parties agree as follows:

ARTICLE 1

DEFINITIONS

Unless otherwise defined herein, capitalized terms used in this Amendment and in the License Agreement amended by this Amendment shall have the meanings assigned to such terms in the License Agreement.

1.1 "Collaboration" shall mean the collaboration between Taisho and Neurocrine to Develop Licensed Products under the terms set forth herein.

1.2 "Development Plan" shall mean the annual worldwide plan for the Development of Products as approved by the JSC.

1.3 "Licensed Territory" shall mean all the world.

1.4 "Milestone Payments" shall mean the payments to be made by Taisho to Neurocrine upon occurrence of certain events as set forth in Sections 5.1B and 5.2B or 5.5B.

1.5 "Net Sales" shall mean the sales of Products or, in the case of multi active components Products, NBI-6024 contributed portion thereof (as determined by a method approved by both Parties), for the sale of Products by Taisho or Affiliates or sublicensees of Taisho to a Third Party other than Affiliates or sublicensees of Taisho, less the amount incurred such as returns and allowances (including, but not limited to, prompt payment and volume discounts, chargebacks from wholesalers and other allowances granted to customers or wholesalers of Products, whether in cash or trade), freight, shipping, packing, insurance, rebates, and sales and other taxes based on sales when included in gross sales, but not including taxes when assessed on income derived from such sales.

1.6 "Rest of World" shall mean all the world other than Asian and European countries listed on Exhibit D.

ARTICLE 2

AMENDEMENTS

2.1 Amendment of Section 1.29. Section 1,29 of the License Agreement ("Neurocrine Territory") is hereby deleted.

2.2 Amendment of Section 2.3. Section 2.3(b) of the License Agreement is hereby amended to read as set forth below.

(b) Indications. Taisho will use Commercially Reasonable Efforts to obtain Governmental Approvals to Develop and Commercialize NBI-6024 in the Licensed Territory for all reasonable indications to the extent regulatively and practically appropriate taking into consideration the circumstances of markets in the Licensed Territory.

2.3 Amendment of Section 2.4. Section 2.4 of the License Agreement is hereby amended to read as set forth below.

(a) Development and Commercialization. Neurocrine covenants to use Commercially Reasonable Efforts to collaborate with Taisho to Develop and Commercialize Products in the Licensed Territory.

(b) Compliance by Neurocrine. Neurocrine covenants that all activities undertaken by Neurocrine in collaborating with Taisho hereunder will comply with all applicable statutes, regulations and guidance of any Governmental Authorities relating to the Development and/or Commercialization of Products.

2.4 Amendment of Section 3.2 (b). Section 3.2(b) of the License Agreement is hereby amended to read as set forth below.

(b) Taisho hereby grants to Neurocrine [XXX]license[XXX] under Licensed Technology and Taisho Technology, [XXX]as set forth in this Agreement.

2.5 Amendment of Section 3.3. Section 3.3 of the License Agreement is hereby amended to read as set forth below.

3.3 Sublicenses. Taisho shall have the right to grant sublicenses to Licensed Technology to Third Parties, provided, however, that Taisho shall remain responsible for the full and complete performance of all obligations hereunder. Taisho shall provide Neurocrine with copies of all agreements sublicensing the Licensed Technology, [XXX]

2.6 Amendment of Section 3.5. Section 3.5 of the License Agreement is hereby deleted.

2.7 Amendment of Section 4.1. Section 4.1 of the License Agreement is hereby amended to delete "for each of the Parties" in Subsection (iii).

2.8 Amendment of Section 4.2. Section 4.2 of the License Agreement is hereby amended to read as set forth below.

4.2 Meetings and Decision of the Joint Steering Committee. The chairperson of the JSC will be designated annually by Taisho and Neurocrine on an alternating basis starting with Neurocrine. A secretary will be appointed for each meeting and shall be responsible for the minutes of the meeting. The JSC shall meet no less frequently than twice per year. Decisions of the JSC shall be made by unanimous vote. In the event the JSC is unable to reach agreement on any issue, the issue shall be referred to the Senior Vice President, Development of Neurocrine and Head of Development of Taisho for resolution. In the event these two persons are unable to reach agreement on the issue, the issue shall be finally decided by Head of Development of Taisho. All decisions of the JSC shall be consistent with the Five Year Plan and will be reached in good faith.

