## 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, 1998 0R

TRANSITION REPORT PURSUANT TO SECTION 13 OR 15(D) OF THE SECURITIES EXCHANGE ACT OF 1934 For the transition period from to

Commission file number: 0-28150 NEUROCRINE BIOSCIENCES, INC. (Exact name of registrant as specified in its charter)

Delaware 33-0525145 (State or other jurisdiction (I.R.S. Employer of incorporation or organization) Identification Number)

10555 Science Center Drive, San Diego, CA 92121 (Address of principal executive office) (Zip Code)

Registrant's telephone number, including area code: (619) 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.

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

The aggregate market value of the voting stock of the issuer held by non-affiliates of the issuer on March 15, 1999 was approximately \$88,054,931, based upon the closing price of such stock of \$6.31 on March 15, 1999. As o based upon the closing price of such stock of \$6.31 on March 15, 1999. As of March 15, 1999, 18,960,581 shares of Common Stock of the registrant were outstanding.

#### DOCUMENTS INCORPORATED BY REFERENCE

Certain information required by Parts I and 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 21, 1999 (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, 1998.

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PART I

ITEM 1. BUSINESS

**BACKGROUND** 

Neurocrine Biosciences, Inc. 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, Alzheimer's disease, insomnia, stroke, glioblastoma, sclerosis, obesity and diabetes.

The following Business section contains forward-looking statements concerning the continuation of the Company's strategic alliances and the receipt of payments thereunder, the identification of drug targets and selection of lead compounds for clinical development, the commencement and successful conclusion of clinical trials, the receipt of regulatory approvals, and the potential development of future commercial products. Such forward-looking statements necessarily involve risks and uncertainties. The Company's actual results could differ materially from those anticipated in these forward-looking statements as a result of cortain factors, including without limitation that receases a result of certain factors, including, without limitation, that research

funding and development will continue under the Company's collaborations, that research and development candidates will successfully proceed through pre-clinical and early stage clinical trials, that development candidates will prove effective for treatment in humans in later stage clinical trials, the timely receipt of regulatory clearances required for clinical testing, manufacturing and marketing of products, the potential adverse impact of competitive technologies, products, and intellectual property rights of third parties, and the failure to achieve product development and commercialization goals. Actual results and the timing of certain events could differ materially from those indicated in the forward-looking statements as a result of these and other factors. See "Risk Factors."

Neurocrine currently has five programs in clinical development. The Company's CRF receptor antagonist project is currently in Phase II clinical development with its partner, Janssen Pharmaceutica, for anxiety/depression. Neurocrine and its partner, Novartis Pharmaceuticals, are conducting their second Phase II clinical trial with Neurocrine's Altered Peptide Ligand (APL) compound in patients with multiple sclerosis. Neurocrine is conducting a Phase I/II trial with for its IL-4 Fusion Toxin for glioblastoma (malignant brain tumors). The Company has also completed a Phase Ib clinical trial in insomnia with a GABA receptor subtype agonist and recently announced that it commenced a Phase I safety and dose escalating clinical study with an APL compound for Type I Diabetic patients.

#### PRODUCTS UNDER DEVELOPMENT

The following table summarizes Neurocrine's most advanced products in research and clinical development. This table is qualified in its entirety by reference to the more detailed descriptions appearing elsewhere in this Form 10-K.

Program	Indication	Status	Commercial Rights
CRF Receptor Antagonist	Anxiety/Depression	Phase II	Janssen/Neurocrine
Altered Peptide Ligand	Multiple Sclerosis	Phase II	Novartis/Neurocrine
IL-4 Fusion Toxin	Glioblastoma	Phase I/II	Neurocrine
GABA Receptor Subtype Agonist	Insomnia	Phase I/II	Neurocrine
Altered Peptide Ligand	Type I diabetes	Phase I	Neurocrine
CRF Receptor Antagonist	Stroke	Development	Neurocrine
CRF / Urocortin Agonist	Alzheimer's/Obesity	Research	Lilly/Neurocrine
Excitatory Amino Acid Transporters	Stroke	Research	Wyeth-Ayerst/Neurocrine
Melanocortin Receptor Antagonist	Obesity	Research	Neurocrine
Chemokine Antagonist	Inflammatory Disorders	Research	Neurocrine
GNRh	Endometriosis	Research	Neurocrine
Neurogenomics	Neurodegenerative	Research	NPI/Neurocrine

(1) "Research" indicates identification and evaluation of compounds in in vitro and animal models.

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

"Phase I" indicates that Neurocrine or its collaborative partner is conducting clinical trials to determine safety, the maximally tolerated dose and pharmacokinetics of the compound in human volunteers.

"Phase II" indicates that the Company has received FDA approval to evaluate one of the Company's products in humans to determine safety and efficacy in an expanded patient population.

 $\label{lem:neurocrine} \textbf{Neurocrine's Research and Development Programs}$ 

Corticotropin Releasing Factor ("CRF")

Corticotropin releasing factor, the central regulator of the body's overall response to stress, affects multiple systems by functioning both as an endocrine factor and a neurotransmitter. CRF acts as a hormone at the pituitary gland causing the secretion of the steroid cortisol from the adrenal glands resulting in a number of metabolic effects, including suppression of the immune system. CRF also functions as a neurotransmitter in the brain and plays a critical role in coordinating psychological and behavioral responses to stress such as increased heart rate, anxiety, arousal and reduced appetite. In addition to neuroendocrine and neurotransmitter roles, accumulating evidence suggests that CRF may also integrate actions between the immune and central nervous systems in response to physiological and psychological stressors.

The body has several mechanisms to regulate the effects of CRF. The Company's cloning of human CRF receptors and binding proteins suggests that the diverse functions of CRF are mediated through distinct receptor subtypes which are differentially distributed in specific brain areas and in tissues outside of the central nervous system. These targets may offer a mechanism to modulate specific actions of CRF without affecting the broad range of its activities. There are several diseases and disorders such as anxiety, depression and

substance abuse in which CRF levels are increased. The deleterious effects of high levels of CRF may be countered by the administration of selective CRF receptor antagonists.

#### Anxiety

Anxiety is among the most commonly observed group of CNS disorders, which includes phobias or irrational fears, panic attacks, obsessive-compulsive disorders and other fear and tension syndromes. Estimates by the National Institute of Mental Health suggest that the most commonly diagnosed forms of anxiety disorders may affect 10% of the United States population. Of the pharmaceutical agents that are currently marketed for the treatment of anxiety disorders, a class of compounds known as the benzodiazepines, which includes Valium, is the most frequently prescribed. In spite of their therapeutic efficacy, several side effects limit the utility of these anti-anxiety drugs. Most problematic among these are drowsiness, ataxia (the inability to stand up), amnesia, drug dependency and withdrawal reactions following the cessation of therapy.

Neurocrine is developing a new class of therapeutics that targets stress-induced anxiety. In view of the evidence implicating CRF in anxiety-related disorders, Neurocrine is developing small molecule CRF receptor antagonists as anti-anxiety agents that block the effects of overproduction of CRF. The Company believes that these compounds represent a class of molecules based on a novel mechanism of action that may offer the advantage of being more selective, thereby providing increased efficacy with reduced side effects. In animal studies used to evaluate anti-anxiety drugs, Neurocrine scientists have demonstrated the efficacy of its clinical compound candidates following oral administration without evidence of apparent side effects. Neurocrine's corporate partner, Janssen, selected a CRF-1 receptor antagonist drug candidate for preclinical testing in 1996 and commenced and completed Phase I clinical trials on the compound in late 1998. Results in animal models of anxiety are not necessary predictive of efficacy in human clinical trials and there can be no assurance that these compounds will demonstrate clinical efficacy in humans. In addition, no assurance can be given that Janssen will successfully initiate and complete Phase II clinical testing or progress to later clinical trials in a timely manner.

#### Depression

Depression is one of a group of neuropsychiatric disorders that includes extreme feelings of elation and despair, loss of body weight, decreased aggressiveness and sexual behavior, and loss of sleep. This condition is believed to result from a combination of environmental factors, including stress, as well as an individual's biochemical vulnerability, which is genetically predetermined. The biochemical basis of depression is thought to involve elevated secretion of CRF and abnormally low levels of other neurotransmitters in the brain such as serotonin. Clinical depression was reported to affect 6% of the population or approximately 25 million individuals in the United States in 1998. Current antidepressant therapies, including Prozac, increase the levels of serotonin and several other chemicals in the brain. Because these drugs affect a wide range of neurotransmitters, they have been associated with a number of side effects. While newer, more selective drugs offer some safety improvement, side effects remain problematic. Another limitation to most existing antidepressant therapies is slow onset of action.

Neurocrine and its corporate partner are developing small molecule therapeutics to block the effects of overproduction of CRF for the treatment of depression. The Company has developed several distinct chemical series of CRF receptor antagonists. Janssen selected a drug candidate in 1996 for preclinical testing and commenced Phase I clinical trials on the compound in late 1997 and completed these in 1998. In late 1998 a Phase II open label trial was initiated in patients with major depression. Results from this trial are expected to be available in second half of 1999. No assurance can be given that Janssen will successfully complete Phase II clinical testing of this candidate or that the Phase II data will support continuation of the program and additional clinical trials.

# Stroke

Stroke is an acute neurologic event caused by blockage or rupture of vessels, which supply blood to the brain leading to nerve cell death. Neuronal damage progresses over a period of four to six hours. According to the National Institutes of Health ("NIH") estimates, approximately 500,000 patients experience a stroke in the United States each year, with an approximately equal incidence in the rest of the world. Stroke results in an estimated 150,000 fatalities each year, making it the leading cause of death behind heart disease and cancer, and an estimated additional 150,000 stroke victims suffer permanent neurological damage. Survivors of stroke are at significantly increased risk of suffering another episode. Current treatments for stroke consist of surgery, steroid therapy and anti-platelet therapy. These treatments may help increase blood flow but do not affect the secondary mechanisms which cause nerve cell death.

Neurocrine believes its CRF receptor antagonist program may have utility in the treatment of stroke. Preliminary experiments in animal models of stroke show enhancement of neuronal survival following treatment with a CRF receptor antagonist. Results obtained in animals are not necessarily predictive of results obtained in humans, and no assurance can be given that the Company will successfully complete pre-clinical development of CRF antagonist drug candidates appropriate for stroke and enter into or complete clinical trials in a timely manner, if at all.

#### Altered Peptide Ligands

In North America, five percent of adults, more than two-thirds of them

women, suffer from autoimmune diseases (including multiple sclerosis, rheumatoid arthritis, Type I diabetes, systemic lupus erythematosus, and thyroiditis). The body's immune system employs highly specific T cells that recognize and attack foreign antigens that invade the body. Occasionally, certain T cells arise that inappropriately recognize the body's own tissues as foreign. While virtually every individual possesses these self-reactive T cells, in only a fraction of these people do the immune cells actually attack healthy tissue and cause an autoimmune disease. In a healthy individual, the activity of these self-reactive T cells is held in check by other T cells that regulate their function (regulatory T cells). If a defect in regulatory T cell function occurs, or the environment favors the activity of self-reactive T cells, an autoimmune disease results. While it is not clear what triggers the immune attack, a current hypothesis suggests that people who are genetically predisposed to autoimmune diseases come in contact with certain infectious viruses or bacteria. In the process of controlling the infection, the immune system targets an antigen on the infectious agent that resembles a self-antigen. These cells then begin to attack self-tissue, resulting in autoimmune disease. Thus, a failure in regulation of the immune system at the level of dysfunctional regulatory T cells predisposes an individual to autoimmune disease. Current reasoning suggests that the development of immune specific drugs that suppress the action of self-reactive T cells and/or restore the function of regulatory T cells might prove advantageous for the prevention/cure or treatment of an autoimmune disease.

The T cells involved in the autoimmune disease achieve specificity in their various functions via their cell surface molecules known as T cell antigen receptors ("TCR"). Each T cell expresses its own specific TCR on its surface. T cells recognize antigens, whether foreign or self-derived in the context of a MHC molecule. This then represents the ligand that hooks up and binds to such a TCR. In this manner, a peptide fragment can send a signal to the T cell via an antigen-specific TCR that binds specifically to this antigen. After receiving this signal through its TCR, the T cell will divide, proliferate, secrete cytokines and/or destroy healthy cells.

If the structure of such a peptide fragment is altered, such that it binds to its specific TCR with much less affinity, this altered peptide ligand ("APL") sends an incomplete signal to the T cell. This incomplete or altered signal can trick a T cell and prevent it from dividing, proliferating, secreting cytokines and/or destroying normal cells. Indeed, if such an APL can be designed to prevent "killer" T cells from destroying healthy cells, it would represent a very useful antigen-specific therapy to prevent the onset of an autoimmune disease.

#### Multiple Sclerosis ("MS")

Multiple sclerosis is a chronic immune mediated disease characterized by recurrent attacks of neurologic dysfunction due to damage in the central nervous system ("CNS"). The classic clinical features of MS 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. The cause of MS is unknown but immunologic or infectious factors have been implicated. According to the National Multiple Sclerosis Society, there are an estimated 350,000 cases of multiple sclerosis in the United States and an equal number of patients in Europe with approximately 20,000 new cases diagnosed worldwide each year. Currently available treatments for MS offer only limited efficacy. Steroids have been used to reduce the severity of acute flare-ups and speed recovery. Experimental therapy with other immunosuppressive agents has shown limited success. Betaseron (a form of beta-interferon) has been shown to delay the onset of flare-ups of the symptoms in patients and has been approved for marketing by the FDA. In addition, Avonex, a similar form of beta-interferon, and Copaxone, a random peptide polymer, have received FDA approval for relapsing remitting MS. In clinical trial with the beta-interferon products, these therapies slowed progression of disease in MS patients, yet lead to a variety of side effects including "flu-like" symptoms.

Neurocrine's cofounder, Dr. Lawrence Steinman, identified the dominant invading T cell in the brains of patients who had died of MS. Dr. Steinman further identified the dominant target or recognition site on the myelin sheath to which invading T cells bind. Neurocrine has exclusively licensed this technology and has designed altered peptide ligands, which resemble native disease-causing molecules of the myelin sheath. These molecules have been altered to attract and bind to disease-causing T cells and inhibit their destructive capabilities. Neurocrine's altered peptide ligand for the treatment of MS has been shown to reverse disease in animal models of MS and decrease the production of cytokines such as gamma interferon and tumor necrosis factor-alpha which contribute to the disease. These same molecules demonstrate the ability to silence pathogenic T cells from MS patients in vitro. Together with Novartis, the Company's collaborative partner for this program, Neurocrine filed an IND and received approval in 1996 to commence clinical trials. The Company and Novartis subsequently completed Phase I clinical trials, and two Phase II clinical trials currently underway in North America and Europe and are scheduled to complete by the fourth quarter of 1999 or the first quarter 2000. Results obtained in animal models of MS are not necessarily predictive of results obtained in man, and Phase I trials are not designed to predict efficacy. No assurance, therefore, can be given that Novartis will successfully complete the current Phase II clinical studies or that results of these studies will warrant additional clinical development of potential product.

# Type I Diabetes

Utilizing its experience in the development of APL for Multiple Sclerosis, Neurocrine has extended this approach to Type I or juvenile-onset diabetes. Like MS, in Type I diabetes the immune system has erroneously targeted healthy tissue, in this case the pancreatic cells responsible for the production of insulin. Type I diabetes is one of the most prevalent chronic conditions in the North America, afflicting approximately 890,000 patients in 1997. Diabetics suffer from a number of complications of the disease including heart disease, circulatory problems, kidney failure, neurologic disorders and blindness.

Current therapy for Type I diabetes consists of daily insulin injections to regulate blood glucose levels.

The Company believes 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 a leading Diabetologist at the Barbara Davis Center for Childhood Diabetes at the University of Colorado, Neurocrine scientists have engineered one of the dominant pancreatic antigens which is no longer recognized by the pathogenic immune cell. In preclinical models this APL was capable of eliciting a protective immune response by generating cells that secrete factors capable of regulating the destructive cells reducing the incidence of diabetes. In addition, experiments using immune cells derived from the blood of Type 1 diabetes patients indicate that APL are recognized by immune cells response to insulin, suggesting that the APL may have the potential to intervene in the disease process in humans. Neurocrine is currently conducting a Phase I safety and dose escalating clinical program in diabetic patients in Europe. The results of the Company's preclinical studies in animals and cells derived from Type I diabetes patients are not necessarily predictive of the results the Company will see treating Type I diabetes patients. There can be no assurance that the APL will prove safe in Phase I studies or that the Company will conduct additional clinical trials.

#### IL-4 Fusion Toxin

IL-4 receptors are highly expressed in malignant brain tumors as well as in cancers of the breast, kidney, lung, colon, stomach, ovary, prostate, and in melanoma and mesothelioma. Immunotoxins are a novel form of anticancer therapy under investigation in a variety of clinical situations. The immunotoxin is designed to carry a cellular toxin, such as Pseudomonas exotoxin, to a target antigen, expressed on cancer cells. Targeted toxins have several theoretical advantages over conventional chemotherapy in that they may be extremely potent and effective in chemotherapy-resistant T cells.

Malignant brain tumors, both primary and metastatic, are a major cause of cancer death. Despite current therapeutic options such as surgery, radiation, and chemotherapy, the median survival rate for malignant brain cancer is only in the range of 9-12 months. Approximately 17,400 new cases of primary brain cancer and 75,000 cases of metastatic brain tumor are diagnosed in the United States each year, with comparable incidence numbers in Europe. According to the American Cancer Society, the incidence of malignant brain tumors is rising. Glioblastoma (grade 4 astrocytoma) is the most common primary malignant brain tumor. These tumors arise within the brain and generally remain confined to the brain. The clinical course of glioblastoma is characterized by relentless loss of vital neurological functions and death within approximately twelve months.

In 1998, the Company exclusively licensed from the National Institutes of Health an anti-cancer compound, referred to as IL-4 Fusion Toxin. NBI-3001, or IL-4 Fusion Toxin is an immunotoxin which fuses interleukin-4 ("IL-4"), a cytokine, to Pseudomonas exotoxin. This molecule was designed as a result of a collaboration between the FDA and the National Cancer Institute. IL-4 receptors Fusion Toxin is a chimeric protein in which a cytokine (blood cell growth factor) known as interleukin 4 (IL-4) has been joined together with another molecule, an exotoxin that can destroy cancer cells. The IL-4 portion of the Fusion Toxin preferentially binds to human cancer cells, which express elevated levels of high affinity receptors for IL-4 on their surface. The advantage of targeting the IL-4 receptor is that expression of the receptor is absent or undetectable in normal brain tissue.

In the preclinical setting, NBI-3001 has been found to be highly cytotoxic to brain tumor cell lines in vitro, and exhibits anti-tumor activity in in vivo models of brain tumor. NBI-3001 has completed a Phase I safety trial under an Investigator sponsored IND in which (9) patients with recurrent malignant glioblastoma were treated. Results were presented at The Society for Neuro-Oncology Meeting in an abstract entitled "A Circularly Permuted Interleukin-4 Pseudomonas Exotoxin for Treatment of Malignant Gliomas." In this study, NBI-3001 produced no evident systemic or neurological toxicities as documented by serum chemistry, hematology screen including liver panels and neurological examinations. A physician-IND clinical trial does not replace the need for Company-sponsored clinical trials, but can provide a preliminary indication as to whether further clinical trials are warranted. However, results from the Physician IND sponsored clinical study may not be repeated in a larger study. NBI-3001 is currently undergoing a Phase I/II trial targeting enrollment of thirty (30) subjects with recurrent glioblastoma in which the primary endpoints are safety, tumor regression, and progression free survival. The Company intends to complete enrollment of this trial in 1999, and if results warrant, commence an efficacy trial for NBI-3001 in early 2000. No assurance can be given that the Company will successfully complete clinical testing or progress to later clinical trials in a timely manner, or at all.

# GABA Subtype Receptor Agonists

#### Insomnia

The term "insomnia" is used to describe all conditions related to the perception of inadequate or non-restful sleep by the patient. According to a Gallup Survey conducted on behalf of the National Sleep Foundation, 49% of all Americans say that they have trouble sleeping. Often undiagnosed or dismissed, insomniacs have trouble falling asleep, remaining asleep or staying awake. Insomnia was also shown to be related to the age and sex of the individuals, the prevalence of which is higher in older individuals and females. While insomnia is reported to be a major problem in the adult population worldwide, only approximately 10% of such patients seek prescription sleeping medications for their condition. This fact may result from the perceived side effect profile of currently marketed sedative-hypnotics.

In the recent past, the majority of patients treated for insomnia have utilized non-benzodiazepine compounds, which show an improved side effect

profile over the benzodiazepine class of sedative-hypnotics utilized during the 1980's. However, currently marketed products continue to exhibit certain unfavorable side effects, including synergy with other CNS depressants (especially alcohol), the development of tolerance upon repeat dosing, rebound insomnia following discontinuation of dosing, hangover effects the next day, and impairment of psychomotor performance 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. The elderly population, which represent a large portion of the insomnia market, would especially benefit from a novel therapeutic with an improved safety profile, rapidity of onset, and decrease in memory impairment.

In 1998 the Company signed an exclusive worldwide licensing agreement with DOV Pharmaceuticals, Inc. for a compound in clinical development for the treatment of insomnia. The compound, NBI-34060, works through the activation of the benzodiazepine site on a GABA receptor subtype. It is through this mechanism that the currently marketed therapeutics produces their sleep-promoting effects. However, NBI-34060, a next generation compound, is chemically distinct from the benzodiazepines with a potentially improved pharmacokinetic profile and receptor subtype selectivity, which may reduce the side effects characteristic of the currently marketed products.

Receptor binding studies and preclinical animal studies on NBI-34060 indicate that it is a highly potent GABAA receptor agonist specific for the Type 1 site. In animal studies, NBI-34060 shows a reduced tolerance to sedation, suggesting a lower potential for abuse, and a reduced tendency to potentiate the deleterious effects of alcohol. In addition, in animal models NBI-34060 appears to be devoid of next day hangover effects and is expected to have a considerably reduced amnestic potential.

Prior to licensure by the Company, a Phase I clinical trial was conducted in forty-two (42) subjects. The study was designed to determine the safety and tolerance of NBI-34060, and provide a preliminary evaluation of the sedative-hypnotic potential in normal volunteers as reflected in self-ratings of drowsiness, disruption of memory, and impairment of psychomotor performance. NBI-34060 was well tolerated, with no serious or unexpected adverse events ("AEs") reported. The only consistently reported side effect was drowsiness, indicating strong potential for the sedative-hypnotic properties of the compound.

Based on results from this Phase I study, in the first quarter of 1999, Neurocrine completed a Phase Ib clinical trial in thirty (30) healthy volunteers to further explore the safety and kinetic profile of NBI-34060. As demonstrated in the first Phase I trail, NBI-34060 demonstrated an adequate safety profile. The Company currently intends to conduct a Phase II clinical program in 1999 to evaluate the efficacy of NBI-34060 in subjects with chronic insomnia, and if results warrant, initiate a pivotal Phase III trial in 2000. There can be no assurance that the side effects and efficacy profile of NBI-34060 seen in the Company's animal models and Phase I trials will be confirmed in the Phase II trial or that the results of the Phase II trial will warrant further study.

#### CRF / Urocortin Agonist

The body has several mechanisms to regulate the effects of CRF. CRF-binding protein ("CRF-BP") binds to CRF and holds it in an inactive state, tightly regulating levels of CRF in certain brain regions. CRF-BP may provide a novel target to selectively increase levels of CRF in diseases that are associated with decreased levels of CRF, such as Alzheimer's disease and obesity. In addition, agonists of the CRF-2 receptor may represent a therapeutic strategy to elevate CRF and a related neuropeptide urocortin for the treatment of these disorders.

#### Alzheimer's Disease

Alzheimer's disease is a neurodegenerative brain disorder that leads to progressive memory loss and dementia. Alzheimer's disease generally follows a predictable course of deterioration over eight years or more, with the earliest symptom being impairment of short-term memory. Gradually, memory loss increases, reasoning abilities deteriorate, and individuals become depressed, agitated, irritable and restless. In the final stages of the disease, patients become unable to care for themselves. According to the National Alzheimer's Association, in 1994 over four million individuals in the United States suffered from Alzheimer's disease. Alzheimer's disease is the fourth leading cause of death for adults, responsible for over 100,000 deaths in 1994. Marketed therapies currently available for the treatment of Alzheimer's disease are severely limited. Tacrine and Aricept have been recently approved for this indication, but, show limited memory improvement in Alzheimer's patients; concerns regarding drug-induced elevations in liver enzymes and other side effects have limited the widespread use of these products.

Neurocrine scientists have found that there are significant decreases in CRF levels in the brain areas that are affected in Alzheimer's disease. In spite of reduced CRF concentrations, CRF-BP levels are not decreased in areas of the brain affected by Alzheimer's disease, thereby providing the Company with a novel target for drug intervention. Consequently, Neurocrine is developing CRF-BP antagonists to displace CRF from the binding protein and effectively increase the amount of "free CRF" available to interact with the CRF receptors. This strategy is expected to selectively raise the concentration of CRF in brain areas involved in learning and memory processes. Because the therapeutic is designed to restore normal levels of CRF only in these areas, the Company believes that the drug will not induce the side effects associated with administering CRF directly, such as anxiety. Current efforts are underway to identify and optimize molecules through high-throughput screening of small molecule libraries. However, no assurance can be given that the Company and its corporate partner, Eli Lilly, will successfully identify suitable candidate compounds for development in a timely manner, or at all.

Obesity is the most common nutritional disorder in Western societies. As many as three in ten adult Americans weigh at least 20% in excess of their ideal body weight, and 35 million people in the United States are characterized as clinically obese. Increased body weight is a significant public health problem because it is associated with a number of serious diseases, including Type II diabetes, hypertension, hyperlipidemia and several cancers. Although obesity has been commonly considered to be a behavioral problem, there is now evidence that body weight is physiologically regulated. The regulation of body weight is complex and appears to consist of both centrally and peripherally acting mechanisms.

Preliminary data indicates that CRF and a related neuropeptide, urocortin, may act as central regulators of both appetite and metabolism. Neurocrine has evaluated CRF-BP antagonists and CRF receptor agonists in various animal models of obesity and have shown effects of reduced food intake and weight loss. Neurocrine and its corporate partner Eli Lilly are screening and optimizing small molecule compounds for evaluation in confirmatory preclinical studies. However, no assurance can be given that the Company and its corporate partner will successfully identify CRF and urocortin agonists suitable as anti-obesity therapeutics in a timely manner, or at all. Further, even if the Company and Lilly are successful in identifying drug candidates, the results obtained in animals are not necessarily predictive of results obtained in humans, and no assurance can be given that the Company will progress to clinical trials or successfully complete clinical trials in a timely manner, if at all.

#### Excitatory Amino Acid Transporters ("EAATs")

EAATs serve as novel targets for the development of drugs, which modulate toxic levels of glutamate in the brain. Neurotransmitter transporters play an important role in regulating the levels of neurotransmitters, and some of the most successful CNS drugs are ones that selectively target these transporters. For example, the Selective Serotonin Reuptake Inhibitors ("SSRIs") such as Prozac selectively inhibit the serotonin transporter modulating the serotonin levels for therapeutic benefit. Similarly, Neurocrine is targeting the EAATs to selectively modulate the levels of the excitatory neurotransmitter glutamate to produce a therapeutic benefit in disorders where glutamate levels are abnormal such as in stroke, head trauma, retinal ischemia, schizophrenia and other neurodegenerative and psychiatric disorders. Neurocrine has entered into collaboration with Wyeth-Ayerst focusing on modulating glutamate transporter function as a novel strategy for the treatment of neurodegenerative disorders. Neurocrine and Wyeth-Ayerst will target the EAATs to selectively modulate the levels of the excitatory neurotransmitter glutamate to produce a therapeutic benefit in disorders where glutamate levels are abnormal. These activities will include basic research to understand the function and regulation of the transporters, the identification of suitable chemical hits, along with the identification and characterization of chemical and biological leads. There can be no assurance that the Company and Wyeth-Ayerst will be successful in demonstrating EAATs as therapeutic targets or that they will identify any product candidates for pre-clinical or subsequent clinical development.

#### Melanocortin Receptor Antagonists

Melanocortin receptors are involved in the control of endocrine, autonomic and central nervous system function. To date, a family of five melanocortin receptor subtypes has been identified; several of which have been cloned by the Company's consultants and scientists. One of the melanocortin receptor subtypes, MC4, has recently been identified as an important regulating mechanism for appetite, body weight and insulin secretion which represents a novel target for the treatment of obesity and diabetes. This technology combined with Neurocrine's expertise in obesity, anorexia nervosa and diabetes provides additional avenues for the discovery of effective therapies for the treatment of other endocrine functions and brain disorders.

#### Chemokines

Chemokines are immune / inflammatory mediators considered central to the trafficking of leukocytes. Restricted and sub-type specific expression of their receptors in different pathologies and on T lymphocytes, dendritic cells and CNS tissue, suggests a role for these mediators in diseases characterized by CNS inflammation and leukocyte invasion. All ligand-receptor interactions lead to migration of the cell types expressing the receptor, hinting at a central role for these molecules in the recruitment / invasion of the diseased tissue by these cells and their potential role in the ensuing destruction. Antagonism of this effect may, therefore, be of benefit. In addition to an in-depth program of discovery research, the Company has decided to screen our library against these receptor systems in order to identify small molecule antagonists. Since chemokines are large proteins and have multiple interaction sites with their receptors, the design of specific, high-affinity competitive antagonists will be required. Antagonists are being tested in inflammatory animal models including experimental autoimmune encephalomyelitis (EAE, for MS), arthritis, and diabetes.

Given the complexity of the chemokine area, Neurocrine has focused on the more recently discovered receptors in an attempt to generate small molecule antagonists. To that end, numerous chemokine receptors have been expressed, screened against our small molecule library, and structure activity studies undertaken. There can be no assurance that the Company's research in this area will lead to product candidates.

#### Gonadotrophin-Releasing Hormone (GnRH) Receptor

Gonadotrophin-releasing hormone is a hypothalamic decapeptide that stimulates the secretion of the pituitary gonadotropins, luteinizing hormone (LH) and follicle-stimulating hormone (FSH). The gonadotropins, in turn, are necessary for gonadal steroid production and normal reproductive function. Chronic administration of GnRH superagonist peptides has been found to cause down regulation of the GnRH receptor resulting in a paradoxical reduction in circulating levels of testosterone or estrogen, equivalent to surgical castration or oophorectomy, respectively. This reversible shutdown of the reproductive endocrine axis has proven clinically useful in treating hormone dependent proliferative diseases such as endometriosis, prostate carcinoma, and breast cancer, and resulted in several peptide drugs such as Lupron and Zoladex, with an estimated market in excess of \$1 billion. However, current peptide agonist based drugs have several drawbacks. They require 3-4 weeks before the regulatory activities are observed, and during this period their stimulatory effects can result in a worsening of the disease. Being peptides they also require subcutaneous injection or nasal administration and are expensive to manufacture.

The Company has screened its small molecule library and has conducted structure activity studies aimed at producing a small molecule GnRH antagonist. Several series of small molecule compounds have been identified and are being evaluated as candidates for further development.

#### Neurogenomics

The brain and spinal cord are comprised of two major cell types - glial cells and neurons. Glial cells are the most prevalent cell types in the central nervous system, comprising over 75% of all brain cells. The gene products from these cells are crucial for the survival and development of neurons. Neurons are CNS cells that transmit and receive complex electrical and chemical messages from other neurons to control all cognitive processes. In certain pathological states, excessive glial activity results in the activation of cytosine and related genes. The proteins encoded by these genes may be implicated in the degenerative cascade leading to neurological disorders such as Alzheimer's disease, stroke, multiple sclerosis, Parkinson's disease, epilepsy and AIDS dementia. For example, in AIDS, the HIV virus does not attack neurons but does infect glial cells which in turn release inflammatory cytokines and other factors which are toxic to neurons. Similarly, in Alzheimer's disease, accumulating evidence suggests complex interactions between neurons, glia and a protein fragment known as beta amyloid leading to formation of senile plaques and neurodegeneration. Currently, it is estimated that only a small fraction of genes involved in neurodegeneration or regeneration has been identified. The identification of novel CNS genes involved in the neurodegenerative process may yield new therapeutic opportunities.

#### Neurodegenerative Diseases and Disorders

Neurodegenerative diseases and disorders involve damage to the cellular structure of the brain either acutely, as in stroke or trauma, or chronically, as in epilepsy and Alzheimer's disease. To date, only a limited number of effective therapeutics exists to treat neurological disorders, resulting in significant economic and social costs. In 1998, over 26 million people are estimated in the United States to be affected by neurological disorders.

Activation of glial cells is a common feature of many neurodegenerative diseases. The primary goal of Neurocrine's Neurogenomics program is to identify and characterize novel genes that are induced in glial cells under conditions that lead to neurodegeneration or regeneration. The Company is focusing on stroke, multiple sclerosis, AIDS dementia, epilepsy, Parkinson's disease and Alzheimer's disease. The unique conditions leading to neurodegeneration in each of the disorders have been established in both animal and cellular models of the disease. Neurocrine is actively isolating and analyzing genes associated with neuronal cell death utilizing state of the art molecular biology, gene sequencing and bioinformatics. In addition, activated genes that are neuroprotective or allow for the regeneration of neurons may also be identified.

Novel neurodegenerative genes that are discovered may include proteins, enzymes or receptors. Protein signaling molecules or the genes encoding such molecules may be utilized as therapeutics, while enzymes and receptors may serve as new targets for drug discovery. Neurocrine currently intends to place the receptors and enzymes encoded by these genes in high-throughput screens in an attempt to discover small molecule therapeutics to treat neurodegenerative disorders. To date, the Company has identified novel genes of which a number are undergoing biological evaluation in in vitro and animal models. The Company currently intends to identify candidate genes as drugs or drug targets for one or more neurological diseases. However, there can be no assurance that the Company will successfully identify suitable gene candidates for development in a timely manner, or at all.

#### **BUSINESS STRATEGY**

The Company's strategy is to utilize its understanding of the biology of the central nervous, immune and endocrine systems to identify and develop novel therapeutics. There are five key elements to the Company's business strategy:

Target Multiple Product Platforms. The Company believes certain central nervous system drug targets, such as CRF, EAATs and MCH represent significant market opportunities in psychiatric, neurologic and metabolic disorders. Immunological targets, such as altered peptide ligands, offer therapeutic strategies related to autoimmune diseases. Neurogenomics and chemokines allow the Company to combine its neuroscience and immunology expertise with new drug discovery technologies to identify novel gene-related product or gene therapy opportunities.

Identify Novel Neuroscience and Immunology Drug Targets for the Development of Therapeutics Which Address Large Unmet Market Opportunities. Neurocrine employs molecular biology as an enabling discipline to identify novel drug targets such as receptors, genes and gene-related products. The Company uses advanced technologies, including combinatorial chemistry, high-throughput screening, gene sequencing and bioinformatics, to discover and develop novel small molecule therapeutics for diseases and disorders of the central nervous and immune systems including anxiety, depression, Alzheimer's disease, multiple sclerosis, neurodegeneration, diabetes, obesity and insomnia.

Leverage Strategic Alliances to Enhance Development and Commercialization Capabilities. Neurocrine intends to leverage the development, regulatory and commercialization expertise of its corporate partners to accelerate the development of its potential products, while retaining commercial or co-promotion rights in North America. The Company intends to further leverage its resources by continuing to enter into strategic alliances and novel financing mechanisms to enhance its internal development and commercialization capabilities.

To date, Neurocrine has entered into strategic alliances with Janssen focusing on CRF receptor antagonists to treat anxiety, depression, and substance abuse; with Novartis to develop altered peptide ligands for the treatment of MS; and with Lilly to collaborate in the discovery, development and commercialization of CRF-BP antagonists and CRF agonists for the treatment of central nervous system disorders including obesity and dementias such as Alzheimer's disease. More recently, the Company entered into a collaboration with Wyeth-Ayerst Laboratories for the research; development and commercialization of compounds with modulate excitatory amino acid transporters. The Company has also formed NPI, a research and development subsidiary, to finance its Neurosteroid clinical development program, which has been discontinued and its Neurogenomics programs. In 1999 the Company entered into a collaboration agreement with Wyeth-Ayerst to research, develop and commercialize compounds which modulate excitatory amino acid transporters ("EAATs") for the treatment of neurodegenerative and psychiatric diseases.

In addition, in 1998 Neurocrine entered into two alliances with other companies to enhance its drug discovery and development capabilities. The first alliance is with Medtronic Inc. to study the stability and compatibility of IL-4 Fusion Toxin in Medtronic's implantable drug pump and catheter system. The second alliance is with Caliper Technologies. Neurocrine and Caliper are collaborating to apply Caliper's microfluidics technology to the ultra-high throughput screening of Neurocrine's proprietary targets.

Outsource Capital Intensive and Non-Strategic Activities. Neurocrine intends to focus its resources on research and development activities by outsourcing its requirements for manufacturing, preclinical testing and clinical monitoring activities. The Company utilizes contract current Good Manufacturing Processes ("CGMP") manufacturing for clinical programs including the IL-4 Fusion Toxin program, insomnia and diabetes. Neurocrine believes that availability of skilled contract manufacturers and contractors will allow the Company to focus on its core discovery and development programs to generate additional product opportunities.

Acquire Complementary Research and Development Drug Candidates. Neurocrine plans to continue to selectively acquire rights to products in various stages of

research and clinical development in the fields of neurology and immunology to take advantage of the development and future commercialization capabilities it is developing in cooperation with its strategic partners. In 1998 the Company licensed from the National Institutes of Health an IL-4 Fusion Toxin which is currently in Phase I/II clinical trials for recurrent glioblastoma. In May 1998 the Company completed the acquisition of Northwest NeuroLogic, Inc. (NNL), acquiring the intellectual property surrounding the Excitatory Amino Acid Transporters (EAATs) 1 through 5 and Melanocortin receptors. In addition, the scientific founders of NNL, Drs. Roger Cone and Susan Amara, of the Vollum Institute became exclusive consultants to the Company. Also in June 1998, the Company exclusively licensed worldwide commercial rights from DOV Pharmaceuticals, Inc. for a compound which has completed Phase I clinical development for the treatment of insomnia.

#### **TECHNOLOGY**

Neurocrine utilizes advanced technologies to enhance its drug discovery capabilities and to accelerate the drug development process. These technologies include:

High-Throughput Screening ("HTS"). Neurocrine has assembled a chemical library of diverse, low molecular weight organic molecules for lead compound identification. The Company has implemented robotics screening capabilities linked to its library of compounds that facilitate the rapid identification of new drug candidates for multiple drug targets. The Company believes that the utilization of high-throughput screening and medicinal and peptide chemistry will enable the rapid identification and optimization of lead molecules.

Combinatorial Chemistry. Recent developments in both computational and combinatorial chemistry have shown that it is now possible to design small libraries focused around hits emerging from HTS both to evaluate rapidly the quality of such hits and also subsequently optimize the selected hits into advanced lead candidates. The approach involves learning from the set of hits as a whole and using this information to design libraries of compounds that may be structurally independent of the original hits. Neurocrine is acquiring the necessary technologies to facilitate the process of library design, parallel synthesis and rapid purification and characterization of compounds. Neurocrine will use the same process to supplement the corporate compound library with structures relevant for internal projects and hence improve the likelihood that HTS will discover a meaningful array of useful hits.

Molecular Biology. Neurocrine scientists have utilized novel techniques for examination of gene expression in a variety of cellular systems. The company has developed a sophisticated technique to evaluate the type and quantity of genes in various cellular systems prior to the isolation of genes. Neurocrine has also developed unique expression vectors and cell lines that allow for the highly efficient protein expression of specific genes.

Gene Sequencing. Neurocrine applies integrated automated DNA sequencing and gene identification technology in its Neurogenomics program. The systems utilized by Neurocrine allow for extended gene analysis in a rapid, high-throughput format with independent linkage into a sequence identification database. Neurocrine has optimized gene sequencing instrumentation for "differential display," a technique that may facilitate the rapid identification of novel genes.

Bioinformatics. Neurocrine's Neurogenomics program creates a significant amount of genetic sequence information. Applied genomics relies on information management systems to collect, store and rapidly analyze thousands of gene sequences. Neurocrine has developed a bioinformatics system, which the Company believes will allow it to identify novel genes, which are involved in neurodegeneration. Data are collected by automated instruments and stored and analyzed by Neurocrine using customized computational tools. To date, Neurocrine's molecular biologists have identified over 4,500 novel genes.

# STRATEGIC ALLIANCES

The Company's business strategy is to utilize strategic alliances and novel financing mechanisms to enhance its development and commercialization capabilities. To date, Neurocrine has completed the following alliances:

#### JANSSEN PHARMACEUTICA, N.V.

On January 1, 1995, Neurocrine entered into a research and development agreement with Janssen to collaborate in the discovery, development and commercialization of CRF receptor antagonists focusing on the treatment of anxiety, depression and substance abuse (the "Janssen Agreement"). The collaboration utilizes Neurocrine's expertise in cloning and characterizing CRF receptor subtypes, CRF pharmacology and medicinal chemistry. Pursuant to the Janssen Agreement, the Company has received \$2.0 million in license payments. In connection with the Janssen Agreement, Johnson & Johnson Development Corporation ("JJDC") purchased \$5 million of the Company's Common Stock. The collaborative research portion of the Janssen Agreement was completed as scheduled in 1997.

In 1996 Janssen selected a clinical candidate and commenced clinical trials in Europe. Under the Janssen Agreement, Neurocrine 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 milestone payments for other indications, in each case upon achievement of certain development and regulatory goals. As of December 31, 1998 the Company has received \$3.5 million in milestone payments from Janssen. Janssen is responsible for funding all clinical development and marketing activities, including reimbursement to Neurocrine for its promotional efforts, if any. The Company has granted Janssen an exclusive worldwide license to manufacture and market products developed under the Janssen

Agreement. The Company is entitled to receive royalties on Janssen product sales throughout the world. The Company has certain rights to co-promote such products in North America. There can be no assurance that the Company and its corporate partner will be successful in developing, receiving regulatory approvals or commercializing any potential products discovered under the Janssen Agreement. As a result, there can be no assurance that any product development milestone or royalty payments will be made.

In January 1996, the Company entered into a binding letter agreement with Ciba-Geigy (which subsequently became Novartis) to develop altered peptide ligand therapeutics for the treatment of MS based upon the Company's drug development candidates and expertise in immunology and protein chemistry. December 1996, the Company and Novartis entered into a definitive agreement (the "Novartis Agreement") incorporating the terms and conditions set forth in the letter agreement and certain other terms and conditions agreed to by the Company and Novartis. Novartis paid the Company a \$5.0 million non-refundable fee prior to executing the Novartis Agreement. In connection with the Novartis Agreement, Novartis purchased \$10.0 million of the Company's Common Stock. Pursuant to the Novartis Agreement, Novartis is obligated to provide the Company with \$3.5 million in research and development funding, plus certain other program expenses, each year for five years ending on December 31, 2000. In event that no biological license application ("BLA") has been filed as a result of the collaboration by December 31, 2000, then Novartis may be obligated to provide the Company with an additional \$2.5 million per year thereafter until a Product License Application is filed, except in certain circumstances. As of December 31, 1998 the Company has received a total of \$20.2 million in license fees and research funding under the Novartis Agreement (including the \$5.0 million non-refundable fee). Neurocrine is also entitled to receive milestone payments if certain research, development and regulatory milestones are achieved. Milestone payments were \$3.8 million and \$2.3 million in 1997 and 1998, respectively. Novartis has the right to terminate the Novartis Agreement on six months' notice, which may be given at any time after December 30, 1997.

The Company has granted Novartis an exclusive license outside of the United States and Canada to market altered peptide ligand products developed under the Novartis Agreement for multiple sclerosis. Neurocrine is entitled to receive royalties on product sales in these territories. The Novartis Agreement provides that the Company and Novartis will collaborate in the marketing of products developed under the Novartis Agreement in the United States and Canada. Neurocrine is entitled to receive a share of the profits resulting from sales of altered peptide ligand products in the United States and Canada subject to the recoupment of a portion of Novartis's development costs. Neurocrine retains the right to convert its profit share to the right to receive royalty payments at its sole discretion in which case no repayment of development costs are due to Novartis and Novartis will have exclusive marketing rights. Neurocrine is obligated to repay a portion of the development costs of any potential product developed pursuant to the collaboration unless the Company elects to convert to the right to receive royalty payments. There can be no assurance that the Company and Novartis will be successful in developing or commercializing any potential products. As a result, there can be no assurance that any product development milestone, royalty, or profit sharing payments will be made.

# ELI LILLY AND CO.

On October 15, 1996, Neurocrine entered into a research and license agreement (the "Lilly Agreement") with Lilly to collaborate in the discovery, development and commercialization of CRF binding protein ligand inhibitors for the treatment of central nervous system disorders including obesity and dementias such as Alzheimer's disease and CRF-2 agonists for CNS mediated diseases and disorders. Neurocrine has received \$14.5 million in research payments under the Lilly Agreement, of which \$4.0 million was received in 1998. Neurocrine expects to receive an additional \$3.0 million in research payments through October 31, 1999, as well as additional sponsored research payments over the subsequent two-year period if certain milestones are met, and up to an additional \$49.0 million in milestone payments for the first two products for dementia or obesity if certain development and regulatory milestones are achieved. The Company has granted Lilly an exclusive worldwide license to manufacture and market CRF binding protein ligand antagonists and CRF-2 agonist products. Lilly is obligated to fund clinical development and marketing expenses (except as set forth below) and is responsible for clinical development, regulatory compliance, and manufacturing of products. Neurocrine is entitled to royalties on product sales. At its option, Neurocrine is entitled to receive a portion of the profits resulting from sales of products for the treatment of dementia in the United States (subject to the Company's obligation to pay a portion of the development costs for such product). Lilly has agreed to provide the Company with access to a portion of its chemical compound library for screening against targets outside of the field of the Lilly Agreement and other Lilly program areas, subject to the Company's obligation to pay Lilly royalties on sales of products developed based on compounds in such library and milestone payments based upon certain development and regulatory milestones for such products. There can be no assurance that the Company's research under the Lilly Agreement will be successful in discovering any potential products or that Lilly will be successful in developing, receiving regulatory approvals, or commercializing any potential products that may be discovered. As a result there can be no assurance that any product development milestone, royalty, or profit sharing payments will be made.