2.9 Amendment of Section 4.3. Section 4.3 of the License Agreement is amended to read as set forth below.

4.3 Development Plan. Prior to the Effective Date the Parties worked together to coordinate a development plan for a global five year plan (the "Five Year Plan" as set forth on Exhibit E). The goal of the FiveYear Plan is to maximize Product potential through coordinated, efficient and cost effective Development and Commercialization. The FiveYear Plan includes outline timelines for pre-clinical and clinical studies and Regulatory Filings. The Five Year Plan will be updated on an annual basis and, when necessary in consideration of the progress of the Development, from time to time additionally by mutual agreement of the Parties. On or before September 15 of each year the JSC will adopt a plan for the Development of Products for the Licensed Territory in the next following year (the "Development Plans"). The Development Plans will be consistent with the then valid FiveYear Plan.

2.10 Amendment of Section 4.4. Section 4.4 of the License Agreement is hereby amended to read as set forth below.

4.4 Data. On each meeting of the JSC, and upon written request at any other time, the Parties will exchange written summaries of all Development Data obtained to the date. All Development Data shall be considered Confidential Information of the disclosing Party. The Parties shall maintain all Development Data, related records, documents and raw data in sufficient detail and in good scientific manner as will properly reflect all works done and results achieved in the performance of the Development.

2.11 Amendment of Section 4.5. Section 4.5 of the License Agreement is hereby deleted.

2.12 Amendment of Section 4.6. Section 4.6 of the License Agreement is hereby amended to read as set forth below.

4.6 Collaboration.

(a) Taisho will fund conduct of the Collaboration by no less than [XXX] Neurocrine FTEs (full time equivalents equal to [XXX] hours per year) for a period of [XXX]. Taisho will compensate Neurocrine for the Neurocrine FTEs at a rate of [XXX] per FTE per [XXX]. The Neurocrine FTEs will be devoted [XXX]. The number of Neurocrine FTEs may be increased or decreased and/or extended beyond the initial [XXX]term upon mutual agreement of the Parties.

(b) Taisho may request that Neurocrine conduct on Taisho's behalf certain research, pre-clinical studies, and/or clinical studies on Products set forth in Development Plan as a part of the Collaboration. In the event such research, pre-clinical studies, and/or clinical studies shall not be covered by the Neurocrine FTEs set forth in (a) above, Taisho will compensate Neurocrine for additional Neurocrine FTEs devoted to such research, pre-clinical studies, and/or clinical studies at a rate of [XXX].

2.13 Amendment of Section 4.8. Section 4.8 of the License Agreement is hereby amended to read as set forth below.

4.8 Development Cost. [XXX]of all studies and activities and in-house study costs approved by the JSC based upon the Five Year Plan and the Development Plan, which are conducted after (effective date of this Amendment), [XXX]. The outside costs of all studies and activities [XXX] approved by the JSC based upon the Five Year Plan and the Development Plan, which are conducted from the execution of this Agreement until (effective date of this Amendment), shall be [XXX] in accordance with [XXX] to be agreed by the Parties. Additionally, Taisho shall reimburse Neurocrine [XXX] of all development expenses for the Licensed Territory that occurred from December 25, 1999 to the execution of this Agreement. Such reimbursement will be due within thirty (30) days of the execution of this Agreement.

2.14 Amendment of Section 4.9. Section 4.9 of the License Agreement is

hereby amended to read as set forth below.

4.9 Commercialization. The JSC shall monitor the Commercialization of Products. All matters relating to Commercialization of Products in the Licensed Territory shall be decided by Taisho in Taisho's sole business judgment.

2.15 Amendment of Section 4.10. Section 4.10 of the License Agreement is hereby amended to read as set forth below.

4.10 Reporting. Neurocrine and Taisho shall each promptly notify the other of any events that come to their attention which shall be reported to any Governmental Authorities under any laws and regulations including 21 CFR 314.80, 600.12, 600.14 and 600.80 of the United States (as such requirements may be amended from time to time) and any similar or equivalent reporting requirements to other Governmental Authorities. As for the events that occur in the context of clinical trials, both Parties shall comply with provisions of Exhibit F.

2.16 Amendment of Article 5. Article 5 of the License Agreement is hereby amended to read as set forth below.

ARTICLE 5

LICENSE FEES AND MILESTONE PAYMENTS

5.1 LICENSE FEES AND MILESTONE PAYMENTS FOR ASIA AND EUROPE.

5.1A Data Purchase. On execution of this Agreement, Taisho shall purchase from Neurocrine rights to the Neurocrine CTX filing for NBI-6024 and all supporting data and information for use in exploitation of the Asian rights granted hereunder for a one-time payment of [XXX] and rights to the Neurocrine CTX filing for NBI-6024 and all supporting data and information for use in exploitation of the European rights granted hereunder for a one-time payment of [XXX]. The above payments shall be made within thirty (30) days of execution of this Agreement.

5.1B Milestone Payments. At the first occurrence of the events as to the Product first applicable to the events set forth below, within thirty (30) days after Taisho becomes aware of it, Taisho shall pay the corresponding amounts as the Milestone Payments for the rights in Asian countries and European countries to Products granted to it as long as this Agreement is in force and effect, provided, however, as to the events which occurred before the execution of this Agreement, Taisho shall pay the corresponding amount within thirty (30) days of the execution of this Agreement:

a) for the rights in Japan and other Asian countries total $[XXX]

- o [XXX] Phase II [XXX] $[XXX]
- o [XXX] Pediatric Phase II [XXX] $[XXX]
- o [XXX] Phase III [XXX] $[XXX]
- o Regulatory Filing of New Drug Application or any other comparable filing [XXX] $[XXX]
- o Governmental Approval for [XXX] $[XXX]

b) for the rights in European countries total $[XXX]

- o [XXX] Phase II [XXX] $[XXX]
- o [XXX] Pediatric Phase II [XXX] $[XXX]
- o [XXX] Phase III [XXX] $[XXX]
- o Regulatory Filing of New Drug Application or any other comparable filing in [XXX] $[XXX]
- o Governmental Approval for Commercialization [XXX] $[XXX]

Each Milestone Payment shall be made only once. [XXX] upon Regulatory Filing of New Drug Application or any other comparable filing in any country in Asian and European countries listed on Exhibit D.

5.2 LICENSE FEES AND MILESTONE PAYMENTS FOR REST OF WORLD.

5.2A. License Issue Fee. In consideration of the licenses to the Licensed Technology in the Rest of World, Taisho will pay to Neurocrine a license fee of [XXX]. The above payment shall be made within thirty

(30) days of execution of this Amendment.

5.2B Milestone Payments. At the first occurrence of the events as to the Product first applicable to the events set forth below, within thirty (30) days after Taisho becomes aware of it, Taisho shall pay the corresponding amounts as the Milestone Payments for the rights in the Rest of World to Products granted to it as long as this Agreement is in force and effect, provided, however, as to the events which occurred before(effective date of this Amendment), Taisho shall pay the corresponding amount within thirty (30) days from (effective date of this Amendment):

- Completion of [XXX] Phase I [XXX] $[XXX]
- [XXX] Phase II [XXX] $[XXX]
- [XXX] Pediatric Phase II [XXX] $[XXX]
- [XXX] Phase III [XXX] $[XXX]
- Regulatory Filing of New Drug Application [XXX] $[XXX]
- Governmental Approval for Commercialization [XXX] $[XXX]

Each Milestone Payment shall be made only once. [XXX] upon Regulatory Filing of New Drug Application in the United States.

5.3 Third Party Royalties. [XXX] shall bear any payments (license fees, milestone payments and royalties and so on) owed or to be owed to the Third Parties with respect to Existing Royalty Obligations in the Licensed Territory. In consideration of [XXX] Existing Royalty Obligations [XXX] will pay to [XXX] bear any other payments (license fees, milestone payments and royalties and so on) owed or to be owed to Third Parties other than their Affiliates with respect to patents or patent applications in the Licensed Territory, that are owned or controlled by such Third Parties and that would [XXX]on the basis [XXX] directed to [XXX]. [XXX] shall bear any payments (license fees, milestone payments and royalties and so on) owed or to be owed to Third Parties other than [XXX] Affiliates with respect to such Third Parties' patents or patent applications in the Licensed Territory other than those described in above two cases.

5.4 Sublicense Fee. Within thirty (30) days of the date upon which [XXX] or its Affiliate shall grant a sublicense to the [XXX] to any Third Party other than [XXX] shall pay [XXX] per each of such Third Parties as executing parties of sublicense agreement with [XXX]. In the event a sublicensee of [XXX] (other [XXX] shall further sublicense the Licensed Technology, [XXX] will be payable for such further sublicense unless under the circumstances [XXX] that would have been more [XXX].