#### WYETH-AYERST

Effective January 1, 1999, the Company entered into a Collaboration and License Agreement relating to the research, development and commercialization of compounds which modulate excitatory amino acid transporters ("EAATs") for the treatment of neurodegenerative and psychiatric diseases. Pursuant to the agreement, Wyeth-Ayerst will provide the Company with up to \$13 million in research and development funding. The initial term of the funded research will be three years, subject to earlier termination or extension upon achievement of certain benchmarks upon mutual agreement of the parties. The Company is also

entitled to receive up to \$69.2 million in milestones upon achievement of certain research, development and regulatory events.

In addition, under certain circumstances the Company may have the opportunity to co-promote products with Wyeth-Ayerst in the United States and Canada. There can be no assurance that the Company and Wyeth-Ayerst will be successful in research and drug discovery based on this technology, that any pre-clinical and clinical drug candidates arising from the collaboration will generate commercial product candidates that have viable clinical, regulatory and intellectual property profiles or that any commercial products arising from the collaboration will enjoy market acceptance. Therefore, there can be no assurance that any milestones or royalty income will be payable to the Company under its agreement with Wyeth-Ayerst.

#### NEUROSCIENCE PHARMA INC.

In March 1996, Neurocrine formed Neuroscience Pharma, Inc. ("NPI"), research and development company. Neurocrine licensed to NPI certain technology and Canadian marketing rights to the Company's Neurosteroid and Neurogenomics programs in exchange for 49% of the outstanding Common Stock of NPI. A group of Canadian institutional investors invested approximately \$9.5 million in NPI in exchange for Preferred Stock of NPI, which could be exchanged for shares of Neurocrine's Common Stock. During 1997 and 1998 these investors redeemed the Preferred Stock for an aggregate of 1,279,758 shares of Common Stock of the Company. Pursuant to a Research and Development Agreement with a wholly owned subsidiary of the Company, NPI committed to expend an aggregate amount of \$9.5 million for clinical development of DHEA, a neurosteroid for Alzheimer's Disease. The DHEA Neurosteroid Program was discontinued in March 1999 following results from the Phase II/III trial. Despite suggestion of efficacy from a previously completed 60 patient Phase II trial, the results of its Phase II/III trial did not demonstrate a difference in efficacy between patients treated with DHEA versus placebo. Based on these results, NPI has discontinued further development of DHEA. NPI will continue its research activities in the area of neurogenomics. Pursuant to such Research and Development Agreement, NPI is entitled to receive royalties on sales of products developed in these programs as well as exclusive Canadian marketing rights for such products in the event that the Company has not terminated the technology license and the marketing rights. In connection with their initial investment in NPI, such investors also received warrants exercisable for 383,875 shares of the Company's Common Stock and are eligible to receive additional warrants in the future in the event that NPI receives certain Canadian government incentives for research activities.

#### RISK FACTORS

#### DEPENDENCE ON STRATEGIC ALLIANCES

The Company is dependent upon its corporate partners to provide adequate funding for certain of its programs. Under these arrangements, the Company's corporate partners are responsible for (i) selecting compounds for subsequent development as drug candidates, (ii) conducting preclinical testing and clinical trials and obtaining required regulatory approvals for such drug candidates, and/or (iii) manufacturing and commercializing any resulting drugs. Failure of these partners to select a compound discovered by the Company for subsequent development into marketable products, gain the requisite regulatory approvals or successfully commercialize products would have a material adverse effect on the Company's business, financial condition and results of operations. The Company's strategy for development and commercialization of certain of its products is dependent upon entering into additional arrangements with research collaborators, corporate partners and others, and upon the subsequent success of these third parties in performing their obligations. There can be no assurance that the Company will be able to enter into additional strategic alliances on terms favorable to the Company, or at all. Failure of the Company to enter into additional strategic alliances would have a material adverse effect on the Company's business, financial condition and results of operations.

The Company cannot control the amount and timing of resources that its corporate partners devote to the Company's programs or potential products. If any of the Company's corporate partners breach or terminate their agreements with the Company or otherwise fail to conduct their collaborative activities in a timely manner, the preclinical testing, clinical development or commercialization of product candidates will be delayed, and the Company will be required to devote additional resources to product development and commercialization, or terminate certain development programs. The Company's strategic alliances with Janssen, Novartis, Lilly, and Wyeth-Ayerst are subject to termination by Janssen, Novartis, Lilly, or Wyeth-Ayerst, respectively. There can be no assurance that Janssen, Novartis, Lilly, or Wyeth-Ayerst will not elect to terminate its strategic alliance with the Company prior to its scheduled expiration. In addition, if the Company's corporate partners effect a merger with a third party, there can be no assurance that the strategic alliances will not be terminated or otherwise materially adversely affected. The termination of any current or future strategic alliances could have a material adverse effect on the Company's business, financial condition and results of operations. Neurocrine's corporate partners may develop, either alone or with others, products that compete with the development and marketing of the Company's products. Competing products, either developed by the corporate partners or to which the corporate partners have rights, may result in their withdrawal of support with respect to all or a portion of the Company's technology, which would have a material adverse effect on the Company's business, financial condition and results of operations. There can be no assurance that disputes will not arise in the future with respect to the business, ownership of rights to any products or technology developed with corporate partners. These and other possible disagreements between corporate partners and the Company could lead to delays in the collaborative research, development or commercialization of certain product candidates or could require or result in litigation or arbitration, which would be time-consuming and expensive, and would have a material adverse effect on the Company's business, financial

#### MANUFACTURING

The Company has in the past utilized, and intends to continue to utilize, third party manufacturing for the production of material for use in clinical trials and for the potential commercialization of future products. The Company has no experience in manufacturing products for commercial purposes and does not have any manufacturing facilities. Consequently, the Company is solely dependent on contract manufacturers for all production of products for development and commercial purposes. In the event that the Company is unable to obtain or retain third-party manufacturing, it will not be able to commercialize its products as planned. The manufacture of the Company's products for clinical trials and commercial purposes is subject to cGMP regulations promulgated by the FDA. No assurance can be given that the Company's third-party manufacturers will comply with cGMP regulations or other regulatory requirements now or in the future. The Company's current dependence upon third parties for the manufacture of its products may adversely affect its profit margin, if any, on the sale of future products and the Company's ability to develop and deliver products on a timely and competitive basis.

#### MARKETING, SALES, AND PHARMACEUTICAL PRICING ISSUES

Neurocrine has retained certain marketing or co-promotion rights in North America to its products under development, and plans to establish its own North American marketing and sales organization. The Company currently has no experience in marketing or selling pharmaceutical products and does not have a marketing and sales staff. In order to achieve commercial success for any product candidate approved by the FDA, Neurocrine must either develop a marketing and sales force or enter into arrangements with third parties to market and sell its products. There can be no assurance that Neurocrine will successfully develop such experience or that it will be able to enter into marketing and sales agreements with others on acceptable terms, if at all. If the Company develops its own marketing and sales capabilities, it will compete with other companies that currently have experienced and well funded marketing and sales operations. To the extent that the Company enters into co-promotion or other marketing and sales arrangements with other companies, any revenues to be received by Neurocrine will be dependent on the efforts of others, and there can be no assurance that such efforts will be successful.

The Company's business may be materially adversely affected by the continuing efforts of government and third party payers to contain or reduce the costs of health care through various means. For example, in certain foreign markets, pricing or profitability of prescription pharmaceuticals is subject to government control. In the United States, there have been, and the Company expects that there will continue to be, a number of federal and state proposals to implement similar government control in such jurisdictions. In addition, an increasing emphasis on managed care in the United States has put, and will continue to put, pressure on pharmaceutical pricing. Such initiatives and proposals, if adopted, could decrease the price that the Company receives for any products it may develop and sell in the future, and thereby have a material adverse effect on the Company's business, financial condition and results of operations. Further, to the extent that such proposals or initiatives have a material adverse effect on other pharmaceutical companies that corporate partners or prospective corporate partners for certain of the Company's potential products, the Company's ability to commercialize its potential products may be materially adversely affected.

The Company's ability to commercialize pharmaceutical products may depend in part on the extent to which reimbursement for the costs of such products and related treatments will be available from government health administration authorities, private health insurers and other third-party payers. Significant uncertainty exists as to the reimbursement status of newly approved health care products, and third-party payers are increasingly challenging the prices charged for medical products and services. There can be no assurance that any third-party insurance coverage will be available to patients for any products developed by the Company. Government and other third-party payors are increasingly attempting to contain health care costs by limiting both coverage and the level of reimbursement for new therapeutic products, and by refusing, in some cases, to provide coverage for uses of approved products for disease indications for which the FDA has not granted marketing approval. If adequate coverage and reimbursement levels are not provided by government and third party payors for the Company's products, the market acceptance of these products would be materially adversely affected.

#### COMPETITION

The biotechnology and pharmaceutical industries are subject to rapid and intense technological change. The Company faces, and will continue to face, competition in the development and marketing of its product candidates from academic institutions, government agencies, research institutions and biotechnology and pharmaceutical companies. Competition may arise from 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. There can be no assurance that developments by others will not render the Company's product candidates or technologies obsolete or noncompetitive.

Betaseron and Avonex, similar forms of beta-interferon marketed by Berlex BioSciences and Biogen, Inc., respectively, and Copaxone a peptide polymer marketed by Teva, have been approved for the marketing in the United States and certain other countries for the treatment of relapsing remitting multiple sclerosis. Tacrine, marketed by Warner-Lambert Co., and Aricept, marketed by Pfizer Inc, have been approved for the treatment of Alzheimer's dementia. Sales of these drugs may reduce the available market for any product developed by the Company for these indications. The Company is developing products for the treatment of anxiety disorders, which will compete with well-established products in the benzodiazepine class, including Valium, marketed by Hoffman-La

Roche, Inc., and depression, which will compete with well-established products in the anti-depressant class, including Prozac, marketed by Eli Lilly & Co. Certain technologies under development by other pharmaceutical companies could result in treatments for these and other diseases and disorders being pursued by the Company. For example, a number of companies are conducting research on molecules to block CRF to treat anxiety and depression. Other biotechnology and pharmaceutical companies are developing compounds to treat obesity. In the event that one or more of these products and/or programs are successful, the market for the Company's products may be reduced or eliminated.

In addition, if Neurocrine receives regulatory approvals for its products, manufacturing efficiency and marketing capabilities are likely to be significant competitive factors. At the present time, Neurocrine has no commercial manufacturing capability, sales force or marketing experience. In addition, many of the Company's competitors and potential competitors have substantially greater capital resources, research and development resources, manufacturing and marketing experience and production facilities than does Neurocrine. Many of these competitors also have significantly greater experience than does Neurocrine in undertaking preclinical testing and clinical trials of new pharmaceutical products and obtaining FDA and other regulatory approvals.

#### PATENTS AND PROPRIETARY RIGHTS

The Company files patent applications both in the United States and in foreign countries, as it deems appropriate, for protection of its proprietary technology and products. As of December 31, 1998, 4 patents have been issued to the Company; and the Company has received licenses to 5 issued patents. The Company owns or has exclusive rights to a total of approximately 122 patent applications pursuant to license agreements with academic and research institutions, including the Beckman Research Institute of the City of Hope, the Salk Institute for Biological Studies, and Leland Stanford Junior University. The Company intends to file additional United States and foreign applications and license additional technologies from third parties in the future as appropriate. However, there can be no assurances that licenses to third party technologies that may be required by or advantageous to the Company will be obtained on commercially reasonable terms or at all.

The Company's success will depend on its ability to obtain patent protection for its products, preserve its trade secrets, prevent third parties from infringing upon its 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, the Company intends to seek patent protection for its proprietary technology and compounds. There can be no assurance as to the success or timeliness in obtaining any such patents, that the breadth of claims obtained, if any, will provide adequate protection of the Company's proprietary technology or compounds, or that the Company will be able to adequately enforce any such claims to protect its proprietary technology and compounds. Since patent applications in the United States are confidential until the patents issue, and publication of discoveries in the scientific or patent literature tend to lag behind actual discoveries by several months, the Company cannot be certain that it was the first creator of inventions covered by pending patent applications or that it was the first to file patent applications for such inventions. Litigation, which could result in substantial cost to the Company, may be necessary to enforce the Company's patent and license rights.

The degree of patent protection afforded to pharmaceutical inventions is uncertain and any patents that may issue with regard to the Company's potential products will be subject to this uncertainty. There can be no assurance that competitors will not develop competitive products outside the protection that may be afforded by the claims of the Company's patents. Other potential products that the Company may develop may not consist of novel compounds and therefore would not be covered by composition of matter patent claims. In addition, the Company is aware of a number of patent applications, both domestic and European, relating to neurological compounds, and in particular CRF receptor antagonist potential therapeutics, that have been filed by or are controlled by other entities, including competitors and potential competitors of the Company. There can be no assurance that the Company's potential products can be commercialized without a license to any patents which may issue from such applications.

The Company may be required to obtain licenses to patents or proprietary rights of others. As the biotechnology industry expands and more patents are issued, the risk increases that the Company's potential products may give rise to claims that such products infringe the patent rights of others. At least one patent containing claims covering compositions of matter consisting of certain altered peptide ligand therapeutics for use in modulating the immune response has issued in Europe, and the Company believes that this patent has been licensed to a competitor of the Company. There can be no assurance that a patent containing corresponding claims will not issue in the United States. Although the Company is engaged in an opposition proceeding with respect to the European patent, there can be no guarantee that the Company will be successful in this opposition. Further, there can be no assurance that the claims of the European patent or any corresponding claims of any future United States patents or other foreign patents which may issue will not be infringed by the manufacture, use or sale of any potential altered peptide ligand therapeutics developed by the Company or Novartis. Although the Company has been granted claims to a European patent covering altered peptide ligand therapeutics, there can be no assurance that the Company or Novartis would prevail in any legal action seeking damages or injunctive relief for infringement of any such claims or any patent that might issue under such applications or that any license required under any such patent would be made available or, if available, would be available on acceptable terms. Failure to obtain a required ligand products that they may develop.

The Company is aware of an issued U.S. patent directed toward an excitatory amino acid transporter included within the subject matter of its corporate collaboration with Wyeth-Ayerst. Although the Company believes that it will be found to have superior rights to this transporter through an anticipated interference proceeding, there can be no assurance that the Company will be successful in such an interference.

In 1998 a patent application filed by a third party outside of the United States pursuant to the Patent Cooperation Treaty was published claiming priority from a United States patent application and came to the attention of the Company and Janssen, the Company's corporate partner in the field of corticotropin-releasing factor antagonists. This application claims a genus of chemical compounds that includes the lead product candidate currently under development by Janssen. This application appears to predate the filing by the Company and Janssen with respect to such compound. The Company and Janssen are engaged in discussions with the third party with regard to a licensing arrangement. There can be no assurance that such discussions will be successful or that such a license will be available on commercially reasonable terms. If the third party's patent application was determined to predate the filing by the Company and Janssen and were to issue in its current form, Janssen may be unable to commercialize the current lead compound in the countries which the third party patent issues and may elect to select a new lead clinical candidate. While the Company and Janssen have filed patent applications directed to chemical compounds not covered by the third party's application, selection of a new lead clinical candidate may delay the Company's realization of milestone and royalty income under its agreement with Janssen. As noted above, the patent positions of pharmaceutical and biotechnology companies, including the Company, involve complex legal and factual issues. It is not certain that, with respect to the United States, the third party's date of invention will pre-date that of the Company, that outside of the United States the third party's patent application will be determined to predate filing by the Company and Janssen or that the third party application will issue as a patent. In addition, if the third party's patent does eventually issue, it is not certain that the form in which it issues will present an impediment to Janssen's CRF antagonist development and commercialization program or lead to delays in the Company's realization of milestone and royalty income derived therefrom. The Company's independent CRF antagonist program is not impacted and will continue without regard to this application.

No assurance can be given that any licenses required under any patents or proprietary rights of third parties would be made available on terms acceptable to the Company, or at all. If the Company does not obtain such licenses, it could encounter delays in product introductions while it attempts to design around such patents, or could find that the development, manufacture or sale of products requiring such licenses could be foreclosed. Litigation may be necessary to defend against or assert such claims of infringement to enforce patents issued to the Company to protect trade secrets or know-how owned by the Company, or to determine the scope and validity of the proprietary rights of others. 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 patent applications of the Company or its licensors. Litigation or interference proceedings could result in substantial costs to and diversion of effort by, and may have a material adverse impact on, the Company In addition, there can be no assurance that these efforts by the Company would be successful.

The Company also relies upon unpatented trade secrets and improvements, unpatented know-how and continuing technological innovation to develop and maintain its competitive position, which it seeks to protect, in part, by confidentiality agreements with its commercial partners, collaborators, employees and consultants. The Company also has invention or patent assignment agreements with its employees and certain, but not all, commercial partners and consultants. There can be no assurance that a person not bound by an invention assignment agreement will not develop relevant inventions. There can be no assurance that binding agreements will not be breached, that the Company would have adequate remedies for any breach, or that the Company's trade secrets will not otherwise become known or be independently discovered by competitors.

As is commonplace in the biotechnology industry, the Company employs individuals who were previously employed at other biotechnology or pharmaceutical companies, including competitors or potential competitors of the Company. To the extent such Company employees are involved in research areas at the Company which are similar to those areas in which they were involved at their former employer, the Company may be subject to claims that such employees and/or the Company have inadvertently or otherwise used or disclosed the alleged trade secrets or other proprietary information of the former employers. Litigation may be necessary to defend against such claims, which could result in substantial costs and be a distraction to management, and which may have a material adverse effect on the Company, even if the Company was successful in defending such claims.

#### **GOVERNMENT REGULATION**

Regulation by government authorities in the United States and foreign countries is a significant factor in the development, manufacture and marketing of the Company's proposed products and in its ongoing research and product development activities. All of the Company's products will require regulatory approval by government agencies prior to commercialization. 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 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. Any failure by the Company or its collaborators or licensees to obtain, or any delay in obtaining

or maintaining, regulatory approval could adversely affect the marketing of any products developed by the Company, its ability to receive product or royalty revenues and its liquidity and capital resources.

Preclinical testing is generally conducted in laboratory animals to evaluate the potential safety and the efficacy of a product. The results of these studies are submitted to the FDA as a part of an IND, which must be approved before clinical trials in humans can begin. Typically, clinical evaluation involves a time consuming and costly three-phase process. In Phase I, clinical trials are conducted with a small number of subjects to determine the early safety profile, the pattern of drug distribution and metabolism. In 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. In 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 and may, at its discretion, re-evaluate, alter, suspend or terminate the testing based upon the data which have been accumulated to that point and its assessment of the risk/benefit ratio to the patient.

The results of preclinical testing and clinical trials are submitted to the FDA in the form of an NDA or BLA for approval to commence commercial sales. In responding to an NDA or BLA, the FDA may grant marketing approval, request additional information or deny the application if the FDA determines that the application does not satisfy its regulatory approval criteria. There can be no assurance that approvals will be granted on a timely basis (or at all). If approved, there can be no assurance that such approval will include acceptable labeling to adequately commercialize the product. Similar regulatory procedures must also be complied with in countries outside the United States.

To date, the Company or its collaborators have submitted five IND or equivalent applications in the United States, Canada and/or Europe with regard to its product candidates and has commenced clinical trials. Even if Canadian or European regulatory authorities approve the product, the Company will be required to undertake additional clinical testing to obtain FDA regulatory approval in the United States. No assurance can be given that the Company will be able to obtain FDA or other governmental regulatory approval for any products.

Neurocrine currently has five programs in clinical development. The Company's CRF receptor antagonist project is currently in Phase II clinical development with its partner, Janssen Pharmaceutica, for anxiety/depression. Neurocrine and its partner, Novartis Pharmaceuticals, are conducting their second Phase II clinical trial with Neurocrine's APL compound in patients with multiple sclerosis. Neurocrine is conducting a Phase I/II trial with an IL-4 Fusion Toxin for glioblastoma (malignant brain tumors). The Company has also completed a Phase Ib clinical trial for insomnia and recently announced that it commenced a Phase I safety and dose escalating clinical study for and APL compound for Type I diabetics.

The results from preclinical testing and early clinical trials may not be predictive of results obtained in later clinical trials. As a result, there can be no assurance that clinical trials conducted by the Company or its corporate partners will demonstrate sufficient safety and efficacy to obtain the requisite regulatory approvals or will result in marketable products or marketable indications. In addition, 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. A number of companies in the biotechnology and pharmaceutical industries have suffered significant setbacks in advanced clinical trials, even after promising results in earlier trials. If the Company's drug candidates are not shown to be safe and effective in clinical trials, the resulting delays in developing other compounds and conducting related preclinical testing and clinical trials, as well as the potential need for additional financing, would have a material adverse effect on the Company's business, financial condition and results of operations.

The rate of completion of clinical trials conducted by the Company or its corporate partners may be delayed by many factors, including slower than expected patient recruitment or unforeseen safety issues. Any delays in, or termination of, the Company's clinical trials would have a material adverse effect on the Company's business, financial condition and results of operations. There can be no assurance that Neurocrine or its corporate partners will be permitted by regulatory authorities to undertake clinical trials for its products or, if such trials are conducted, that any of the Company's product candidates will prove to be safe and efficacious or will receive regulatory approvals.

The Company is required to conduct its research activities in compliance with good laboratory practice regulations enforced by FDA. The Company is also subject to various Federal, state and local laws, regulations and recommendations relating to safe working conditions, laboratory manufacturing practices, and the use and disposal of hazardous or potentially hazardous substances, including radioactive compounds and infectious disease agents, used in connection with the Company's research. The extent of government regulation that might result from future legislation or administrative action cannot be predicted accurately.

# SCIENTIFIC ADVISORY BOARD

Neurocrine has assembled a Scientific Advisory Board that currently consists of 16 individuals. Members of the Scientific Advisory Board are leaders in the fields of neurobiology, immunology, endocrinology, psychiatry and medicinal chemistry. Scientific Advisory Board members meet at least yearly to advise the Company in the selection, implementation and prioritization of its

research programs. Certain members meet more frequently to advise the Company with regard to its specific programs.

The Scientific Advisory Board presently consists of the following individuals:

- Susan G. Amara, Ph.D. a Senior Scientist and Professor, 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. He is the current editor of the journal, Science.

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.

Iain Campbell, Ph.D., is an Associate Member of the Department of Neuropharmacology at The Scripps Research Institute. Dr. Campbell is an expert in cytosine activation in autoimmune diseases and neuronal degeneration.

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.

George P. Chrousos, M.D., Sc.D., is Chief of the Pediatric Endocrinology Section at the National Institute of Child Health and Human Development. He has investigated the role of stress hormones in pathological conditions such as Cushing's disease, anxiety-related disorders and rheumatoid arthritis.

Caleb E. Finch, Ph.D., is the Arco and William F. Kieschnick Professor of Neurobiology of Aging at the University of Southern California. He is an internationally recognized expert in the field of molecular gerontology and the genomic control of mammalian development and aging. His recent work has focused on the role of cytokines in neuronal protection and aging.

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.

Phillip J. Lowry, Ph.D., is Professor and Head of the Department of Biochemistry and Physiology at the University of Reading in Great Britain. Dr. Lowry is an internationally recognized biochemical endocrinologist whose work has focused on the purification and characterization of some of the key hormonal mediators of the endocrine response to stress. Dr. Lowry is a member of the European Neuroscience Steering Committee, the European Neuroendocrine Association and the Committee of British Endocrinology

Bruce S. McEwen, Ph.D., is Professor and Head of the Harold and Margaret Milliken Hatch Laboratory of Neuroendocrinology at The Rockefeller University. Dr. McEwen has identified and studied the function of intracellular receptors for neuroactive steroid hormones in the brain and immune system, in relation to stress and sex differences. Dr. McEwen is also President of the Society for Neuroscience.

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 of the Company and a member of Neurocrine's Founding Board of Scientific and Medical Advisors and its Executive Committee.

Wylie W. Vale, Ph.D., is Chief Scientific Advisor, Neuroendocrinology of the Company and a member of Neurocrine's Founding Board of Scientific and Medical Advisors and its Executive Committee. See "Item 10 -- Executive Officers and Directors of the Registrant."

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

#### 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, 1998, the Company had 149 employees, consisting of 135 full-time and 14 part-time employees. Of the full-time employees, 46 hold Ph.D., M.D., or equivalent degrees. None of the Company's employees are represented by a collective bargaining arrangement, and the Company believes its relationship with its employees is good. The Company is highly dependent on the principal members of its management and scientific staff. The loss of services of any of these personnel could impede the achievement of the Company's development objectives. Furthermore, recruiting and retaining qualified scientific personnel to perform research and development work in the future will also be critical to the Company's success. There can be no assurance that the Company will 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, the Company relies on members of its Scientific Advisory Board and a significant number of consultants to assist the Company in formulating its research and development strategy.

# ITEM 2. PROPERTIES

The Company leases approximately 93,000 square feet of space at its headquarters facility, of which approximately 80% is laboratory facilities dedicated to research and development. The facility was constructed in 1998 and is under lease through August 2013. The Company has sublet approximately 13,000 square feet of this facility through August 2000. In addition, the Company leases approximately 19,000 square feet of laboratory and office space, which has been sublet to a third party. The lease and sublease on this property expire in June 2000. The Company's facilities are located in San Diego, California.

The Company believes that its property and equipment are generally well maintained, in good operating condition and adequate for its current needs.

#### ITEM 3. LEGAL PROCEEDINGS

Not Applicable.

## 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

The Company's Common Stock has been traded on the Nasdaq National Market System under the symbol NBIX since the Company's initial public offering on May 23, 1996. Prior to that time there was no established public trading market for the Company's 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.

1998 1997

	 High	Low	High	Low
1st Quarter	\$ 10.13	\$ 7.56	\$ 13.25	\$ 8.63
2nd Quarter	 9.06	7.38	10.50	7.00
3rd Quarter	 8.13	4.00	10.75	7.88
4th Quarter	 8.00	4.13	11.88	7.50

As of March 15, 1999, there were approximately 211 stockholders of record of the Company's Common Stock. The Company has not paid any cash dividends on its Common Stock since its inception and does not anticipate paying cash dividends in the foreseeable future.

## ITEM 6. SELECTED FINANCIAL DATA

The following selected financial data have been derived from the Financial Statements of the Company, which have been audited by Ernst & Young LLP, whose reports appear elsewhere herein. The information presented below should be read in conjunction with the Company's Financial Statements and Notes thereto included elsewhere in this Form 10-K. See "Management's Discussion and Analysis of Financial Condition and Results of Operations."

The following tables set forth certain financial data with respect to the Company (in thousands, except per share data). The selected financial data should be read in conjunction with the consolidated financial statements and notes thereto.

_	Year Ended December 31,				
	1998(1)	1997	1996	1995	1994
STATEMENT OF OPERATIONS DATA Revenues					
Sponsored research and development Sponsored research and development from	\$ 8,751	\$ 14,985	\$ 9,092	\$ 3,000	\$
related party	3,610				
Milestones and license fees	2,500	10,250	9,000	2,750	
Grant income and other revenues	1,176	909	1,124	356	162
Total revenues	16,037	26,144	19,216	6,106	162
Research and development	21,803	18,758	12,569	7,740	6,231
General and administrative	6,594	5,664	3,697	2,728	2,223
and development and licenses	4,910				
Total operating expenses	33,307	24,422	16,266	10,468	8,454
Income (loss) from operations	(17,270)	1,722	2,950	(4,362)	(8,292)
Interest income, net	`4,000´	3,931	2,598	` 839´	`´627´
Other income (expense)	504	818	574	177	(41)
Equity in NPI net losses and other adjustments	(7,188)	(1,130)			`'
Net income (loss) before income taxes	(19,954)	5,341	6,122	(3,346)	(7,706)
Income taxes	1	214	248		
Net income (loss)	\$(19,955)	\$ 5,127	\$ 5,874	\$ (3,346)	\$ (7,706)
Earnings per shares					
Basic	\$ (1.10)	\$ 0.30	\$ 0.39	\$ (0.29)	\$ (0.70)
Diluted Shares used in calculation of earnings per share	\$ (1.10)	\$ 0.28	\$ 0.36	\$ (0.29)	\$ (0.70)
Basic	18,141	16,930	14,971	11,684	10,933
Diluted	18,141	18,184	16,127	11,684	10,933
BALANCE SHEET DATA					
Cash, cash equivalents and short-term investments(2)	62,670	75,092	69,920	18,696	18,228
Total assets	80,529	91,903	77, 957	24,012	22,344
Long-term debt and capital lease obligations	2,247	722	847	1,631	1,733
Accumulated deficit	(24,850)	(4,895)	(10,022)	(15,895)	(12,549)
Total stockholders' equity	71,958	83,152	72,767	19,225	18,743

- (1) Includes results of operations and financial position of Northwest NeuroLogic, Inc. from May 28, 1998, the date of acquisition (See Note 2 of the Notes to the Consolidated Financial Statements).
- (2) Excludes funds held by NPI, which is available to fund certain of the Company's research and development activities.

# 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 of Neurocrine Biosciences, Inc. ("Neurocrine" or the "Company"), as well as the preceding sections of this Annual Report on Form 10-K, contain forward-looking statements which involve risks and uncertainties, pertaining generally to the expected continuation of the Company's 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 and profit-sharing payments, the anticipated dates of commencement of selection of development candidates and the commencement of clinical trials, the successful continuation of the Company's

research and development programs and the potential development of future products, the period of time the Company's existing capital resources will meet its funding requirements, and the Company's financial results of operations. Actual results could differ materially from those anticipated in such forward-looking statements as a result of various factors, including those set forth below, and those outlined in the Business section of Item 1.

#### Overview

Since the founding of the Company in January 1992, Neurocrine has been engaged in the discovery and development of novel pharmaceutical products for diseases and disorders of the central nervous and immune systems. To date, Neurocrine has not generated any revenues from the sale of products, and does not expect to generate any product revenues for the foreseeable future. The Company's revenues are expected to come from its strategic alliances. Neurocrine has incurred a cumulative deficit of approximately \$25 million as of December 31, 1998 and expects to incur additional operating losses in the future, which are potentially greater than losses in prior years.

#### Results of Operations

The Company's revenue from collaborative research and development agreements was \$16.0 million for the year ended December 31, 1998 compared with \$26.1 million in 1997, and \$19.2 million in 1996. The decline in 1998 revenues compared to 1997 revenues resulted primarily from non-recurring 1997 revenues related to the completion of the sponsored research portion of the Janssen collaboration, a one-time research support payment received under the Eli Lilly collaboration, sponsored development payments received under the Novartis collaboration and the timing of milestone achievements received under all three collaborations. Revenues in 1998 included \$3.6 million of sponsored development received from the Company's Canadian affiliate, NPI. The increase in 1997 revenues compared to 1996 revenues resulted primarily to increased sponsored research, license fees and milestone revenues recognized under the Janssen, Novartis and Eli Lilly collaborations.

Research and development expenses increased to \$21.8 million during 1998 compared with \$18.8 million in 1997 and \$12.6 million in 1996. These increases reflect higher costs associated with the addition of scientific personnel and costs to advance compounds into preclinical and clinical trials. The Company expects to incur significant increases in future periods as compounds are advanced through the clinical development process.

General and administrative expenses increased to \$6.6 million during 1998 compared with \$5.7 million in 1997 and \$3.7 million in 1996. These increases resulted primarily from additional administrative personnel, business development and professional service expenses to support the expanded clinical development efforts. The Company anticipates slight increases in general and administrative expenses over the next few years as the Company's clinical efforts continue to expand.

During 1998, the Company wrote-off acquired in-process research and development costs of \$4.9 million. In May 1998, the Company acquired the assets, liabilities and the in-process research and development programs of Northwest Neurologic, Inc. ("NNL") in exchange for Company's Common Stock and stock options valued at \$4.2 million. The acquired in-process research and development consisted of Melanocortin ("MCR"), a brain receptor technology relating to obesity and Excitatory Amino Acid Transporters ("EAATs"), a technology relating to neurodegeneration and stroke. In June 1998, the Company purchased licenses for the use of technology in programs relating to insomnia ("NBI-34060") from DOV Pharmaceuticals and brain cancer ("IL-4 Fusion Toxin") from the National Institute of Health for \$710,000. The acquired in-process research and development projects and the licensed technologies are in the early stages of development, have not reached technological feasibility and have no known alternative uses.

The nature and efforts required to develop the acquired in-process research and development into commercially viable products include completion of the development stages of a compound, pre-clinical development, clinical trial testing, FDA approval and commercialization. Due to the nature of the pharmaceutical development process, the Company anticipates incurring substantial costs to develop the compounds into products. However, there is no certainty that any of these development efforts will result in commercially viable products. During the upcoming fiscal year, the Company anticipates research and development expenditures of \$2.8 million for EAATs, \$1.7 million for MCR, \$6.1 million for IL-4 Fusion Toxin and \$5.0 million for NBI-34060.

The value of the acquired in-process research and development was determined by estimating the projected net cash flows related to such products, including costs to complete the development, and future revenues to be earned upon commercialization of the products. These cash flows were discounted back to their net present value using a discount factor of 35%. The resulting projected net cash flows from such projects were based on management's estimates of revenues and operating profits related to such projects. Management also reviewed the probability of product success, which were estimated using certain probability factors for each stage of development.

Interest income increased to \$4.2 million during 1998 compared with \$4.1 million for 1997 and \$2.9 million in 1996. The increase over 1997 primarily resulted from higher effective interest yields on the Company's investment portfolio during 1998. The increase over 1996 primarily resulted from higher effective interest yields in addition to higher average cash balances throughout the year. Management anticipates lower interest income in future periods as clinical efforts increase operating requirements and cash available for investment declines.

million in 1997. In addition to the equity in NPI losses during 1998, the Company recorded a write-down in the value of its investment in NPI, totaling \$3.8 million.

Net loss for 1998 was \$20.0 million or \$1.10 per share compared to net income of \$5.1 million or \$0.30 per share for 1997 and \$5.9 million or \$0.39 per share in 1996. Management expects to incur substantial operating losses in future periods as its clinical development efforts continue to grow.

To date, the Company's 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-date revenues and earnings. Accordingly, results and earnings of one period are not predictive of future periods.

#### LIOUIDITY AND CAPITAL RESOURCES

As of December 31, 1998, the Company had cash, cash equivalents and short-term investments of \$62.7 million. 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. The primary market risk associated with such investments is vulnerability to changes in short-term and long-term U.S. prime interest rates. For further information regarding the Company's investments, see Notes 1 and 3 of the Notes to the Consolidated Financial Statements.

Net cash used by operating activities during 1998 was \$10.7 million compared with net cash provided of \$11.0 million in 1997 and \$6.7 million in 1996. The increase in cash used in operations during 1998 compared with 1997, resulted primarily from increased sponsored research and milestone revenues received under the Company's collaborations during 1997 and an increase in 1998 operating expenses as the Company expands its clinical development activities. The increase in cash provided during 1997 compared with 1996, resulted primarily from increased sponsored research and milestone revenues received under the Company's collaborations during 1997.

Net cash provided by investing activities during 1998 was \$4.7 million compared with net cash used of \$7.2 million and \$48.6 million in 1997 and 1996, respectively. The cash provided by investing activities during 1998 resulted primarily from sales of short-term investments. The cash used in investing activities during 1997 and 1996 resulted from the purchase of short-term investments with proceeds from the Company's prior financings and the sale of Common Stock to corporate collaborators.

Net cash provided by financing activities during 1998 was \$1.9 million compared with \$659,000 and \$46.8 million during 1997 and 1996, respectively. Cash provided during 1998 resulted from proceeds received under capital lease financing of equipment purchases. Cash provided during 1997 resulted from the issuance of the Company's Common Stock upon the exercises of stock options and warrants and proceeds received from a note payable used to finance the purchase of land. Cash provided during 1996 resulted from proceeds received from the Company's initial public offering and sale of the Company's Common Stock to corporate collaborators in May 1996.

Neurocrine has primarily financed its operations through proceeds received from the sale of its Common Stock in various private and public offerings, as well as revenues received under corporate collaborations.

In February 1995, the Company entered into a three year collaborative research and development agreement with Janssen for the development of CRF receptor antagonists for the treatment of anxiety, depression and substance abuse. Janssen paid the Company \$3.7 million and \$3.0 million for sponsored research during 1997 and 1996, respectively. Milestone payments totaled \$250,000, \$1.5 million and \$1.0 million during 1998, 1997 and 1996, respectively. 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. The Company may continue to receive milestone payments and royalties upon the successful continuation of the development portion of the agreement.

In January 1996, the Company entered into an agreement with Novartis to develop altered peptide ligands for the treatment of multiple sclerosis. Novartis paid the Company for license fees and research funding totaling \$4.5 million, \$7.2 million and \$8.5 during 1998, 1997 and 1996, respectively. Milestone payments were \$2.3 million, \$3.8 million and \$3.0 million during 1998, 1997 and 1996, respectively.

In March 1996, the Company participated in the formation of a research and development company, Neuroscience Pharma, Inc. ("NPI"), with a group of Canadian investors. At the same time, 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. During 1998, the Company recognized \$3.6 million in revenues associated with costs of research on the Neurogenomics and DHEA programs.

In May 1997, the Company purchased two adjacent parcels of land in San Diego for approximately \$5.0 million in cash. One parcel was sold to Science Park Center, LLC. ("LLC"), of which the Company owns a minority interest, in exchange for a note receivable of \$3.5 million plus interest. 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, 1998 and 1997 was \$3.8 million and \$3.5 million, respectively. During 1998, the LLC constructed an expanded laboratory and office complex on the property and leased the facility to the Company under a 15 year operating lease. The Company has the option to purchase the facility at any time during the lease at a predetermined price. The Company will hold the remaining parcel until such time as the Company's growth requires

additional expansion.

The Company believes that its existing capital resources, together with interest income and future payments due under the strategic alliances, will be sufficient to satisfy its current and projected funding requirements at least through the year 2000. However, no assurance can be given that such capital resources and payments will be sufficient to conduct its research and development programs as planned. The amount and timing of expenditures will vary depending upon a number of factors, including progress of the Company's research and development programs.

#### INTEREST RATE RISK

The Company is exposed to changes in interest rates primarily from its investments in certain available-for-sale securities and secondarily from its long-term debt. Under its current policies, the Company does not use interest rate derivative instruments to manage exposure to interest rate changes.

The Company's investments are primarily in fixed income, investment-grade securities and are not restricted. The investment policy emphasizes return on principal and liquidity and is focused on fixed returns, which limit volatility and risk of principal. At December 31, 1998, the Company had available-for-sale securities of \$51.0 million. Interest risk exposure on long-term debt relates to the Company's note payable which bears of floating interest rate of prime plus one quarter percent (8.00% at December 31, 1998). At December 31, 1998, the note balance was approximately \$610,000, payable in equal monthly installments through January 2003. The Company believes that a hypothetical 100 basis point adverse move in interest rates along the entire interest rate yield curve would not materially effect the fair value of interest sensitive financial instruments nor the costs associated with the long-term debt.

#### IMPACT OF YEAR 2000

The Year 2000 Issue is the result of computer programs being written using two digits rather than four to define the applicable year. Any of the Company's computer programs or hardware that have date-sensitive software or embedded chips may recognize a date using "00" as the year 1900 rather than the year 2000. This could result in a system failure or miscalculations causing disruptions of operations, including, among other things, a temporary inability to process transactions, send invoices, or engage in similar normal business activities.

Based on recent assessments, the Company determined that it will not be required to modify or replace significant portions of hardware and software so that those systems will properly utilize dates beyond December 31, 1999. The Company presently believes that with modifications and replacement of existing hardware and software, the Year 2000 Issue can be mitigated. However, if such modifications and replacements are not made, or are not completed timely, the Year 2000 Issue could have a material impact on the operations of the Company.

The Company's plan to resolve the Year 2000 Issue involves the following four phases: assessment, remediation, testing, and implementation. To date the Company has fully completed its assessment of all systems that could be significantly affected by the Year 2000. The completed assessment indicated that most of the Company's significant information technology systems are Year 2000 compliant. That assessment did, however, indicated that software and hardware (embedded chips) used in some scientific equipment were at risk. Affected systems include several robotics systems used for high through-put screening. The Company is currently assessing cost comparisons on whether to remediate or replace this equipment and expects to have the equipment corrected and re-tested by May 1, 1999. The Company has gathered information about the Year 2000 compliance status of its significant suppliers and contractors and continues to monitor their compliance.

For its information technology exposures, to date the Company is 99% complete on the remediation phase and expects to complete software reprogramming and replacement no later than April 15, 1999. To date, the Company has completed 100% of its testing and has implemented 90% of its remediated systems for its scientific equipment. The remediation phase for all significant systems is expected to be complete by May 1, 1999, with all remediated systems fully tested by June 1, 1999.

The Company has queried its important suppliers and contractors that do not share information systems with the Company (external agents). To date, the Company is not aware of any external agent Year 2000 issue that would materially impact the company's results of operations, liquidity, or capital resources. However, the Company has no means of ensuring that external agents will be Year 2000 ready. The inability of external agents to complete their Year 2000 resolution process in a timely fashion could materially impact the Company. The effect of non-compliance by external agents is not determinable.

The Company will utilize both internal and external resources to reprogram, or replace, test and implement the software and scientific equipment for Year 2000 modifications. The total cost of the Year 2000 project is estimated at approximately \$175,000 and is being funded through operating cash flows and capital equipment financing. To date, the Company has incurred approximately \$100,000 related to all phases of the Year 2000 project. Of the total remaining project costs, approximately \$40,000 is attributable to the purchase of new software, \$25,000 for new scientific equipment, which will be capitalized, and \$10,000 for the repair of hardware and software.

The Company plans to complete the Year 2000 modifications are based on management's best estimates, which were derived utilizing numerous assumptions of future events including continued availability of certain resources, and other factors. Estimates on the status of completion and the expected completion dates are based on costs incurred to date compared to total expected costs.

However, there can be no guarantee that these estimates will be achieved and actual results could differ materially from those plans. Specific factors that might cause such material differences include, but are not limited to, the availability and cost of personnel trained in this area, the ability to locate and correct all relevant computer codes, and similar uncertainties.

The Company has not completed a formal contingency plan for non-compliance, but it is developing a plan based on the information obtained from third parties and an on-going evaluation of the Company's own systems. The Company anticipates having a contingency plan in place by mid-1999, which will include development of backup procedures, identification of alternate suppliers and possible increases in supplies inventory levels. The Company has not identified its most reasonably likely worst case scenario with respect to possible losses in connection with Year 2000 related problems. The Company plans on completing this analysis in mid-1999.

The information above contains forward-looking statements including, without limitation, statements relating to the Company's plans, strategies, objectives, expectations, intentions, and adequate resources that are made pursuant to the "safe harbor" provisions of the Private Securities Litigation Reform Act of 1995. Readers are cautioned that forward-looking statements about the Year 2000 should be read in conjunction with the Company's disclosures under the heading: "Caution on forward-looking statements".

#### CAUTION ON FORWARD-LOOKING STATEMENTS

The Company's business is subject to significant risks, including but not limited to, the risks inherent in its research and development activities, including the successful continuation of the Company's 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 its 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 the Company's 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.

Neurocrine will require additional funding for the continuation of its research and product development programs, for progress with preclinical testing and clinical trials, for operating expenses, for the pursuit of regulatory approvals for its 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 may require additional funding for establishing manufacturing and marketing capabilities in the future. The Company may seek to access the public or private equity markets whenever conditions are favorable. The Company may also seek additional funding through strategic alliances and other financing mechanisms, potentially including off-balance sheet financing. There can be no assurance that adequate funding will be available on terms acceptable to the Company, if at all. If adequate funds are not available, the Company may be required to curtail significantly one or more of its research or development programs or obtain funds through arrangements with collaborative partners or others. This may require the Company to relinquish rights to certain of its technologies or product candidates.

Continued profitability is not expected as the Company's operating expenses are anticipated to rise significantly in future periods as products are advanced through the various development and clinical stages. Neurocrine expects to incur additional operating expenses over the next several years as its research, development, preclinical testing and clinical trial activities increase. To the extent that the Company is unable to obtain third party funding for such expenses, the Company expects that increased expenses will result in increased losses from operations. There can be no assurance that the Company's products under development will be successfully developed or that its products, if successfully developed, will generate revenues sufficient to enable the Company to earn a profit.

#### 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, on page 26 of this report.

# ITEM 8. FINANCIAL STATEMENTS AND SUPPLEMENTAL 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

Information required by this item will be contained in the Company's Notice of 1999 Annual Meeting of Stockholders and Proxy Statement, Regulation 14A, to be filed with the Securities and Exchange Commission within 120 days after December 31, 1998. 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 1999 Annual Meeting of Stockholders and Proxy Statement, pursuant to Regulation 14A, to be filed with the Securities and Exchange Commission within 120 days after December 31, 1998. 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 1999 Annual Meeting of Stockholders and Proxy Statement, Regulation 14A, to be filed with the Securities and Exchange Commission within 120 days after December 31, 1998. 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 1999 Annual Meeting of Stockholders and Proxy Statement, pursuant to Regulation 14A, to be filed with the Securities and Exchange Commission within 120 days after December 31, 1998. Such information is incorporated herein by reference.