5.5 PROFIT SHARING OPTION FOR REST OF WORLD

5.5A Profit Sharing Option. At any time after [XXX] and before [XXX] shall have the option to elect to change the agreement for Rest of World from a royalty bearing arrangement as provided in Section 5.2, to a profit sharing structure as set forth in this Section 5.5 (the "Option"). At the time [XXX] to exercise the Option the Parties will [XXX] Development and Commercialization of Products in the Rest of World. [XXX]completed prior to [XXX], provided, however, that such [XXX] shall be [XXX].

5.5B Milestone Payments.

In the event [XXX] on or before the date of the first occurrence of the events [XXX] to the events [XXX], Section 5.2B will not apply irrespective of its provision and the following provision will apply instead. In the event [XXX] after the date of the first occurrence of the events [XXX] to the events stipulated [XXX], Section 5.2B irrespective of its provision shall no longer apply and the following provision will apply instead.

At the first occurrence of the events as to the Product first applicable to the events set forth below, within thirty (30) days after Taisho becomes aware of it, Taisho shall pay the corresponding amounts as the Milestone Payments for the rights in the Rest of World to Products granted to it as long as this Agreement is in force and effect, provided, however, as to the events which occurred before (effective date of this Amendment), Taisho shall pay the corresponding amount within thirty (30) days from (effective date of this Amendment):

- Completion of [XXX] Phase I [XXX] $[XXX]
- [XXX] Phase II [XXX] $[XXX]
- [XXX] Pediatric Phase II [XXX] $[XXX]
- [XXX] Phase III [XXX] $[XXX]

o Regulatory Filing of New Drug Application [XXX] $[XXX]

o Governmental Approval for Commercialization [XXX] $[XXX]

Each Milestone Payment shall be made only once. [XXX] upon Regulatory Filing of New Drug Application in the United States.

If any Milestone Payments [XXX] in any country in the world have been made pursuant to Section 5.2B prior to the exercise of the Option, the amount of each subsequent Milestone Payment under this Section 5.5B for the rights in the Rest of World shall [XXX] so that the total Milestone Payments under this Section 5.5B for the rights in the Rest of World [XXX]. For clarity, the license fee of [XXX] payable under Section 5.2A [XXX].

5.5C Royalties. Neurocrine shall be paid a royalty of [XXX]of Net Sales of Products in the United States and a royalty [XXX] of Net Sales of Products in the Rest of World excluding the United States until the time set forth in 6.4 (c).

5.5D Profit Sharing. Taisho and Neurocrine will [XXX] the net profits from sales of Products in the Rest of World. The net profits will be calculated by subtracting [XXX]other than those [XXX] to calculate Net Sales, the royalties due [XXX] set forth in [XXX] Net Sales in the United States as Neurocrine's Existing Royalty Obligation [XXX], from Net Sales of Products [XXX]. For clarity, any payments [XXX] other than [XXX] of Net Sales in the United States [XXX] Neurocrine's Existing Royalty Obligation [XXX] shall not be subtracted from Net Sales of Products in the Rest of World [XXX].

5.5E Third Party Royalties. In the event [XXX] the Option before any [XXX], Section 5.3 will not apply irrespective of its provision and the following provision will apply instead. In the event [XXX] on or after [XXX], Section 5.3 irrespective of its provisions shall no longer apply and the following provision will apply instead.

[XXX] shall bear any payments (license fees, milestone payments and royalties and so on) owed or to be owed to the Third Parties with respect to Existing Royalty Obligations in the Licensed Territory ([XXX] which shall be paid as set forth [XXX]any other payments (license fees, milestone payments and royalties and so on) owed or to be owed to Third Parties other than their Affiliates with respect to patents or patent applications in the Licensed Territory, that are owned or controlled by such Third Parties and that would [XXX] Products on the basis of [XXX] directed to [XXX]. With respect to Third Parties patents or patent applications in the Licensed Territory other than those described in above two cases, [XXX] shall bear any payments (license fees, milestone payments and royalties and so on) owed or to be owed to such Third Parties other than [XXX] in Asian and European countries listed on Exhibit D, and [XXX] any payments (license fees, milestone payments and royalties and so on) owed or to be owed to such Third Parties other than [XXX] in the Rest of World.

5.5F Supply and Manufacturing. In the event [XXX] the Option, the price for supply of NBI-6024 for Commercialization in the Rest of World shall be [XXX] and so the provisions in Section 6.4 with regard to the price for supply for Rest of World, irrespective of the provisions set forth in Section 6.4, will not apply to the supply for the Rest of World and the provisions of Section 6.4 will then apply only to the supply for Asian countries and European countries. Similarly, in the event [XXX] the Option, the provisions in Section 6.7 with regard to the royalty to be paid by Taisho, irrespective of the provisions of Section 6.7, will not apply to the manufacturing by Taisho or its subcontractor of NBI-6024 for the Rest of World (Taisho shall not pay any royalty for the manufacturing by Taisho or its subcontractor of NBI-6024 for the Rest of World) and the provisions of Section 6.7 will then apply only to the manufacturing by Taisho or its subcontractor of NBI-6024 for Asian countries and European countries.