#### PART TV

#### ITEM 14. EXHIBITS, FINANCIAL STATEMENT SCHEDULES AND REPORTS ON FORM 8-K

(a) Documents filed as part of this report

- 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, 1998 and 1997 Consolidated Statement of Operations for the years ended December 31, 1998, 1997 and 1996 Consolidated Statement of Stockholders' Equity for the years ended December 31, 1998, 1997 and 1996 Consolidated Statement of Cash Flows for the years ended December 31, 1998, 1997 and 1996 Notes to the Consolidated Financial Statements
- 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. No reports on Form 8-K were filed during the quarter ended December 31, 1998.
- (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*	Registration Rights Agreement dated May 28, 1998, between certain investors and the Registrant (7)
2.3	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 Lock-Up Agreement (1)
4.2	Form of Common Stock Certificate (1)
4.3	Form of warrant issued in existing warrant holders (1)
4.4	Form of Series A warrant issued in connection with the execution by the Company of the Unit Purchase Agreement (see below) (1)
4.5	New Registration Rights Agreement dated March 29, 1996 among the Company and the investors signatory thereto (1)
4.6	Letter of Intent between Northwest NeuroLogic, Inc. and the Company dated February 27, 1998 (2)
10.1	Purchase and Sale Agreement and Escrow Instructions between MS Vickers II, LLC and the Company dated February 13, 1997 (3)
10.2	1992 Incentive Stock Plan, as amended
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 (4)
10.7 10.8	Employment Agreement dated March 1, 1997, between the Registrant and Errol B. De Souza, as amended (4) Employment Agreement dated March 1, 1997, between the Registrant and Paul W. Hawran (4)

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Employment Agreement dated March 1, 1997, between the Registrant and Stephen Marcus, MD (4)
10.10
                  Consulting Agreement dated September 25, 1992, between the Registrant and Wylie A. Vale, Ph.D. (1)
10.11
                  Consulting Agreement effective January 1, 1992, between the Registrant and Lawrence J. Steinman, MD (1)
                  Lease Agreement dated June 1, 1993, between the Registrant and Hartford Accident and Indemnity Company,
                  as amended (1)
10.13
                  Exclusive License Agreement dated as of July 1, 1993, by and between the Beckman Research Institute of
                  the City of Hope and the Registrant covering the treatment of nervous system degeneration and
                  Alzheimer's disease (1)
                  Exclusive License Agreement dated as of July 1, 1993, by and between the Beckman Research Institute of the City of Hope and the Registrant covering the use of Pregnenolone for the enhancement of memory (1) License Agreement dated May 20, 1992, by and between The Salk Institute for Biological Studies and the
10.14
10.15
                  Registrant (1)
10.16
                  License Agreement dated July 17, 1992, by and between The Salk Institute for Biological Studies and
                  the Registrant (1)
                  License Agreement dated November 16, 1993, by and between The Salk Institute for Biological Studies
10.17
                  and the Registrant (1)
10.18
                  License Agreement dated October 19, 1992, by and between the Board of Trustees of the Leland Stanford
                  Junior University and the Registrant (1)
10.19
                  Agreement dated January 1, 1995, by and between the Registrant and Janssen Pharmaceutica, N.V. (1)
                  Letter Agreement dated January 19, 1996, by and between the Registrant and Ciba-Geigy Limited (1)
Unit Purchase Agreement dated March 29, 1996, by and between Neuroscience Pharma, Inc. the Registrant
10.20
10.21*
                  and the investors signatory thereto (1)
10.22*
                  Exchange Agreement dated March 29, 1996, by and between Neurocrine Biosciences (Canada), Inc., the
                  Registrant and the investors signatory thereto (1)
10.23*
                  Research and Development Agreement dated March 29, 1996, by and between Neurocrine Biosciences
                  (Canada), Inc. and Neuroscience Pharma, Inc. (1)
10.24*
                  Intellectual Property and License Grants Agreement dated March 29, 1996, by and between the Registrant
                  and Neurocrine Biosciences (Canada), Inc. (1)
10.25*
                  Development and Commercialization Agreement dated December 20, 1996, by and between Ciba-Geigy Ltd.
                  And the Registrant (5)
Letter and Purchase Order dated June 7, 1996, by and between Ciba-Geigy and the Registrant (5)
10.26*
                  Third Lease Amendment dated June 6, 1996, by and between Talcott Realty I Limited Partnership and the
10.27
                  Registrant (5)
10.28*
                  Research and License Agreement dated October 15, 1996, between the Registrant and Eli Lilly and
                  Company (5)
10.29*
                  Lease between Science Park Center LLC and the Company (6)
10.30*
                  Option Agreement between Science Park Center LLC (Optionor) and the Company (Optionee) (6)
10.31*
                  Construction Loan Agreement (6)
                  Secured Promissory Note (6)
Operating Agreement for Science Park Center LLC (6)
10.32
10.33*
10.34
                  Information and Registration Rights Agreement dated September 15, 1992, as amended to date (1)
10.35
                  Form of incentive stock option agreement and nonstatutory stock option agreement for use in connection
                  with 1992 Incentive Stock Plan (1)
                  Patent License Agreement dated May 7, 1998, between the US Public Health Service and the Registrant (7) Patent License Agreement dated April 28, 1998, between and among Ira Pastan, David Fitzgerald and the
10.36*
10.37*
                  Registrant (7)
10.38*
                  Sub-License and Development Agreement dated June 30, 1998, by and between DOV Pharmaceutical, Inc. and
                  the Registrant (7)
                  Warrant Agreement dated June 30, 1998, between DOV Pharmaceutical, Inc. and the Registrant (7)
10.39
                  Warrant Agreement dated June 30, 1998, between Jeff Margolis and the Registrant (7) Warrant Agreement dated June 30, 1998, between Stephen Ross and the Registrant (7)
10.40*
10.41*
10.42+
                  Collaboration and License Agreement dated January 1, 999, by and between American Home Products
                  Corporation acting through its Wyeth-Ayerst Laboratories Division and the Registrant
10.43+
                  Employment Agreement dated January 1, 1999, between the Registrant and Margaret Valeur-Jensen
10.44+
                  Employment Agreement dated February 9, 1998, between the Registrant and Bruce Campbell
21
                  Subsidiaries of the Company
                  Consent of Ernst & Young LLP, Independent Auditors
23
24
                  Power of Attorney (see page 33)
                  Financial Data Schedule
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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 8-K filed
- on March 13, 1998.
- (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
- Incorporated by reference to the Company's Report on Form 10-K for the fiscal year ended December 31, 1996 Incorporated by reference to the Company's Quarterly Report on Form 10-Q filed on November 14, 1997 Incorporated by reference to the Company's Quarterly Report on Form 10-Q filed on November 16, 1998. (5)
- (6)
- (7)
  - 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.

10.9

#### 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

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

President and Chief Executive Officer

Date

Date: March 31, 1999

#### 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.

Title

Signature

	President, Chief Executive Officer and - Director (Principal Executive Officer)		31,	1999
Gary A. Lyons	J1. 0000. ( 1.101pul 2.0000110 0 1001.)			
	Chief Financial Officer - (Principal Financial and Accounting Of	March ficer)	31,	1999
/s/ Joseph A. Mollica Joseph A. Mollica.	Chairman of the Board of Directors	March	31,	1999
/s/ Richard F. Pops	Director -	March	31,	1999
Richard F. Pops /s/ Harry F. Hixson, Jr.	Director	March	31,	1999
Harry F. Hixson, Jr.	-			
/s/ Wylie W. Vale 	Director -	March	31,	1999

# NEUROCRINE BIOSCIENCES, INC. INDEX TO THE CONSOLIDATED FINANCIAL STATEMENTS

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Consolidated Statement of Cash Flows	39
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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, 1998 and 1997, and the related consolidated statements of operations, stockholders' equity, and cash flows for each of the three years in the period ended December 31, 1998. 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 generally accepted auditing standards. 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, 1998 and 1997, and the consolidated results of its operations and its cash flows for each of the three years in the period ended December 31, 1998, in conformity with generally accepted accounting principles.

/s/ ERNST & YOUNG LLP ERNST & YOUNG LLP

San Diego, California January 26, 1999, except for Note 13, as to which the date is March 2, 1999

# NEUROCRINE BIOSCIENCES, INC. Consolidated Balance Sheet (in thousands) December 31,

December 31,		
	1998	1997
ASSETS Current assets:		
Cash and cash equivalents	\$ 11,708 50,962 863 544 1,556	\$ 15,771 59,321 194 156 936
Total current assets	65,633	76,378
Property and equipment, net	10,899 967 1,411 1,619	8,846 1,185 3,343 2,151
Total assets	\$ 80,529 ======	\$ 91,903 ======
LIABILITIES AND STOCKHOLDERS' EQUITY Current liabilities:		
Accounts payable Accrued liabilities Deferred revenues Current portion of long-term debt Current portion of capital lease obligations	2,077 169 149 693	\$ 1,822 2,402 1,919 149 724
Total current liabilities	5,569	7,016
Long-term debt, net of current portion	461 1,786 257 498	597 125 659 354
Total liabilities	8,571	8,751
Commitments and contingencies		
Stockholders' equity: Preferred Stock, \$0.001 par value; 5,000,000 shares authorized; no shares issued and outstanding Common Stock, \$0.001 par value; 100,000,000 shares authorized; issued and outstanding shares were		
18,930,865 in 1998 and 17,686,802 in 1997	19 97,064 (187) (119) 31 (24,850)	18 88,586 (439) (120) 2 (4,895)
Total stockholders' equity	71,958	83,152
Total liabilities and stockholders' equity	\$ 80,529 ======	\$ 91,903 ======

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

	Year-ended December 31,		
	1998	1997	1996
Revenues:			
Sponsored research and developmentSponsored research and development from related party	\$ 8,751 3,610	\$ 14,985 	\$ 9,092
Milestones and license fees	1,176	10,250 909	9,000 1,124
Total revenues	16,037	26,144	19,216
Research and development	21,803 6,594	18,758 5,664	12,569 3,697
development and licenses	,		
Total operating expenses	33,307	24,422	16,266
Income (loss) from operations	(17,270)	1,722	2,950
Interest income	4,151 (151)	4,084 (153)	2,870 (272)
Equity in NPI losses and other adjustments Other income	(7,188) 504	(1,130) 818	 574
Income (loss) before taxes	(19,954) 1	5,341 214	6,122 248
Net income (loss)	\$(19,955) ======	\$ 5,127 ======	\$ 5,874
Earnings (loss) per common share:	======		======
Basic Diluted	\$ (1.10) \$ (1.10)		\$ 0.39 \$ 0.36
Shares used in the calculation of earnings (loss) per common share:			
Basic	18,141 18,141	16,930 18,184	14,971 16,127

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

			Paid In	Compen-	Notes d Receivable from	Accumulated Other Comprehensive		
	Shares	Amount	Capital		Stockholders	Income (Loss)	Delicit	Equity
BALANCE AT DECEMBER 31, 1995	11,723		\$ 35,586	\$(342)	\$(138)		\$(15,896)	\$ 19,225
Net income Unrealized gain on short-term investments						39	5,874 	5,874 39
Comprehensive income	 5,054	 5	 47,535					5,913 47,540
Payments received on stockholder notes Deferred compensation and related					10			10
amortization, net			113	(34)				79
BALANCE AT DECEMBER 31, 1996	16,777	17 	83,234	(376)	(128)	42 	(10,022) 5,127	72,767 5,127
Unrealized loss on short-term investments						(40)	5,127	(40)
Comprehensive income								5,087
Issuance of common stock for warrants  Issuance of common stock for option exercises  Issuance of common stock pursuant to the	182 106		59 453					59 453
Employee Stock Purchase Plan	22		175					175
NPI Preferred Stock	600	1	4,473					4,474
Payments received on stockholder notes Deferred compensation and related					8			8
amortization, net			192	(63)				129
BALANCE AT DECEMBER 31, 1997 Net loss	17,687	18	88,586	(439)	(120)	2	(4,895)	83,152
Unrealized gain on short-term investments						29	(19,955) 	(19,955) 29
Comprehensive loss								(19,926)
Issuance of common stock for warrants	60		142					142
Issuance of common stock for option exercises Issuance of common stock pursuant to the	81		286					286
Employee Stock Purchase Plan Issuance of common stock in exchange for	30		205					205
NPI Preferred Stock	679	1	3,854					3,855
Issuance of common stock for NNL Acquisition	392 2		4,032 17					4,032
Issuance of common stock for milestone achievement Payments received on stockholder notes			17 		1			17 1
Amortization of deferred compensation, net			(58)	252				194
BALANCE AT DECEMBER 31, 1998	,		\$ 97,064	\$(187) ======	\$(119) =======	\$ 31 ========	\$(24,850) =====	,

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

	Twelve Months Ended Decembe		,
	1998	1997	1996
CASH FLOW FROM OPERATING ACTIVITIES  Net (loss) income	\$(19,955)	\$ 5,127	\$ 5,874
Provided by (used in) operating activities:     Acquisition of Northwest NeuroLogic for Common Stock     Equity in NPI losses and other adjustments     Depreciation and amortization     Loss on abandonment of assets     Gain on sale of equipment     Deferred revenues     Deferred rent     Compensation expenses recognized for stock options     Change in operating assets and liabilities, net of acquired business:	4,200 7,188 1,720 460 (15) (1,750) (402) 194	1,130 1,322 76  1,000 384 129	981 25  419 61
Accounts receivable and other current assets  Other non-current assets  Accounts payable and accrued liabilities	(2,898) 291 271	885 (1,274) 2,213	(936) (486) 665
Net cash flows (used in) provided by operating activities $\ldots$	(10,696)	10,992	6,682
CASH FLOW FROM INVESTING ACTIVITIES Purchases of short-term investments Sales/maturities of short-term investments Proceeds from sale of equipment	(41,618) 50,006 72	(113,080) 112,315	(85,171) 38,918
Purchases of property and equipment	(3,755)		(2,304)
Net cash flows provided by (used in) investing activities	4,705	(7,205)	(48,557)
CASH FLOW FROM FINANCING ACTIVITIES Issuance of Common Stock	433 2,500 (1,006) 1	687 747 (783) 8	47,540  (742) 10
Net cash flows provided by financing activities	1,928	659	46,808
Net decrease in cash and cash equivalents	(4,063)	4,446	4,933
Cash and cash equivalents at beginning of the period	15,771	11,325	6,392
Cash and cash equivalents at end of the period		\$ 15,771 ======	\$ 11,325 ======
SUPPLEMENTAL DISCLOSURES Supplemental disclosures of cash flow information:	\$ 150 1	\$ 153 250	\$ 272 40
Conversion of note receivable to investment in NPI Conversion of NPI Preferred Stock to investment in NPI	\$ 1,401 3,855	4,474	

# NEUROCRINE BIOSCIENCES, INC. NOTES TO THE CONSOLIDATED FINANCIAL STATEMENTS (Continued) December 31, 1998

#### . ORGANIZATION AND SUMMARY OF SIGNIFICANT ACCOUNTING POLICIES

BUSINESS ACTIVITIES: Neurocrine Biosciences, Inc. (the "Company") was incorporated in California on January 17, 1992 and was reincorporated in Delaware in March 1996. The Company is engaged in the discovery and development of therapeutics for the treatment of diseases and disorders of the central nervous and immune systems which includes anxiety, depression, Alzheimer's disease, obesity, stroke and multiple sclerosis.

PRINCIPLES OF CONSOLIDATION: The consolidated financial statements include the accounts of Neurocrine Biosciences, Inc. (the "Company") and its wholly owned subsidiary, Northwest NeuroLogic, Inc. ("NNL"). Significant intercompany accounts and transactions have been eliminated in consolidation.

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 a separate component of stockholders' equity. 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. 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 exclusive, worldwide, perpetual 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 Statement 17 "Intangible Assets" and are adjusted to an appropriate amortization period which generally results in immediate write-off. Accumulated amortization at December 31, 1998 and 1997 was \$679,000 and \$461,000, respectively.

IMPAIRMENT OF LONG-LIVED ASSETS: The Company routinely assesses the recoverability of 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 will measure 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.

INDUSTRY SEGMENT AND GEOGRAPHIC INFORMATION: The Company operates in a single industry segment - the discovery and development of therapeutics for the treatment of diseases and disorders of the central nervous and immune. The Company has no foreign operations.

RESEARCH AND DEVELOPMENT REVENUE AND EXPENSES: Revenues under collaborative research agreements are recognized over the period specified in the related agreement. Advance payments received in excess of amounts earned are classified as deferred revenue and recognized as income in the period earned. Revenues from government grants are recognized based on the performance requirements of the grant or as the grant expenditures are incurred. 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 \$12.0 million, \$9.4 million and \$8.3 million during 1998, 1997 and 1996, respectively.

STOCK-BASED COMPENSATION: The Company accounts for stock option grants to employees in accordance with Accounting Principles Board Opinion No. 25, "Accounting for Stock Issued to Employees" (APB 25) and related Interpretations because the Company believes the alternative fair value accounting provided for under SFAS No. 123, "Accounting for Stock-Based Compensation," requires the use of option valuation models that were not developed for use in valuing employee stock options. Deferred compensation is recorded 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. Such deferred compensation is amortized over the vesting

period of the options. Compensation expense recognized during the years ended December 31, 1998, 1997 and 1996 was \$194,000, \$129,000 and \$79,000, respectively.

EARNINGS PER SHARE: Basic and diluted earnings per share is calculated in accordance with FASB Statement No. 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 Statement No. 128.

COMPREHENSIVE INCOME: Comprehensive income is calculated in accordance with FASB Statement No. 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, 1998.

IMPACT OF RECENTLY ISSUED ACCOUNTING STANDARDS: In June 1998, the FASB issued Statement No. 133, "Accounting for Derivative Instruments and Hedging Activities". The Company expects to adopt the new Statement effective January 1, 2000. The Statement will require the Company to recognize all derivatives on the balance sheet at fair value. The Company does not anticipate that the adoption of the Statement will have a significant effect on its results of operations or financial position.

#### 2. ACQUIRED IN-PROCESS RESEARCH AND DEVELOPMENT AND LICENSES

NORTHWEST NEUROLOGIC, INC: In May 1998, the Company acquired the assets and liabilities of Northwest NeuroLogic, Inc. ("NNL"), a neurodegenerative research and development company, in exchange for 392,608 shares of Company's Common Stock and 105,414 of stock options valued at \$4.2 million. The operations of NNL are included in the consolidated statement of operations from the date of acquisition.

The acquisition was accounted for as a purchase and, accordingly, the purchase price has been allocated to the assets acquired and the liabilities assumed based on the estimated fair market value at the date of the acquisition. The amount allocated to in-process research and development was charged to expense because the technology has not reached technological feasibility and has no future alternative uses. The purchase price was allocated as follows (in thousands):

Current assets	\$ 180
Furniture and equipment	49
Liabilities assumed	(207)
In-process research and development	4,200
Total purchase price	\$ 4,222

The acquired in-process research and development consisted of Melanocortin ("MCR"), a brain receptor technology relating obesity and Excitatory Amino Acid Transporters ("EAATs"), a technology relating to neurodegeneration and stroke. Both in-process research and development are in early developmental stages.

The nature and efforts required to develop the acquired in-process research and development into commercially viable products include completion of the development stages of a compound, pre-clinical development, clinical trial testing, FDA approval and commercialization. Due to the nature of the pharmaceutical development process, the Company anticipates substantial further research and clinical expenditures to develop the products. There is, however, no certainty that either of these programs will result in viable products.

The following are the pro forma unaudited results of operations for the years ended December 31, 1998 and 1997, had the purchase of NNL been consummated as of January 1, of the respective years:

	1998	1997
	(in thousands,	except per share data)
Revenues		\$ 26,783 975
Basic		\$ 0.06 0.05

This pro forma information is not necessarily indicative of the actual results that would have been achieved had NNL been acquired on January 1, 1997, nor is it necessarily indicative of future results.

OTHER: During 1998, the Company purchased licenses for technologies relating to insomnia in the amount of \$440,000 and brain cancer in the amount of \$270,000. These projects are 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.

# 3. 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, 1998				
US Government securities	\$ 6,000	\$ 17	\$	\$ 6,017
Certificates of deposit .	260			260
Commercial paper	5,420			5,420
Corporate debt securities	39,141	61	(87)	39,115
Other	110	40		150
Total coourities	ф FO 021	\$ 118	ф (07)	Ф FO 062
Total securities	\$ 50,931 ======	\$ 118 =======	\$ (87) ======	\$ 50,962 ======
December 31, 1997				
US Government securities	\$ 11,975	\$ 54	\$	\$ 12,029
Certificates of deposit .	247			247
Commercial paper	9,850			9,850
Corporate debt securities	37,143	4	(60)	37,087
Other	104	4		108
Total securities	\$ 59,319	\$ 62	\$ (60)	\$ 59,321
	=======	======	=======	=====

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, 1998, are shown below (in thousands).

	Amortized Cost	Estimated Fair Value
Due in one year or less	\$22,883	\$23,002
Due after one year through five years	28,048	27,960
	\$50,931	\$50,962
	======	======

#### 4. PROPERTY AND EQUIPMENT

	1998	1997
Land  Furniture and fixtures  Equipment  Leasehold improvements	\$5,299 1,856 7,356 562	\$4,985 1,204 4,956 717
Less accumulated depreciation and amortization	15,073 (4,174)	11,862 (3,016)
Net property and equipment	\$ 10,899 ======	\$ 8,846 ======

Furniture and equipment under capital leases were \$5.8 million and \$3.3 million at December 31, 1998 and 1997, respectively. Accumulated depreciation of furniture and equipment under capital leases totaled \$3.1 million and \$2.2 million at December 31, 1998 and 1997, respectively. The Company received proceeds of \$2.5 million for equipment that it sold and subsequently leased back under capital lease obligations in 1998. No similar transactions were conducted in 1997.

#### 5. ACCRUED LIABILITIES

	1998	1997
Accrued employee benefits	\$ 1,120	\$ 1,162
Accrued professional fees	438	470
Accrued development costs	333	300
Taxes payable	15	195
Other accrued liabilities	171	275
	\$2,077	\$2,402
	======	======

# 6. 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 (8.00% at December 31, 1998). The note is repayable in equal monthly installments beginning February 1998.

At December 31, 1998, the repayment schedule for the note was \$149,000 for each year 1999 through 2002 and \$13,000 in the year 2003.

## 7. COMMITMENTS AND CONTINGENCIES

CAPITAL LEASE OBLIGATIONS: The Company has financed certain equipment under capital lease obligations which expire on various dates through the year 2002 and bear interest at rates between 7.6% and 11.6%. 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 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, 1998 and 1997 was \$3.8 million and \$3.5 million, respectively.

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. In November 1998, the Company subleased a portion of this facility to an unrelated third party for a term of 20 months. The Company will hold the second parcel of land until such a time as additional facilities are required.

In November 1998, the lease obligation relating to the Company's former operating facility was amended to reduce the amount of square footage leased and to shorten the lease term to conclude in June 2000. The Company currently subleases this space to an unrelated third party and is obligated to continue this arrangement through June 2000.

Repayment schedules for the capital lease obligations and operating lease commitments at December 31, 1998 are as follows (in thousands):

Fiscal Year:	Capital Leases	Operating Leases
113001 10011		
1999	. \$863	\$2,924
2000	. 733	2,731
2001	. 900	2,525
2002	. 350	2,626
2003		2,731
Thereafter		32,721
Total minimum payments	. 2,846	\$46,258
		=======
Less: amounts representing interest	. (367)	
Future minimum payments		
Less: current portion	. (693)	
Future normante en conital lacce obligations	ф1 706	
Future payments on capital lease obligations	. \$1,786	
	=======	

Rent expense was \$2,379,000, \$2,139,000, and \$1,298,00 for the years ended December 31, 1998, 1997 and 1996, respectively. Sublease income was \$837,000, \$917,000 and \$598,000, for the years ended December 31, 1998, 1997 and 1996, respectively.

Future minimum sublease income to be received under non-cancelable subleases at December 31, 1998 will be \$985,000 and \$506,000 for the years ending December 31, 1999 and 2000, respectively.

Licensing and Research Agreements: The Company has entered into licensing agreements with various universities and research organizations. 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.

# 8. 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 \$10.50 per share resulting in aggregate net proceeds of approximately \$72.1 million.

Options: The Company has authorized 5,005,414 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 (collectively "the 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 Plan.

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

1998	1997	1996
Weighted	Weighted	Weighted

	Options (in thousands)	Average Exercise Price	Options (in thousands)	Average Exercise Price	Options (in thousands)	Average Exercise Price
Outstanding at January 1,	2,653	\$5.84	1,739	\$4.48	1,415	\$3.61
Granted	677	\$6.26	1,072	\$7.86	378	\$7.92
Exercised	(81)	\$3.64	(100)	\$4.10	(11)	\$3.60
Canceled	(456)	\$5.76	(58)	\$5.88	(43)	\$4.41
Outstanding at December 31,	2,793	\$6.02	2,653	\$5.85	1,739	\$4.48

A summary of options outstanding as of December 31, 1998 follows:

Options Outstanding				Options Exercisable		
Range of Exercise Prices	Outstanding as of 12/31/98	Weighted Average Remaining Contractual Life	Weighted Average Exercise Price	Exercisable As of 12/31/98	Weighted Average Exercise Price	
\$0.02 to \$2.50 \$4.25 \$5.00 to \$7.01 \$7.38 to \$7.86 \$8.00 to \$10.25	492 553 486 678 584	5.4 years 6.2 years 8.6 years 8.5 years 8.2 years	\$2.24 \$4.25 \$6.36 \$7.62 \$8.73	427 474 104 228 294	\$2.40 \$4.25 \$5.64 \$7.58 \$8.73	
φο.σο το φισ.25	2,793	7.5 years	\$6.02	1,527	\$5.19	· <b>-</b>

The weighted average fair values of the options  $\,$  granted during 1998, 1997 and 1996 were \$5.59, \$5.01 and \$5.79, 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 1998, 1997 and 1996, respectively: risk-free interest rates of 5.5%, 5.8% and 6.1%; a dividend yield of 0.0% (for all years), volatility factors of the expected market price of the Company's common stock of .88, .43 and .41; 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 income loss for 1998 and net income in 1997 and 1996, 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, 1998, 1997 and 1996 follows (in thousands, except for per share data):

	1998	1997	1996
-			
Pro forma net income (loss)	\$(20,758)	\$4,364	\$5,375
Pro forma income (loss) per share (diluted) .	\$(1.14)	\$0.24	\$0.33

EMPLOYEE STOCK PURCHASE PLAN: The Company has reserved 125,000 shares of Common Stock for issuance under the 1996 Employee Stock Purchase Plan (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 start date of an offering period or on the date on which the shares are purchased. Through December 31, 1998, 51,082 shares had been issued pursuant to the Purchase Plan.

WARRANTS: The Company has outstanding warrants to purchase 388,185 shares of Common Stock at exercise prices of \$5.00 and \$10.50 per share. The warrants generally expire between 1998 and 2007. At December 31, 1998, all outstanding warrants were exercisable.

The following shares of Common Stock are reserved for future issuance at December 31, 1998:

Stock option plans Employee stock purchase plan Warrants	73,918 388,185
Total	3,927,568

Of the shares available for future issuance under the Plan, 2,792,987 are outstanding grants and 672,478 remain available for future grant.

## 9. COLLABORATIVE RESEARCH AND DEVELOPMENT AGREEMENTS

JANSSEN: In January 1995, the Company entered into a research and development agreement (the "Janssen Agreement") with Janssen, under which Janssen paid the Company \$2.0 million in up-front license fees and \$9.7 million in sponsored research payments during the three-year term of the collaborative research portion of the agreement. The research portion of the agreement was

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. Milestone payments of \$3.5 million have been received through December 31, 1998. The Company has granted Janssen an exclusive worldwide license to manufacture and market products developed under the Janssen Agreement. 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 reimbursement to Neurocrine for its promotional efforts, if any.

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. 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 is obligated to provide Neurocrine with \$7.0 million in research and development funding during the first two years of the agreement and up to \$15.5 million in further research and development funding thereafter. As of December 31, 1998, the Company has received \$15.2 million in sponsored research and development payments. In addition, the Company is also entitled to receive milestone payments for certain development and regulatory achievements. The Company has received \$9.1 million of milestone payments through December 31, 1998 of which \$2.3 million was received in 1998.

In return, Novartis received manufacturing and marketing rights outside of North America and will receive a percentage of profits on sales in North America. The Company will receive royalties for all sales outside North America and a percentage of profits on sales in North America, which the Company may at its option convert to a right to receive royalties on product sales. Neurocrine is obligated to repay a portion of the development costs for potential products developed in such collaboration unless the Company elects to convert to the right to receive royalty payments. Novartis has the right to terminate the agreement upon six months notice.

ELI LILLY: In October 1996, the Company entered into an agreement with Eli Lilly and Company under which the Company expects to receive \$22.0 million in research payments of which \$14.5 million have been received as of December 31, 1998. 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, which 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.

## 10. RELATED PARTY TRANSACTIONS

Neuroscience Pharma, Inc: In March 1996, the Company along with a group of Canadian institutional investors (the "Canadian Investors") established Neuroscience Pharma Inc. ("NPI"). The Company's contribution was to license certain technology and Canadian marketing rights to NPI. The Canadian Investors contributed approximately \$9.5 million in cash in exchange for Preferred Stock of NPI, which could be converted into 1,279,758 shares of the Company's Common Stock at the option of the investors. Upon conversion of the Preferred Shares, ownership of the shares transfer to the Company and is redeemable for approximately \$9.5 million in cash at the option of the Company.

NPI has committed to use these funds for research and clinical development of certain of the Company's programs in exchange for royalties on sales of products developed, as well as, exclusive Canadian marketing rights for such products in certain situations. The Company has the right to terminate this agreement upon the conversion of the Preferred Shares. In connection with their investment in NPI, the Canadian Investors also received warrants exercisable for 383,875 shares of the Company's Common Stock at an exercise price of \$10.50 per share and are also eligible to receive additional warrants in the future upon attainment of certain additional funding.

During December 1997 and October 1998, the Canadian Investors converted their Preferred Shares to Neurocrine 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 NPI net losses in accordance with the equity method of accounting.

The Preferred Shares are redeemable for approximately \$9.5 million in cash at the Company's option. The redemption feature of the Preferred Shares limits their value to the balance of cash and cash equivalents maintained by NPI. Consequently, the Company reduced the value of its NPI investment by \$3.8 million during 1998. Equity in NPI losses was \$3.4 million and \$1.1 million in 1998 and 1997, respectively. The balance of the Company's investment in NPI was \$1.4 million and \$3.3 million at December 31, 1998 and 1997, 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. During 1998, the Company recognized \$3.6 million in revenues associated with costs of research on the Neurogenomics and DHEA programs.

### 11. INCOME TAXES

At December 31, 1998, the Company had federal and California income tax net operating loss carryforwards of approximately \$9.3 million and \$8.3 million, respectively. The federal and California tax loss carryforwards will begin to expire in 2009 and 2003, respectively, unless previously utilized. The Company also has federal and California research tax credit carryforwards of approximately \$1.6 million and \$271,000, respectively, which will begin to expire in 2007 and 2012, respectively, unless previously utilized. The Company has federal Alternative Minimum Tax credit carryforwards of approximately \$257,000, which will carryforward indefinitely.

Pursuant to Internal Revenue Code Sections 382 and 383, annual use of the Company's net operating loss and credit carryforwards 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 change will have a material impact upon the utilization of these carryforwards.

Significant components of the Company's deferred tax assets as of December 31, 1998 and 1997 are shown below. A valuation allowance of \$6,470,000 and \$3,474,000 at December 31, 1998 and 1997, 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:

	=======	======
Net deferred tax assets	\$	\$
Total deferred tax assets Valuation allowance	,	3,474 (3,474)
Net operating loss carryforwards  Tax credit carryforwards  Capitalized research and development  Other, net	2,069 453	\$ 993 1,176 525 780
Deferred tax assets:	1998	1997 
	1000	1007

The provision for income taxes on earnings subject to income taxes differs from the statutory federal rate at December 31, 1998, 1997 and 1996, due to the following:

		=======	=======	=======
		\$ 1	\$ 214	\$ 248
ΑI	ternative minimum taxes		127 	248
	crease in valuation allowance and other	2,572	(1,837)	(2,098)
Та	x effect on non-deductible expenses	4,213	21	17
St	ate income tax, net of federal benefit	1	87	
Fe	deral income taxes at 34%	\$(6,785)	\$ 1,816	\$2,081
		1998	1997	1996

The provision for taxes based on income at December 31, 1998, 1997 and 1996 consist of the following:

	1998	1997	1996
Current:			
Federal	\$	\$127	\$248
State	1	87	
Deferred:			
Federal			
State			
Total	\$ 1	\$214	\$248
	=====	======	=====

## 12. 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):

	1998	1997	1996
Numerator:			
Net income (loss)	\$(19,955)	\$5,127	\$5,874
Effect of dilutive securities			
Numerator for earnings (loss) per share	\$(19,955)	\$5,127	\$5,874
	=======	=======	=======
Denominator:			
Denominator for basic earnings (loss) per share	18,141	16,930	14,971
Effect of dilutive securities:			
Employee stock options	Antidilutive	909	796
Convertible preferred stock	Antidilutive	204	183
Warrants	Antidilutive	141	177

Year Ended December 31,

Dilutive potential of common shares	-	1,254	1,156
Denominator for diluted earnings (loss) per share .	18,141	18,184	16,127
	======	======	=======
Basic earnings (loss) per share Diluted earnings (loss) per share	\$ (1.10)	\$ 0.30	\$ 0.39
	\$ (1.10)	\$ 0.28	\$ 0.36

### 13. SUBSEQUENT EVENT

On March 2, 1999, the Company entered into a collaboration agreement with Wyeth-Ayerst Laboratories, 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. The agreement, valued up to \$78 million, provided that marketable products for these disorders result from the collaboration, includes sharing proprietary technologies between the two companies; funding for research and milestone achievements and potential royalties on world-wide sales of products resulting from the collaboration. The Company expects to receive three to five years of funding for research and development activities, in addition to access to Wyeth's chemical libraries for screening within the collaborative field.

## COLLABORATION AND LICENSE AGREEMENT

## DATED JANUARY 1, 1999

## BETWEEN

AMERICAN HOME PRODUCTS CORPORATION acting through its WYETH-AYERST LABORATORIES DIVISION

AND

NEUROCRINE BIOSCIENCES, INC.

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#### COLLABORATION AND LICENSE AGREEMENT

THIS COLLABORATION AND LICENSE AGREEMENT (the "Agreement"), dated as of January 1, 1999, is made by and between Neurocrine Biosciences, Inc., a Delaware corporation with its principal place of business at 10555 Science Park Road, San Diego, California 92121-1102 ("Neurocrine") and American Home Products Corporation, acting through its Wyeth-Ayerst Laboratories Division, a Delaware corporation, with a place of business at 555 East Lancaster Avenue St. Davids Pennsylvania 19087 ("Wyeth-Ayerst").

WHEREAS, Wyeth-Ayerst is engaged in the research, development and commercialization of human pharmaceutical products;

WHEREAS, Neurocrine is the owner or licensee of certain patent rights relating to [\*\*\*] which may be useful in the discovery and development of human pharmaceutical products;

WHEREAS, Wyeth-Ayerst and Neurocrine have agreed to collaborate, on the terms and conditions set forth herein, in the research, development and commercialization of compounds [\*\*\*] (each as defined below);

NOW, THEREFORE, in consideration of the mutual representations, warranties and covenants contained herein and other good and valuable consideration, the Parties agree as follows:

## ARTICLE ONE DEFINITIONS

When used in this Agreement, each of the following capitalized terms shall have the meanings set forth in this Article One. Any terms defined elsewhere in this Agreement shall be given equal weight and importance as though set forth in this Article One.

- "Acquisition" shall mean with respect to Neurocrine, the acquisition, directly or indirectly, by any Third Party of (i) securities authorized to cast fifty percent (50%) or more of the votes in any election of directors and/or (ii) the sale or other transfer of all or substantially all of its assets. Notwithstanding the foregoing, the sale or other transfer of substantially all of the assets of Neurocrine to another direct or indirect wholly-owned subsidiary of Neurocrine shall not constitute an Acquisition.
- "Affiliate" shall mean a Person that, directly or indirectly, through one or more intermediates, controls, is controlled by, or is under common control with the Person specified. For the purposes of this definition, control shall mean the direct or indirect ownership of, (a) in the case of corporate entities, securities authorized to cast more than fifty percent (50%) of the votes in any election for directors or (b) in the case of non-corporate entities, more than fifty percent (50%) ownership interest with the power to direct the management and policies of such non-corporate entity. Notwithstanding the foregoing, the term "Affiliate" shall not include subsidiaries in which a Party or its Affiliates owns a majority of the ordinary voting power to elect a majority of the board of directors, but is restricted from electing such majority by contract or otherwise, until such time as such restrictions are no longer in effect.
- "Collaboration Products" shall mean products containing one or more Lead Compounds as an active ingredient(s), provided, however, that if (i) none of the Compounds contained in a product are encompassed within the Collaboration Technology and (ii) such product is not developed by Wyeth-Ayerst, its Affiliates or sublicensees for any indication in which the [\*\*\*] and (iii) identification, development and commercialization of such product does not utilize Collaboration Technology, then such product shall not be a Collaboration Product for purposes of this Agreement. For the purposes of License Fees under Article Eight below and Royalty payments under Article Nine below, all formulations (e.g., tablets, gel caps, topical formulations, parenteral formulations, sustained release formulations, etc.) of a Collaboration Product will be considered to be the same Collaboration Product, regardless of the indications for which such Collaboration Product may be used.
- 1.4 "Collaboration Technology" shall mean all Technology encompassed by the Neurocrine Technology, Wyeth-Ayerst Technology and Joint Technology.
- "Combination Product" shall mean a product that contains, as active ingredients one or more Lead Compounds (or Collaboration Products) and one or more other Compounds that are not Lead Compounds (or Collaboration Products).
- "Commercially Reasonable Efforts" shall mean efforts and resources commonly used by a Party (which efforts will be no less than those used by such Party in the research and development of its products, as described below, in the one year period preceding the Effective Date) for a product owned by it or to which it has rights, which product is at a similar stage in its development or product life and is of similar market potential taking into account efficacy, safety, Regulatory Authority approved labeling, the competitiveness of alternative products in the marketplace, the patent and other proprietary position of the product, the likelihood of Regulatory Approval given the

regulatory structure involved, the profitability of the product including the royalties payable to licensors of patent rights, alternative products and other relevant factors. Commercially Reasonable Efforts shall be determined on a market-by-market basis for a particular product, and it is anticipated that the level of effort will change over time, reflecting changes in the status of the Collaboration Product and the market involved.

- "Competition" shall exist during a given calendar quarter with respect to a Collaboration Product in a county if, during such calendar quarter, one or more Competitive Products shall be commercially available in such country and shall have in the aggregate a [\*\*\*] or greater share of the total market (based on data provided by IMS International, or if such data are not available, based on such other data mutually agreed to by Wyeth-Ayerst and Neurocrine) in that country as measured by unit sales. For purposes of this agreement, the "total market" in a country shall be the sum of (x) the number of units of the affected Collaboration Product sold during such calendar quarter in such country by Wyeth-Ayerst, its Affiliates and sublicensees and (y) the number of units of Competitive Products sold in such country during such calendar quarter.
- "Competitive Products" shall mean and include products (other than Collaboration Products developed and commercialized by Wyeth-Ayerst pursuant to this Agreement) that contain principally the same active chemical entity(ies) as a Collaboration Product and which (a) act through the same mechanism as a Collaboration Product and (b) can reasonably be or are reasonably used for the same indication as a Collaboration Product. Without limitation of the foregoing, compounds that are of the same general formulation type (i.e., oral vs. parenteral vs. topical) as a Collaboration Product would generally be considered Competitive Products while compounds of a different general formulation type from a Collaboration Product would generally not be considered Competitive Products unless the compound and Collaboration Product are reasonably used (other than de minimis usage) for the treatment of the same indication.
- 1.9 "Compound" shall mean a chemical compound or substance together with all complexes, mixtures and other combinations, prodrugs, metabolites, enantiomers, salt forms, racemates, and isomers thereof.
- 1.10 "Confidential Information" shall mean with respect to each Party, non-public proprietary data or information which belong in whole or in part to such Party and/or information designated as Confidential Information of such Party hereunder.
- 1.11 "Controls" or "Controlled" shall mean with respect to Technology, the possession of the ability to grant licenses or sublicenses without violating the terms of any agreement or other arrangement with, or the rights of, any Third Party.
- 1.12 "Default" shall mean with respect to a Party that (i) any representation or warranty of such Party set forth herein shall have been untrue in any material respect when made or (ii) such Party shall have failed to perform any material obligation set forth in this Agreement.
- 1.13 [\*\*\*] shall be as defined in Exhibit A.
- 1.14 "Effective Date" shall mean January 1, 1999.
- 1.15 "European Union" shall mean, from time to time, those countries that are members of the European Union.
- 1.16 "FDA" shall mean the Federal Food and Drug Administration of the United States Department of Health and Human Services or any successor agency thereof.
- 1.17 "Field of Use" shall mean all therapeutic, prophylactic and diagnostic uses.
- "FTE" shall mean full time equivalent scientific person year consisting of a minimum of a total [\*\*\*] per year of scientific work on or directly related to the Research Program. Work on or directly related to the Research Program can include, but is not limited to, experimental laboratory work, recording and writing up results, reviewing literature and references, holding scientific discussions, managing and leading scientific staff, carrying out management duties related to the Research Program, and to the extent specifically approved by Wyeth-Ayerst, writing up results for publications or presentation and attending or presenting appropriate seminars and symposia.
- 1.19 "First Commercial Sale" shall mean with respect to any Collaboration Product approved for commercial sale, the first transfer by Wyeth-Ayerst, its Affiliates and/or its sublicensees of the Collaboration Product to a non-Affiliate Third Party in exchange for cash or some equivalent to which value can be assigned.
- "Force Majeure" shall mean any occurrence beyond the reasonable control of a Party that prevents or substantially interferes with the performance by the Party of any of its obligations hereunder, if such occurs by reason of any act of God, flood, fire, explosion, earthquake, strike, lockout, labor dispute, casualty or accident; or war, revolution, civil commotion, acts of public enemies, blockage or embargo; or any injunction, law, order, proclamation, regulation, ordinance, demand or requirement of any government or of any subdivision, authority or representative of any such government; or

breakdown of plant, inability to procure or use materials, labor, equipment, transportation, or energy sufficient to meet manufacturing needs without the necessity of allocation; or any other cause whatsoever, whether similar or dissimilar to those above enumerated, beyond the reasonable control of such Party, if and only if the Party affected shall have used reasonable efforts to avoid such occurrence and to remedy it promptly if it shall have occurred.

- "Hit(s)" shall mean Compounds derived from the Neurocrine Proprietary Chemical Library, the Wyeth-Ayerst Proprietary Chemical Library or any other library selected by the Parties, which are screened in the conduct of the Research Program and test positive in screening assays [\*\*\*]. For the purposes of this definition, the Steering Committee will determine what shall constitute a positive test with respect to any screening assays selected for the Research Program and it is anticipated that, depending on results obtained in the course of the Research Program, what constitutes a positive test may change from time to time.
- "Interim Clinical Evaluation Point" or "ICE" shall mean, with respect to any Collaboration Product, the development milestone indicating [\*\*\*], as decided by Wyeth-Ayerst's Development Operating Committee. [\*\*\*]. In addition, [\*\*\*]. Notwithstanding the foregoing, in the event Wyeth-Ayerst shall make the decision [\*\*\*], ICE shall be deemed to have been met.
- 1.23 "IND" shall mean an Investigational New Drug Application covering a Collaboration Product filed with the FDA pursuant to 21 CFR 312.20 or an equivalent foreign filing required for the clinical testing of a pharmaceutical product.
- "Joint Confidential Information" shall mean Confidential Information owned jointly by Wyeth-Ayerst and Neurocrine or otherwise designated as Joint Confidential Information hereunder.
- 1.25 "Joint Inventions" shall be as defined in Section 13.1 hereof.
- 1.26 "Joint Technology" shall mean Technology, which is discovered or invented jointly by Neurocrine personnel and Wyeth-Ayerst personnel during the term of this Agreement.
- "Lead Compound(s)" shall mean those Compounds (i) [\*\*\*], (ii) that meet the criteria set forth on Exhibit B hereto and (iii) that are selected by the Steering Committee or Wyeth-Ayerst in accordance with Article Six, provided, however, that Lead Compounds shall specifically exclude any Compounds [\*\*\*]. Notwithstanding the foregoing, for purposes of calculating Net Sales and determining License Fees and Royalty payments under this Agreement, a Lead Compound together with all complexes, mixtures and other combinations, prodrugs, metabolites, enantiomers, salt forms, racemates, isomers, and derivatives thereof, shall be considered to be a single Lead Compound.
- 1.28 "License Fees" shall mean the payments to be made by Wyeth-Ayerst to Neurocrine upon occurrence of certain events as set forth in Article Eight.
- 1.29 "Major European Country" shall mean France, Germany, Italy or the United Kingdom.
- 1.30 "NDA" shall mean a New Drug Application (or Biologics License Application, if applicable) covering a Collaboration Product filed with the FDA pursuant to 21 CFR 314 or an equivalent foreign filing required for marketing approval of a pharmaceutical product.
- 1.31 "Net Sales" shall mean, with respect to a Collaboration Product, all proceeds actually received from the sale or other disposition of a Collaboration Product by Wyeth-Ayerst, its Affiliates or sublicensees to unrelated Third Parties, less the reasonable and customary deductions from such gross amounts actually paid by or charged to the account of Wyeth-Ayerst, including, without limitation,
  - (a) trade, cash and quantity discounts actually allowed and taken directly with respect to such sales;
  - (b) amounts repaid, credits or allowances actually granted for damaged goods, defects, recalls, returns or rejections of Collaboration Product and retroactive price reductions;
  - (c) sales or similar taxes actually paid by or charged to the account of Wyeth-Ayerst, its Affiliates or sublicensees without offset (including, without limitation, duties or other governmental charges levied on, absorbed or otherwise imposed on the sale of Collaboration Product, value added taxes or other governmental charges otherwise measured by the billing amount, when included in billing, but not including national, state or local taxes based on income);
  - (d) charge back payments and rebates granted to (i) managed health care organizations, (ii) federal, state and/or local governments or their agencies, (iii) purchasers and reimbursers, or (iv) trade customers, including, without limitation, wholesalers and chain and pharmacy buying groups; and

(e) freight, postage, shipping, customs duties and insurance charges to the extent included in the proceeds actually received from the customer.

For the purposes of determining Net Sales hereunder, a sublicensee shall include a Third Party who, pursuant to an agreement with Wyeth-Ayerst, distributes Collaboration Products, provided, such Third Party also, as required by such agreement, conducts promotion and/or marketing activities in the applicable territory. Net Sales shall be determined in accordance with United States generally accepted accounting principles consistently applied. A "sale" shall also include the transfer or other disposition of a Collaboration Product for consideration other than cash, in which case such consideration will be valued at the fair market value thereof. In the event that a Collaboration Product is sold either for consideration other than cash or as part of a bundled product, the Net Sales of such Collaboration Product when sold (other than as part of a bundle) in cash transactions in such country. In the event that, on a country-by-country basis, a Collaboration Product is sold in the form of a Combination Product, the Net Sales for such Combination Product will be calculated as follows:

- (i) If Wyeth-Ayerst, its Affiliates and/or sublicensees separately sells, in such country, (x) Collaboration Products containing as their sole active ingredient(s) the same Lead Compound(s) as are contained in such Combination Product and (y) other products containing as their sole active ingredient(s) the other active component or components in such Combination Product, the Net Sales attributable to such Combination Product shall be calculated by multiplying actual Net Sales of the Combination Product by the [\*\*\*], which Collaboration Product contains, as the sole active ingredient(s), the same Lead Compound(s) as are in such Combination Product and [\*\*\*], which product(s) contain, as their sole active ingredient(s) any other active component or components in the Combination Product.
- (ii) If Wyeth-Ayerst, its Affiliates and/or sublicensees separately sells, in such country, Collaboration Products containing as their sole active ingredient(s) the same Lead Compound(s) as are contained in such Combination Product but do not separately sell, in such country, other products containing as their sole active ingredient(s) the other active component or components in such Combination Product, the Net Sales attributable to such Combination Product shall be calculated by multiplying the Net Sales of such Combination Product by the [\*\*\*], which Collaboration Product contains, as the sole active ingredient(s), the same Lead Compound(s) as are in such Combination Product, [\*\*\*].
- [\*\*\*].