2.17 Amendment of Article 6. Article 6 of the License Agreement is hereby amended to delete all references to Independent Studies and Neurocrine Territory.

2.18 Amendment of Section 6.4. Section 6.4 of the License Agreement is hereby amended to add the following subsection (c).

(c) for Rest of World in the Licensed Territory, the expiration of Patent Right last to expire of the Licensed Patent Rights in the United States.

2.19 Amendment of Section 6.7. Section 6.7 of the License Agreement is hereby amended to read as set forth below.

6.7 Manufacturing by Taisho. To the extent of not conflicting with

Sections 6.1 and 6.2 above or after the expiration of Patent Right last to expire of Licensed Patent Rights in the Licensed Territory, Taisho shall have the right to manufacture NBI-6024 for the Licensed Territory and/or have NBI-6024 manufactured on its behalf, which shall be subject to the terms and conditions to be agreed by the Parties [XXX]. In such cases, Taisho shall pay in consideration of the license of Manufacturing Technology (a) the royalty [XXX] of Net Sales in all Asian countries in the Licensed Territory until the time set forth in Section 6.4 (a), (b) the royalty [XXX] of Net Sales in all European countries in the Licensed Territory until the time set forth in Section 6.4 (b) and (c) the royalty [XXX] of Net Sales in Rest of World until the time set forth in 6.4(c), provided however [XXX] to the case in which [XXX] shall manufacture [XXX] and supply it to [XXX]. In case the manufacturing cost incurred [XXX] is [XXX] to meet the above requirements, [XXX] shall seek for [XXX] including [XXX].

2.20 Amendment of Section 8.1. Section 8.1 of the License Agreement is hereby amended to read as set forth below.

8.1 Trademarks. Taisho will market Products under its own Trademarks.

2.21 Amendment of Section 8.2 (b). Section 8.2 (b) of the License Agreement is hereby amended to read as set forth below.

(b) Expenses. All expenses in connection with prosecution and maintenance of the Licensed Patent Rights will be borne by [XXX], provided, however, [XXX] shall bear a) all expenses incurred after the execution of this Agreement in connection with prosecution and maintenance of the Licensed Patent Rights in [XXX] to the extent this Agreement is in force and effect until (effective date of this amendment), and b) all expenses incurred after (effective date of this amendment) in connection with prosecution and maintenance of the Licensed Patent Rights in the Licensed Territory to the extent this Agreement is in force and effect.

2.22 Amendment of Sections 8.3 and 8.4. Sections 8.3 and 8.4 of the License Agreement are hereby amended to delete all references to the Neurocrine Territory And to replace all "the execution of this Agreement" in the both Sections with (effective date of this amendment).

2.23 Amendment of Sections 8.5. Sections 8.5(a) of the License Agreement is hereby amended to read as set forth below.

(a) Intellectual property rights regarding any invention made by either Party during the term of this Agreement shall be solely owned by such Party, and the other Party shall have no rights in or to such invention other than those rights specifically granted to such other Party hereunder. The Party who made the invention shall have the right to prosecute and maintain, in its sole discretion and at its own expenses, all patent application or patent regarding such invention in any country in the world. Taisho, its Affiliates and its sublicensees shall have a non-exclusive right to exercise such invention by Neurocrine free of charge only for the purpose of Development and Commercialization of Products in the Licensed Territory.

2.24 Amendment of Section 11.1. Section 11.1 of the License Agreement is hereby amended to read as set forth below.

11.1 Indemnification.

(a) Non-Patent. Taisho shall indemnify and hold Neurocrine harmless from and against any and all liability, damage, loss, cost (including reasonable attorneys' fees) and expense arising out of the Development and/or Commercialization of Products by Taisho, its Affiliates and/or its sublicensees and including the conduct of the Collaboration by Neurocrine other than those arising out of the infringement of a Patent Right of a Third Party through the making, using or selling of Products by Taisho, its Affiliates and/or its sublicensees, provided, however, in case Neurocrine receives notice of a claim for which indemnification may be sought, Neurocrine shall promptly inform Taisho of such notice. Notwithstanding the foregoing Neurocrine shall not be entitled to indemnification under this subsection (a), against any claim of personal injury or property damage to the extent resulting from Neurocrine's negligence or misconduct.