  (iii) If Wyeth-Ayerst, its Affiliates and/or sublicensees do not separately sell, in such country, Collaboration Products containing as their sole active ingredient(s) the same Lead Compound(s) as are contained in such Combination Product, the Net Sales attributable to such Combination Product shall be calculated by multiplying the Net Sales of such Combination Product by the [\*\*\*].

Notwithstanding the foregoing, Net Sales shall not include any consideration received by Wyeth-Ayerst, its Affiliates or sublicensees in respect of the sale, use or other disposition of a Collaboration Product in a country as part of a clinical trial prior to the receipt of all Regulatory Approvals required to commence full commercial sales of such Collaboration Product in such country.

- 1.32 "Neurocrine Ancillary Transporters" shall mean [\*\*\*] as defined on Exhibit A.
- "Neurocrine Compound" shall mean any Compound, which is (a) within the Neurocrine Proprietary Chemical Library, and (b) is screened under the Research Program for activity against the Neurocrine Transporters together with all complexes, mixtures and other combinations, prodrugs, metabolites, enantiomers, salt forms, racemates, and isomers thereof.
- 1.34 "Neurocrine Confidential Information" shall mean Confidential Information owned by Neurocrine or otherwise designated as Neurocrine Confidential Information hereunder but shall not include Joint Confidential Information.
- 1.35 "Neurocrine Invention" shall have the meaning set forth in Section 13.1 hereof.
- "Neurocrine Materials" shall mean Neurocrine proprietary research materials including, but not limited to, Neurocrine Compounds, the Neurocrine Proprietary Chemical Library, assays, physical databases of chemical structures of Compounds in the Neurocrine Proprietary Chemical Library, reagents and materials derived therefrom. Neurocrine Materials will not include Research Program Materials. Neurocrine will own Neurocrine Materials supplied by Neurocrine to Wyeth-Ayerst hereunder.
- 1.37 "Neurocrine Proprietary Chemical Library" shall mean those Compounds

that Neurocrine, as of the Effective Date owns or Controls, or that come into Neurocrine's Control during the term of the Research Program.

- 1.38 "Neurocrine Researcher" shall mean professional researchers and scientists employed by Neurocrine and having at least a Bachelors Degree in science and other academic and/or professional credentials demonstrating reasonably appropriate expertise for the task to be performed by such Neurocrine Researcher in carrying out the Research Plan.
- 1.39 "Neurocrine Technology" shall mean the Neurocrine Compound Technology, Neurocrine Ancillary Transporter Technology and the Neurocrine Transporter Technology, each as defined below.
  - (a) "Neurocrine Compound Technology" shall mean all Technology (other than Joint Technology) owned or Controlled by Neurocrine on the Effective Date and/or during the term of this Agreement, which (i) claims or describes Lead Compounds and/or Collaboration Products and/or (ii) is developed, discovered or invented by Neurocrine in the conduct of the Research Program and/or (iii) is necessary or useful to develop, make, use or sell Lead Compounds and/or Collaboration Products.
  - (b) "Neurocrine Ancillary Transporter Technology" shall mean all Technology (other than Joint Technology) owned or Controlled by Neurocrine on the Effective Date or during the term of the Research Program that claims, describes or relates to the use of the Neurocrine Ancillary Transporters.
  - (c) "Neurocrine Transporter Technology" shall mean all Technology (other than Joint Technology) owned or Controlled by Neurocrine on the Effective Date or during the term of the Research Program that claims, describes or relates to the use of the Neurocrine Transporters. Neurocrine Transporter Technology will specifically include, without limitation, the Patent Rights set forth on Exhibit C hereto.
- 1.40 "Neurocrine Transporters" shall mean [\*\*\*] as defined on Exhibit A.
- "OHSU Agreement" shall mean the Amended and Restated License Agreement dated January 1, 1999 by and between Oregon Health Sciences University ("OHSU") and Neurocrine (a complete copy of which has been provided to and approved by Wyeth-Ayerst prior to the date this Agreement was signed by the Parties and which is attached hereto as Exhibit D), as such agreement may be amended from time to time (subject to the consent of Wyeth-Ayerst to the extent required under the Agreement dated January 1, 1999 by and among OHSU, Wyeth-Ayerst and Neurocrine.)
- 1.42 "Party" shall mean Wyeth-Ayerst or Neurocrine, as the case may be, and "Parties" shall mean Wyeth-Ayerst and Neurocrine.
- "Patent Rights" shall mean the rights and interests in and to all issued patents and pending patent applications in any country, including, without limitation, all provisional applications, substitutions, continuations, continuations-in-part, divisions, and renewals, all letters patent granted thereon, and all patents-of-addition, reissues, reexaminations and extensions or restorations by existing or future extension or restoration mechanisms, including, without limitation Supplementary Protection Certificates or the equivalent thereof.
- "Person" shall mean any individual, firm, corporation, partnership, limited liability company, trust, unincorporated organization or other entity or a government agency or political subdivision thereto, and shall include any successor (by merger or otherwise) of such Person.
- 1.45 "Pivotal Trial" shall mean clinical trial which, if the pre-defined endpoints are met, is intended to be submitted as part of an application for marketing approval as statistically significant data in support of the product's safety and efficacy for the intended indication.
- 1.46 "Prior Agreement" shall mean the agreement dated August 15, 1996 by and between Northwest NeuroLogic, Inc. and Wyeth-Ayerst, as amended.
- "Proof of Concept" shall mean, with respect to either of the Neurocrine Transporters, the successful achievement of both the in vitro Proof of Concept and the in vivo Proof of Concept criteria for such Neurocrine Transporter, as set forth in Exhibit B.
- "Regulatory Approval" shall mean the technical, medical and scientific licenses, registrations, authorizations and approvals (including, without limitation, approvals of NDAs, supplements and amendments, preand post-approvals, pricing and third party reimbursement approvals, and labeling approvals) of any national, supra-national, regional, state or local regulatory agency, department, bureau, commission, council or other governmental entity, necessary for the development, manufacture, distribution, marketing, promotion, offer for sale, use, import, export or sale of Lead Compounds or Collaboration Product(s) in a regulatory jurisdiction.
- "Regulatory Authority" shall mean any national (e.g., the FDA), supra-national (e.g., the European Commission, the Council of the European Union, or the European Agency for the Evaluation of Medicinal

Products), regional, state or local regulatory agency, department, bureau, commission, council or other governmental entity in each country of the Territory involved in the granting of Regulatory Approval for a Lead Compound or a Collaboration Product.

- 1.50 "Regulatory Filings" shall mean, collectively, INDs, Biologics License Applications, Drug Master Files, NDAs and/or any other comparable filings as may be required by Regulatory Authorities to obtain Regulatory Approvals.
- 1.51 "Research Plan" will be as defined in Section 5.3 below.
- 1.52 "Research Program" shall mean the collaborative research program conducted by Neurocrine and Wyeth-Ayerst and funded, in part, by Wyeth-Ayerst in accordance with the provisions of Article Five below.
- 1.53 "Research Program Funding" will be as defined in Section 5.5 below.
- "Research Program Materials" shall mean and include clones, cell lines, Compounds, assays, databases, electronic and physical databases of chemical structures which, in each case, are developed by Neurocrine and/or Wyeth-Ayerst during the course of conduct of the Research Program. Research Program Materials also will include the Neurocrine Transporters and Neurocrine Ancillary Transporters and clones, cell lines and other materials encompassing, expressing, and/or containing the Neurocrine Transporters and/or Neurocrine Ancillary Transporters.
- 1.55 "Royalties" shall mean those royalties payable by Wyeth-Ayerst to Neurocrine pursuant to Article Nine of this Agreement.
- 1.56 "Steering Committee" shall have the meaning set forth in Section 4.1 hereof.
- 1.57 "Technology" shall mean proprietary data, information and all intellectual property, including but not limited to, trade secrets, know-how, inventions and technology, whether patentable or not, and Patent Rights directed to products, processes, formulations and/or methods.
- 1.58 "Third Party(ies)" shall mean any Person other than Neurocrine, Wyeth-Ayerst and their respective Affiliates.
- "Third Party Royalties" shall mean royalties payable by Neurocrine, Wyeth-Ayerst, its Affiliates or sublicensees to a non-Affiliate Third Party (or multiple non-Affiliate Third Parties) to make, have made, use, sell, offer for sale or import Collaboration Products where the royalty payable to such non-Affiliate Third Party is based on Patent Rights owned or Controlled by such Third Party.
- 1.60 "Unpatented Product" shall mean a Collaboration Product the making, using or sale of which is not claimed or described in at least one Valid Claim included in the Collaboration Technology.
- "Valid Claim" shall mean a claim of an issued and unexpired patent or a claim of a pending patent application which has not been held invalid or unenforceable by a court or other government agency of competent jurisdiction from which no appeal can be or has been taken and has not been admitted to be invalid or unenforceable through re-examination or disclaimer or otherwise, provided, however, that if a claim of a pending patent application shall not have issued within [\*\*\*] after the filing date from which such claim takes priority such claim shall not constitute a Valid Claim for the purposes of this Agreement.
- "Wyeth-Ayerst Compound" shall mean any Compound (a) which is within the Wyeth-Ayerst Proprietary Chemical Library and (b) which is screened under the Research Program or by Wyeth-Ayerst under this Agreement for activity against a Neurocrine Transporter together with all complexes, mixtures and other combinations, prodrugs, metabolites, enantiomers, salt forms, racemates, and isomers thereof.
- 1.63 "Wyeth-Ayerst Confidential Information" shall mean Confidential Information owned by Wyeth-Ayerst or otherwise designated as Wyeth-Ayerst Confidential Information hereunder but shall not include Joint Confidential Information.
- 1.64 "Wyeth-Ayerst Invention" shall have the meaning set forth in Section
  13.1 hereof.
- "Wyeth-Ayerst Materials" shall mean Wyeth-Ayerst proprietary research materials including, but not limited to, Wyeth-Ayerst Compounds, the Wyeth-Ayerst Proprietary Chemical Library, assays, physical databases of chemical structures of Compounds in the Wyeth-Ayerst Proprietary Chemical Library, reagents and materials derived therefrom. Wyeth-Ayerst Materials will not include Research Program Materials. Wyeth-Ayerst will own Wyeth-Ayerst Materials provided to Neurocrine hereunder.
- "Wyeth-Ayerst Proprietary Chemical Library" shall mean those Compounds that Wyeth-Ayerst, as of the Effective Date, owns or Controls, or that come into Wyeth-Ayerst's Control during the term of this Agreement, and any other Compounds not Controlled by Wyeth-Ayerst, but which Wyeth-Ayerst has the right to develop and commercialize, including, without limitation, the right to screen such Compounds for activity against the Neurocrine Transporters without violating the terms of any agreement between Wyeth-Ayerst and a Third Party.
- 1.67 "Wyeth-Ayerst Technology" shall mean all Technology (other than Joint Technology) owned or Controlled by Wyeth-Ayerst on the Effective Date and/or during the term of this Agreement (a) which relates specifically

to, claims or describes Lead Compounds and/or Collaboration Products and/or (b) is developed, discovered or invented by Wyeth-Ayerst in the conduct of the Research Program, (c) is developed, discovered or invented by Wyeth-Ayerst personnel directly resulting from the use of Neurocrine Technology or Joint Technology and/or (d) is necessary or useful to make, use or sell Lead Compounds and/or Collaboration Products.

## ARTICLE TWO REPRESENTATIONS AND WARRANTIES

- 2.1 Mutual Representations and Warranties. Each Party hereby represents, warrants and covenants to the other Party that:
  - the execution, delivery to the other Party and performance by it of this Agreement and its compliance with the terms and provisions of this Agreement does not and will not conflict, in any material respect, with or result in a breach of any of the terms or provisions of (x) any other contractual obligations of such Party, (y) the provisions of its charter, operating documents or bylaws, or (z) any order, writ, injunction or decree of any court or governmental authority entered against it or by which it or any of its property is bound except where such breach or conflict would not materially impact the Party's ability to meet its obligations hereunder, and (ii) it has not granted to any Third Party any right which would conflict in any material respect with the rights granted by it to the other Party hereunder;
  - (b) this Agreement is a legal and valid obligation binding upon such Party and enforceable in accordance with its terms except as (i) enforceability may be limited by bankruptcy, insolvency, reorganization, moratorium or similar laws affecting the enforcement of creditors' rights and (ii) equitable principles of general applicability;
  - (c) such Party is a corporation duly organized, validly existing and in good standing under the laws of the state or other jurisdiction of incorporation or formation and has full corporate power and authority to enter into this Agreement and to carry out the provisions hereof except where failure to be in good standing would not materially impact the Party's ability to meet its obligations hereunder;
  - (d) such Party is duly authorized, by all requisite corporate action, to execute and deliver this Agreement and the execution, delivery and performance of this Agreement by such Party does not require any shareholder action or approval, and the Person executing this Agreement on behalf of such Party is duly authorized to so by all requisite corporate action; and
  - (e) no consent, approval, order or authorization of, or registration, qualification, designation, declaration or filing with, any federal, state or local governmental authority is required on the part of such Party in connection with the valid execution, delivery and performance of this Agreement, except for any filings under any applicable securities laws and except where the failure to obtain any of the foregoing would not have a material adverse impact on the ability of such Party to meets its obligations hereunder.
- 2.2 Additional Neurocrine Representations, Warranties and Covenants.
  Neurocrine represents, warrants and covenants to Wyeth-Ayerst that:
  - (a) it has the full right, power and authority to grant the licenses granted to Wyeth-Ayerst under Article Three hereof;
  - (b) all Patent Rights included within the Neurocrine Transporter Technology and/or the Neurocrine Ancillary Transporter Technology which are existing as of the Effective Date are listed on Exhibit C attached hereto and, as of the Effective Date, the Patent Rights included within the Neurocrine Technology are existing and, to its knowledge, are not invalid or unenforceable, in whole or in part;
  - (c) except as disclosed to Wyeth-Ayerst in writing and except for the nonexclusive licenses granted to Neurocrine pursuant to Article Three of the OHSU Agreement or retained by OHSU, Howard Hughes Medical Institute and the United States Government pursuant to Article Five of the OHSU License Agreement, to its knowledge (i) it is the sole and exclusive owner or the exclusive licensee of the Neurocrine Technology, including, without limitation, all Patent Rights included therein, and (ii) no Person (except OHSU, the Howard Hughes Medical Institute and the United States Government with respect to those Patent Rights licensed to Neurocrine under the OHSU Agreement), has any right, title or interest in or to the Neurocrine Technology;
  - (d) except as disclosed to Wyeth-Ayerst in writing, to its knowledge (i) all inventors (who are known as of the date this Agreement is signed by each of the Parties) of any inventions included within the Neurocrine Technology have assigned their entire right, title and interest in and to such inventions and the corresponding Patent Rights to Neurocrine or, in the case of inventions and Patent Rights licensed by Oregon Health Sciences University to Neurocrine, to Oregon Health Sciences

University, and (ii) no Person, other than those Persons named as inventors on any patent or patent application included within the Neurocrine Technology, is an inventor of the invention(s) claimed in such patent or patent application;

- (e) except as disclosed to Wyeth-Ayerst in writing, to Neurocrine's knowledge, OHSU has (i) complied with all of its obligations under applicable United States Government laws and regulations with respect to any inventions included within the Neurocrine Technology which inventions are subject inventions of a funding agreement between OHSU and the United States Government or any agency thereof and (ii) elected to retain title to any such invention as provided in 37 CFR Part 401;
- (f) as of the date this Agreement is signed by each of the Parties, there are no claims, judgments or settlements against or owed by Neurocrine or, to its knowledge, pending or threatened claims or litigation relating to the Neurocrine Technology and during the term of this Agreement Neurocrine shall promptly notify Wyeth-Ayerst in writing, upon learning of any such actual or threatened claim, judgment or settlement;
- (g) during the term of this Agreement Neurocrine will use Commercially Reasonable Efforts not to diminish the rights under the Neurocrine Technology provided, however, that termination of the OHSU Agreement (i) by reason of the failure by Wyeth-Ayerst, as a sublicensee thereunder, to meet obligations set forth in Articles Nine and Ten thereof or any other obligations of a sublicensee thereunder or (ii) by reason of any default by Wyeth-Ayerst hereunder, shall not, in either instance, constitute a breach of this subparagraph (g);
- (h) except as set forth on Exhibit E, as of the date this Agreement is signed by each of the Parties, it is not aware of any patent, patent application or other intellectual property right of any Third Party which could materially adversely affect the ability of either Party to carry out its respective obligations hereunder or the ability of Wyeth-Ayerst to exercise or exploit any of the rights or licenses granted to it under this Agreement;
- (i) except as set forth on Exhibit F hereof, the terms of this Agreement do not conflict in any material respect with the terms of any other Neurocrine obligations; and
- (j) it has no knowledge of any material information, other than information provided to Wyeth-Ayerst in writing prior to the signing of this Agreement, which would negatively affect the ability of Wyeth-Ayerst to use the Neurocrine Transporters or the Neurocrine Ancillary Transporters.
- 2.3 Representation by Legal Counsel. Each Party hereto represents that it has been represented by legal counsel in connection with this Agreement and acknowledges that it has participated in the drafting hereof. In interpreting and applying the terms and provisions of this Agreement, the Parties agree that no presumption shall exist or be implied against the Party which drafted such terms and provisions.
- 2.4 Neurocrine Disclaimer. EXCEPT AS EXPRESSLY PROVIDED IN SECTIONS 2.1 AND 2.2 HEREOF, NEUROCRINE MAKES NO OTHER REPRESENTATION OR WARRANTY, EITHER EXPRESS OR IMPLIED, INCLUDING, WITHOUT LIMITATION, ANY WARRANTIES OF MERCHANTABILITY OR FITNESS FOR A PARTICULAR PURPOSE WITH RESPECT TO ANY NEUROCRINE MATERIALS, INCLUDING WITHOUT LIMITATION, THE NEUROCRINE TRANSPORTERS AND NEUROCRINE ANCILLARY TRANSPORTERS. ADDITIONALLY, NEUROCRINE MAKES NO REPRESENTATION OR WARRANTY, EITHER EXPRESS OR IMPLIED, THAT THE MANUFACTURE, USE OR SALE OF ANY LEAD COMPOUND OR COLLABORATION PRODUCT WILL NOT INFRINGE THE INTELLECTUAL PROPERTY RIGHTS OF ANY THIRD PARTY.
- Wyeth-Ayerst Disclaimer. EXCEPT AS EXPRESSLY PROVIDED IN SECTION 2.1
  HEREOF, WYETH-AYERST MAKES NO OTHER REPRESENTATION OR WARRANTY, EITHER
  EXPRESS OR IMPLIED, INCLUDING, WITHOUT LIMITATION, ANY WARRANTIES OF
  MERCHANTABILITY OR FITNESS FOR A PARTICULAR PURPOSE WITH RESPECT TO ANY
  WYETH-AYERST MATERIALS, ANY LEAD COMPOUND OR ANY COLLABORATION PRODUCT.
  ADDITIONALLY, WYETH-AYERST MAKES NO REPRESENTATION OR WARRANTY, EITHER
  EXPRESS OR IMPLIED THAT THE DISCOVERY, DEVELOPMENT, MANUFACTURE, USE OR
  SALE OF ANY LEAD COMPOUND OR COLLABORATION PRODUCT WILL NOT INFRINGE
  THE INTELLECTUAL PROPERTY RIGHTS OF ANY THIRD PARTY.