(b) Patent. Subject to Section 5.3 and Article 8, Taisho will indemnify Neurocrine and hold Neurocrine harmless from and against any and all liability, damage, loss, cost (including reasonable attorneys' fees) and expense arising out of any claim of infringement of a Patent Right of a Third Party through the making, having made, using, selling or having sold Products by or on behalf of Taisho which is brought by a Third Party, provided, however, in case Neurocrine receives notice of a claim for which indemnification may be sought, Neurocrine shall promptly inform Taisho of such notice and, provided, further, that .the foregoing shall not apply to any Third Party licensor of Existing

Royalty Patent Rights.

2.25 Amendment of Section 12.2. Section 12.2 of the License Agreement is hereby revised to read as set forth below.

12.2 Termination of Product Development.

Should Taisho [XXX], rights of Taisho to Products (including all data, information, physical manifestations and Regulatory Filings) in the Licensed Territory shall revert and be delivered to Neurocrine, and Taisho shall be free from any and all monetary or developmental obligations thereafter. In addition, Neurocrine shall be granted a royalty-free worldwide non-exclusive license with sublicensing rights under the Taisho Technology to make, have made, use and sell Products. Should [XXX] may retain its all rights of Asian and European countries listed on Exhibit D subject to the terms and the condition of this Agreement originally executed by the Parties (i.e. the original one before being given any amendment).

ARTICLE 3

MISCELLANEOUS PROVISIONS

3.1 Further Actions. Each Party agrees to execute, acknowledge and deliver such further instruments, and to do all such other acts, as may be necessary or appropriate in order to carry out the purposes and intent of this Amendment.

3.2 Counterparts. This Amendment shall be executed in two counterparts, each of which shall contain the signature of the Parties and all such counterparts shall constitute one and the same agreement.

3.3 Descriptive Headings. The descriptive headings of this Amendment are for convenience only, and shall be of no force or effect in construing or interpreting any of the provisions of this Amendment.

3.4 Governing Law. This Amendment shall be governed by and interpreted in accordance with the substantive laws of the State of California.

3.5 Severability. Whenever possible, each provision of this Amendment will be interpreted in such manner as to be effective and valid under applicable law, but if any provision of this Amendment is held to be prohibited by or invalid under applicable law, such provision will be ineffective only to the extent of such prohibition or invalidity, without invalidating the remainder of this Amendment.

3.6 Entire Agreement of the Parties. This Amendment together with the License Agreement will constitute and contain the complete, final and exclusive understanding and agreement of the Parties and cancels and supersedes any and all prior negotiations, correspondence, understandings and agreements, whether oral or written, between the Parties respecting the subject matter hereof.

3.7 Dispute Resolution. The Parties agree that in the event of a dispute between them arising from, concerning or in any way relating to this Amendment, the Parties shall undertake good faith efforts to resolve any such dispute in good faith. In the event the Parties shall be unable to resolve any such dispute, the matter shall be referred to the Chief Executive Officer of Neurocrine and the President of Taisho for further review and resolution. In the event that they shall be unable to resolve the dispute, then the dispute shall be finally settled by arbitration, in San Francisco, California, under the Rules of Conciliation and Arbitration of the International Chamber of Commerce. The award of arbitration shall be final and binding upon both Parties.

IN WITNESS WHEREOF, the Parties hereto have executed this Amendment as of the date first above written.

NEUROCRINE BIOSCIENCES, INC.

/s/ Margaret Valeur-Jensen
- ---------------------------
By: Margaret Valeur-Jensen
Title: Senior Vice President and General Counsel

TAISHO PHARMACEUTICAL CO., LTD.

/s/ Akira Uehara
- ----------------
By: Akira Uehara
Title: President

Exhibit 23.1

CONSENT OF ERNST & YOUNG LLP, INDEPENDENT AUDITORS

We consent to the incorporation by reference in the Registration Statements Form S-3 No. 333-95005 and Forms S-8 Nos. 333-57875 and 333-87127 of our report dated January 27, 2001, with respect to the consolidated financial statements of Neurocrine Biosciences, Inc. included in the Annual Report (Form 10-K) for the year ended December 31, 2000.

/s/ Ernst & Young LLP
Ernst & Young LLP

San Diego, California
March 27, 2001