## ARTICLE THREE LICENSES

- 3.1 License Grant to Wyeth-Ayerst. Except as set forth in Section 3.3 below, Neurocrine hereby grants to Wyeth-Ayerst:
  - (a) the sole and exclusive worldwide right and license, with no right to sublicense (except (i) to Wyeth-Ayerst's Affiliates and (ii) to any sublicensee of a Lead Compound and/or Collaboration Product in so far as reasonably necessary for such sublicensee to develop such Lead Compound and/or Collaboration Product), under both the Neurocrine Technology and Neurocrine's interest in any Joint Technology, to use the Neurocrine Transporters for the identification and/or development of Lead Compounds and Collaboration Products in the Field of Use;

- (b) the sole and exclusive worldwide right and license, with the right to sublicense to Affiliates of Wyeth-Ayerst and/or one or more Third Parties, under both the Neurocrine Technology and Neurocrine's interest in any Joint Technology, to make, have made, use, import, market, offer for sale and sell Lead Compounds and Collaboration Products in the Field of Use;
- (c) during the term of the Research Program, the sole and exclusive right and license, with no right to sublicense (except to Wyeth-Ayerst's Affiliates), under both the Neurocrine Ancillary Transporter Technology and Neurocrine's interest in any Joint Technology, to use the Neurocrine Ancillary Transporters for the [\*\*\*] of Lead Compounds and Collaboration Products;
- (d) after the term of the Research Program, a non-exclusive right and license, with no right to sublicense (except to Wyeth-Ayerst's Affiliates), under the Neurocrine Ancillary Transporter Technology to use the Neurocrine Ancillary Transporters for the [\*\*\*] of Lead Compounds and Collaboration Products:
- (e) during the term of this Agreement, a nonexclusive right and license, with no right to sublicense (except (i) to Wyeth-Ayerst Affiliates and (ii) to any sublicensee of a Lead Compound and/or Collaboration Product in so far as reasonably necessary for such sublicensee to develop such Lead Compound and/or Collaboration Product), to use all data and information generated by or on behalf of Neurocrine in the conduct of the Research Program, including data relating to Hits in the Neurocrine Proprietary Chemical Library, but only as shall be reasonably necessary for Wyeth-Ayerst to conduct research to identify and develop Lead Compounds and Collaboration Products, provided, however, that such license shall become sole and exclusive when a Compound is designated a Lead Compound in accordance with Article Six and shall revert to a non-exclusive license upon determination of the Steering Committee or Wyeth-Ayerst that such Lead Compound will not become a Collaboration Product;
- (f) during the term of this Agreement, an exclusive right and license, with the right to sublicense, to use all data and information generated by or on behalf of Neurocrine in the conduct of the Research Program relating to Lead Compounds and/or Collaboration Products in the Neurocrine Proprietary Chemical Library, but only as shall be reasonably necessary for Wyeth-Ayerst to conduct research to identify and develop Lead Compounds and Collaboration Products; and
- (g) during the term of this Agreement, a non-exclusive right and license, with no right to sublicense (except (i) to Wyeth-Ayerst's Affiliates and (ii) to any sublicensee of a Lead Compound and/or Collaboration Product in so far as reasonably necessary for such sublicensee to develop such Lead Compound and/or Collaboration Product), to use the Neurocrine Materials but only to the extent that such right and license shall be necessary for Wyeth-Ayerst to identify and develop Lead Compounds and Collaboration Products.
- 3.2 License Grant to Neurocrine. Wyeth-Ayerst hereby grants to Neurocrine for the term of the Research Program (i) a non-exclusive right and license, with no right to sublicense, under the Wyeth-Ayerst Technology to the extent that such right and license shall be necessary for Neurocrine to perform its obligations under the Research Program, and (ii) a non-exclusive right and license, with no right to sublicense, to use the Wyeth-Ayerst Materials but only to the extent that such right and license shall be necessary for Neurocrine to perform its obligations under the Research Program and (iii) a nonexclusive right and license to use all data and information generated in the conduct of the Research Program, including data relating to Hits in the Wyeth-Ayerst Proprietary Chemical Library, but only as shall be reasonably necessary for Neurocrine to perform its obligations under the Research Program.
- Neurocrine Retained Rights. The exclusive licenses granted to Wyeth-Ayerst in Section 3.1 above, shall be subject to the retention by Neurocrine of a nonexclusive right and license, with no right to sublicense, in each case, to the extent necessary for Neurocrine to perform its obligations under the Research Program hereunder. Subject to the licenses granted to Wyeth-Ayerst in Section 3.1 above, nothing herein shall be deemed to restrict Neurocrine's right to otherwise exploit the Neurocrine Technology to develop products other than Lead Compounds and Collaboration Products including, without limitation, Neurocrine's right to use and sublicense the use of the Neurocrine Transporters to conduct selectivity testing with respect to products (other than Lead Compounds and Collaboration Products) being developed by Neurocrine or is corporate partners or sublicensees.
- 3.4 Prior Agreement. This Agreement supersedes the Prior Agreement and all Compounds which may have been identified under the Prior Agreement will be governed solely by the terms and conditions of this Agreement.
- 3.5 OHSU Agreement. Patent Rights licensed to Neurocrine pursuant to the OHSU Agreement (the "Sublicensed Rights") are included in the Neurocrine Technology licensed to Wyeth-Ayerst hereunder. Wyeth-Ayerst has approved the terms of the OHSU Agreement and the Parties agree that the terms of the OHSU Agreement are consistent with the terms of this Agreement and no conflict exist with respect to Neurocrine's

obligations under this Agreement and Neurocrine's obligations under the OHSU Agreement. Wyeth-Ayerst will have all of the rights set forth in that agreement to be afforded to Neurocrine's sublicensee of any technology licensed thereunder including, without limitation, in the event of a termination of the OHSU Agreement, the right under Section 4.03 thereof, to enter into a license, with respect to the Sublicensed Rights, directly with OHSU which license would be on the same terms and conditions as the OHSU Agreement. In the event that Wyeth-Ayerst enters into such a license with OHSU, (i) [\*\*\*] of any payments made by Wyeth-Ayerst to OHSU under Paragraph 6.02 thereof (including payments creditable against payments owed under Section 6.02 thereof) and (ii) [\*\*\*] of other payments thereunder shall in each case be deducted from any payments that Wyeth-Ayerst remains obligated or thereafter becomes obligated to make to Neurocrine under this Agreement. Neurocrine agrees that it will not modify or amend the OHSU Agreement, insofar as any such amendment or modification will have any impact on any of the rights or obligations of Wyeth-Ayerst under this Agreement or any agreement entered into between Wyeth-Ayerst and OHSU in accordance with this Section 3.5, without Wyeth-Ayerst's prior written consent which consent (i) may be provided or withheld by Wyeth-Ayerst in Wyeth-Ayerst's sole discretion in the case of any modification that would negatively impact any such rights or obligations of Wyeth-Ayerst, including, without limitation, any increase in payments to be made by Wyeth-Ayerst, any increase in diligence obligations, or any modification of the exclusivity of the Sublicensed Rights, or (ii) will not be unreasonably withheld by Wyeth-Ayerst in the case of any modification that would not negatively impact any such rights or obligations of Wyeth-Ayerst. Neurocrine further agrees that it will promptly provide Wyeth-Ayerst with copies of any notices it receives from or gives to OHSU pertaining to any termination or threatened termination of the OHSU Agreement.

#### ARTICLE FOUR STEERING COMMITTEE

- 4.1 Creation; Authority. Immediately following the signing of this Agreement, Wyeth-Ayerst and Neurocrine will establish a steering committee (the "Steering Committee") consisting of at least three (3) members from each of Wyeth-Ayerst and Neurocrine with Wyeth-Ayerst and Neurocrine having equal representation at all times. The Steering Committee will be responsible for monitoring and reviewing the implementation of the Research Plan by the Parties and for determining the mechanisms for exchange of information and materials between the Parties. From time to time, the Steering Committee may establish subcommittees to oversee specific projects or activities and such subcommittees shall be constituted as the Steering Committee shall determine. The Steering Committee will exist until the termination of the Research Program unless the Parties otherwise agree in writing.
- 4.2 Chairperson. The chairperson of the Steering Committee shall be designated by Wyeth-Ayerst. The chairperson will be responsible for scheduling meetings of the Steering Committee, preparing agendas for meetings, sending to all Steering Committee members notices of all regular meetings and agendas for such meetings. The chairperson shall appoint a secretary for each meeting who will record the minutes of the meeting, circulate copies of meeting minutes to the Parties and each Steering Committee member promptly following the meeting for review, comment and approval and finalize approved meeting minutes.
- 4.3 Meetings. The Steering Committee shall meet at least once each calendar quarter and may meet at additional times as the Parties shall agree. Either Party may call a special meeting of the Steering Committee two (2) times per year, on fifteen(15) days written notice to the other Party. The Party convening a special meeting shall send notices and agenda for such meetings to the other Party and to each Steering Committee member. Meetings will alternate between the offices of the Parties, unless otherwise agreed, or may be held telephonically or by video-conference. Members of the Committee shall have the right to participate in and vote at meetings by telephone and to vote at meetings by proxy. Each Party shall be responsible for expenses incurred by its employees and its members of the Steering Committee incurred in attending or otherwise participating in Steering Committee meetings.
- 4.4 Decisions of the Committee. The goal of the Parties' collaboration shall be the timely identification and development of Lead Compounds and Collaboration Products for commercialization in the Field of Use. All decisions of the Steering Committee shall be made by majority vote, with at least one (1) member from each Party voting with the majority, in the exercise of good faith to further the goal of the Collaboration. In the event that a decision cannot be reached by the Steering Committee, the matter shall be referred to further review and resolution by the Chief Executive Officer of Neurocrine and President of Wyeth-Ayerst Research as set forth in Section 14.1.

## ARTICLE FIVE COLLABORATIVE RESEARCH PROGRAM AND RESEARCH FUNDING

Research Program. Under the terms and conditions set forth herein, Wyeth-Ayerst and Neurocrine will exclusively collaborate in the conduct of a collaborative pre-clinical research program (the "Research Program") to discover, identify and develop modulators of the Neurocrine Transporters for the treatment of central nervous system disorders, [\*\*\*]. The Research Program will be focused on the screening of the Wyeth-Ayerst Proprietary Chemical Library and Neurocrine Proprietary Chemical Library and any other library selected by mutual

agreement of the Parties for the identification of Hits, a medicinal chemistry program for the development of Lead Compound candidates, screening and testing of Lead Compound candidates to identify Lead Compounds and further preclinical research and screening of Lead Compounds to select Collaboration Products for development and commercialization by Wyeth-Ayerst.

- Term. The initial term of the Research Program will be three (3) years unless earlier terminated in accordance with Article Twelve hereof. The initial term of the Research Program will begin on January 1, 1999. Upon the expiration of the initial three (3) year term, the term of the Research Program may, upon mutual written agreement of the Parties, be extended for [\*\*\*] extension terms on substantially the same terms as those set forth herein. Notwithstanding the foregoing, in the event that at the end of the initial term of the Research Program, [\*\*\*] and the Steering Committee or Wyeth-Ayerst has determined that significant additional [\*\*\*] should be conducted and the Steering Committee determines that such additional [\*\*\*] justifies extending the Research Program by an additional [\*\*\*], the Parties will extend the term of the Research Program [\*\*\*], provided, however, that in no event will Wyeth-Ayerst be obligated to fund more than [\*\*\*] Neurocrine Researcher FTEs (at a rate of [\*\*\*]) during [\*\*\*].
- 8.3 Research Plan. Within thirty (30) days following the date this Agreement is signed by each of the Parties and on an annual basis on or before October 31 of each year thereafter, the Steering Committee shall develop and approve, a research plan and budget for the collaborative Research Program (the "Research Plan"). The Research Plan will be updated on an annual basis and shall specifically include both detailed plans for the following year including staffing levels, activities and estimated expenditures as well as more general plans for the remaining term of the Research Program. The Research Plan may only be modified or amended upon the written approval of the Steering Committee. Except as expressly set forth in Section 5.5 below, each Party shall be responsible for its own costs and expenses incurred in their conduct of the Research Program.
- Conduct of the Research Program. Neurocrine and Wyeth-Ayerst shall each use Commercially Reasonable Efforts to perform its obligations under the Research Program in accordance with the Research Plan. Notwithstanding, the foregoing, during the term of the Research Program, Neurocrine shall apply an average of at least [\*\*\*] Neurocrine Researcher FTEs per year in performing its obligations under the Research Program, which minimum number of Neurocrine Researcher FTEs shall be increased to [\*\*\*] upon the successful completion of the first [\*\*\*] (according to the criteria set forth in Exhibit B, Part 2(a)) [\*\*\*] Lead Compound (as defined in Exhibit B attached hereto) and to [\*\*\*] upon the successful completion of the first [\*\*\*] (according to the criteria set forth in Exhibit B, Part 2(b)) of [\*\*\*] Lead Compound, provided, however, that neither increase shall become effective prior to the beginning of the [\*\*\*] of the Research Program. While it is anticipated that Neurocrine and Wyeth-Ayerst will each devote to the Research Program efforts consistent with the goals set forth in the Research Program more than the number of Neurocrine Researcher FTEs funded by Wyeth-Ayerst pursuant to Section 5.5 below, in and of itself, constitute a failure by Neurocrine to use Commercially Reasonable Efforts to conduct the Research Program. In addition, the Parties have agreed that the Research Plan will at all times allocate to Neurocrine sufficient responsibilities to allow Neurocrine to devote to the Research Program, the number of Neurocrine Researcher FTEs funded by Wyeth-Ayerst hereunder.
- 5.5 Funding of the Research Program.
  - Funding by Wyeth-Ayerst. During the initial term of the Research Program, Wyeth-Ayerst will provide to Neurocrine the funds in the amount of [\*\*\*] per calendar quarter, which funds are to be used by Neurocrine solely to fund the conduct of the Research Program by [\*\*\*] Neurocrine Researcher FTEs. The funding amount set forth in the preceding sentence shall be increased to [\*\*\*] per calendar quarter upon the successful completion of the first [\*\*\*] (according to the criteria set forth in Exhibit B, Part 2(a)) [\*\*\*] Lead Compound which funds are to be used by Neurocrine solely to fund the conduct of the Research Program by [\*\*\*] Neurocrine Researcher FTEs and to [\*\*\*] per calendar quarter upon the successful completion of the [\*\*\*] (according to the criteria set forth in Exhibit B, Part 2(b)) of [\*\*\*] Lead Compound [\*\*\*] which funds are to be used by Neurocrine solely to fund the conduct of the Research Program by [\*\*\*] Neurocrine Researcher FTEs, provided, however, that (i) neither increase shall become effective prior to [\*\*\*] of the Research Program and (ii) subject to clause (i) above, each such increase shall become effective on the first day of the calendar quarter following the calendar quarter in which the event resulting in such increase occurs. Wyeth-Ayerst will provide the funding set forth in this Section 5.5(a) to Neurocrine [\*\*\*] during the term of the Research Program, provided however, that the first payment will be due on [\*\*\*] business day following the date the Parties shall have both signed this Agreement.
  - (b) Reporting and Reconciliation. Within thirty (30) days after the end of each calendar quarter during the term of the Research Program, Neurocrine will provide to Wyeth-Ayerst a report setting forth the number of Neurocrine Researcher FTEs devoted to the Research Program in such calendar quarter along with their names and titles. In the event that Neurocrine

shall, in any calendar quarter, devote to the conduct of the Research Program fewer than the number of Neurocrine Researcher FTEs funded by Wyeth-Ayerst for the such calendar quarter as required under Section 5.4 hereof, Neurocrine shall in good faith endeavor to devote, at its own expense, additional Neurocrine Researcher FTEs to the conduct of the Research Program in subsequent calendar quarters to make up for the shortfall. If, despite Neurocrine's good faith efforts to make up any shortfall in number of Neurocrine Researcher FTEs devoted to the Research Program versus the funded number of Neurocrine Researcher FTEs set forth in Section 5.5, it is determined at the end of the term of the Research Program, utilized less than the number of Neurocrine Researcher FTEs funded by Wyeth-Ayerst hereunder, Neurocrine shall within thirty (30) days after such determination refund to Wyeth-Ayerst the excess Research Program funding provided to Neurocrine under Section 5.5(a) above, which refund shall be equal to [\*\*\*] multiplied by the difference between (x) the number (in the aggregate) of Neurocrine Researcher FTEs that were funded by Wyeth-Ayerst [\*\*\*] Research Program. For example, if the number of Neurocrine Researcher FTEs funded by Wyeth-Ayerst [\*\*\*] Research Program. For example, if the number of Neurocrine Researcher FTEs funded by Wyeth-Ayerst [\*\*\*] of the Research Program was [\*\*\*] and Neurocrine, in fact, only utilized [\*\*\*] Neurocrine Researcher FTES [\*\*\*] of the Research Program, Neurocrine Researcher FTES [\*\*\*] of the Research Program, Neurocrine Researcher

- Records and Audits. During the term of the Research Program and for a period of three (3) years thereafter, Neurocrine (c) shall keep and maintain accurate and complete records showing the time devoted and activities performed by each Neurocrine Researcher in performing Neurocrine's obligations under the Research Program in sufficient detail such that the number of Neurocrine Researcher FTEs applied to the Research Program during each calendar quarter thereof can be accurately determined. Upon fifteen (15) days prior written notice from Wyeth-Ayerst, Neurocrine shall permit an independent certified public accounting firm of nationally recognized standing selected by Wyeth-Ayerst and reasonably acceptable to Neurocrine, to examine the relevant books and records of Neurocrine and its Affiliates as may be reasonably necessary to verify the accuracy of the reports submitted to Wyeth-Ayerst under Section 5.5(b) hereof and the number of Neurocrine Researcher FTEs applied to the performance of Neurocrine's obligations under the Research Program. An examination under this Section 5.5(c) shall not occur more than once in any calendar year and no such examination may be conducted more than eighteen (18) months after the expiration or earlier termination of the Research Program. The accounting firm shall provide both Neurocrine and Wyeth-Ayerst a written report disclosing whether the reports submitted by Neurocrine are correct or incorrect and the specific details concerning any discrepancies. No other information shall be provided to Wyeth-Averst.
- 5.6 Invention Assignment Agreements. Each Neurocrine Researcher and each scientist of Wyeth-Ayerst conducting the Research Program will have executed Neurocrine's or Wyeth-Ayerst's, as the case may be, standard non-disclosure and invention assignment agreement.

### 5.7 Reporting and Disclosure.

- (a) Reports. Prior to each quarterly meeting of the Steering Committee, Neurocrine and Wyeth-Ayerst will each provide the other with written copies of all materials they intend to present at the Steering Committee meeting plus, to the extent not set forth in the Steering Committee materials, a written report summarizing any other material data and information arising out of the conduct of the Research Program. In the event that after receipt of any such report, either Party shall request additional data or information relating to Research Program data or Collaboration Technology licensed hereunder, the Party to whom such request is made shall promptly provide to the other Party such data or information that such Party reasonably believes is necessary for the continued conduct of the Research Program.
- (b) Quarterly Meetings. At the quarterly meetings of the Steering Committee, Wyeth-Ayerst and Neurocrine will review in reasonable detail (i) all data and information generated in the conduct of the Research Program by each Party, and (ii) all Collaboration Technology licensed hereunder developed by the Parties.
- (c) Disclosure. During the term of the Research Program, the Parties will promptly disclose to one another all data, information, inventions, techniques and discoveries (whether patentable or not) arising out of the conduct of the Research Program and all inventions, techniques and discoveries (whether patentable or not) included in Collaboration Technology licensed hereunder.

## 5.8 Data.

(a) Neurocrine Data. All data and information arising out of the

Research Program which relates specifically to Compounds from the Neurocrine Proprietary Chemical Library will be owned by Neurocrine, will be Neurocrine Confidential Information and, subject to the licenses granted to Wyeth-Ayerst, if any, as set forth herein, may be used by Neurocrine for any purpose.

- (b) Wyeth-Ayerst Data. All data and information arising out of the Research Program which relates specifically to Compounds from the Wyeth-Ayerst Proprietary Chemical Library will be owned by Wyeth-Ayerst, will be Wyeth-Ayerst Confidential Information and, subject to the licenses granted to Neurocrine, if any, as set forth herein, may be used by Wyeth-Ayerst for any purpose.
- (c) Other Research Program Data. All data and information arising out of the Research Program which is not Neurocrine Data or Wyeth-Ayerst Data as set forth in (a) and (b) above, will be jointly owned by the Parties and will be Joint Confidential Information and, subject to the licenses granted or to be granted by one Party to the other, if any, as set forth herein, may be used by the Parties for any purpose.
- (d) Wyeth-Ayerst Research, Clinical Development and Commercialization Data. All data and information arising out of Wyeth-Ayerst's research and preclinical development of Lead Compounds and/or Collaboration Products after the term of the Research Program and all data and information arising out of the clinical development and commercialization of Collaboration Products by Wyeth-Ayerst will belong to Wyeth-Ayerst and shall be Wyeth-Ayerst Confidential Information.

#### 5.9 Materials.

- (a) Research Program Materials. During the term of this Agreement, upon request by either Party, the Party to whom the request is made will promptly provide to the other Party such quantities of Research Program Materials as shall be reasonably available in excess of its own needs for such other Party to carry out its respective responsibilities under this Agreement. Subject to the licenses set forth in Article Three, each Party may use the Research Program Materials created or developed by such Party for any purpose.
- (b) Neurocrine Materials. During the term of this Agreement, Neurocrine will supply to Wyeth-Ayerst Neurocrine Materials reasonably (both in quantity and identity) requested by Wyeth-Ayerst provided (i) such Neurocrine Materials are reasonably and readily available to Neurocrine in excess of Neurocrine's own requirements, and (ii) supply of such Neurocrine Materials will not, in Neurocrine's sole judgment, (A) conflict with Neurocrine's internal or collaborative research programs, (B) conflict with Neurocrine's internal policies regarding such materials or (C) violate any agreement to which Neurocrine is a party. Any Neurocrine Materials provided to Wyeth-Ayerst hereunder together with materials derived therefrom thereof (i) may only be used by Wyeth-Ayerst and Wyeth-Ayerst's permitted sublicensees in the conduct of the Research Program and/or in the discovery and/or development of Lead Compounds and/or Collaboration Products, (ii) may not be supplied to Third Parties, other than Third Parties that, with the approval of the Steering Committee, are under contract with one of the Parties to perform services in support of the Research Program, without Neurocrine's prior written consent which can be withheld for any reason in Neurocrine's sole discretion and (iii) will, at Neurocrine's option and at Neurocrine's request be returned to Neurocrine or destroyed. The provision of Neurocrine Materials hereunder will not constitute any grant, option or license under any Neurocrine Patent Rights, except as expressly set forth herein.
- (c) Wyeth-Ayerst Materials. During the term of the Research Program, Wyeth-Ayerst will supply to Neurocrine Wyeth-Ayerst Materials reasonably (both in quantity and identity) requested by Neurocrine, provided that (i) such Wyeth-Ayerst Materials are reasonably and readily available in excess of Wyeth-Ayerst's own requirement and (ii) supply of such Wyeth-Ayerst owned Materials will not, in Wyeth-Ayerst's sole judgment, (A) conflict with Wyeth-Ayerst's internal or collaborative research programs, (B) conflict with Wyeth-Ayerst's internal policies regarding such materials or (C) violate any agreement to which Wyeth-Ayerst is a party. Any Wyeth-Ayerst Materials provided to Neurocrine hereunder together with any materials derived therefrom (i) may only be used by Neurocrine in the conduct of the Research Program, (ii) may not be supplied to Third Parties without Wyeth-Ayerst's prior written consent which can be withheld for any reason in Wyeth-Ayerst's sole discretion and (iii) will, at Wyeth-Ayerst's option and at Wyeth-Ayerst's request, be returned to Wyeth-Ayerst or destroyed. The provision of Wyeth-Ayerst Materials hereunder will not constitute any grant, option or license under any Wyeth-Ayerst Patent Rights, except as expressly set forth herein.

- 6.1 Selection of Lead Compounds During Term of Research Program. Lead Compounds may be selected by the Steering Committee during the term of the Research Program from Hits in the Neurocrine Proprietary Chemical Library, Wyeth-Ayerst Proprietary Chemical Library or any other library the Parties shall agree to screen in connection with the Research Program. Additionally, if any Compound in the Neurocrine Proprietary Chemical Library is identified as a Hit during the term of the Research Program, Wyeth-Ayerst may, upon written notice to Neurocrine, select such Compound as a Lead Compound at any time during [\*\*\*].
- 6.2 Selection of Lead Compounds After Term of Research Program. Lead Compounds may be selected by Wyeth-Ayerst after the term of the Research Program from Compounds in the Wyeth-Ayerst Proprietary Chemical Library or any other library Wyeth-Ayerst shall elect to screen in connection with the development of Lead Compounds and Collaboration Products using the Collaboration Technology. Notwithstanding the foregoing, except as expressly provided in Section 6.1 above, in no event will Wyeth-Ayerst be entitled after the term of the Research Program to select Compounds from Compounds in the Neurocrine Proprietary Chemical Library as Lead Compounds or Collaboration Products.
- 6.3 Selection of Collaboration Products. Lead Compounds will become Collaboration Products upon Wyeth-Ayerst's decision that the Lead Compound is a suitable clinical candidate or Wyeth-Ayerst shall elect to file an IND with respect to such Lead Compound. Wyeth-Ayerst's determination that a Lead Compound is a suitable clinical candidate will be based on its preclinical profile and competitive and other commercial considerations.
- Designation of Lead Compounds and Collaboration Products. It is the Parties' intention that the licenses set forth in Articles Three and Twelve and all rights granted by either Party hereunder be limited to Lead Compounds and Collaboration Products and neither Party grants to the other any right or license in or to Patent Rights or any other rights a Party may have in its Proprietary Chemical Library or any Compounds included therein that are not Lead Compounds or Collaboration Products. The Parties agree that during the term of the Research Program (a) a compound may only be designated a Lead Compound upon the determination of the Steering Committee, as recorded in the minutes of a Steering Committee meeting or by written consent of the Steering Committee, that such compound meets the criteria set forth herein for a Lead Compound and (b) a Lead Compound may only be designated a Collaboration Product upon Wyeth-Ayerst's written notice to the Steering Committee that Wyeth-Ayerst has elected to initiate clinical development with respect to the Lead Compound. After the term of the Research Program, a compound will only be designated a Lead Compound or a Collaboration Product hereunder upon timely written notice (within sixty (60) days after the determination or election set forth below) from Wyeth-Ayerst to Neurocrine describing the compound and setting forth Wyeth-Ayerst's determination that such compound meets the criteria set forth herein for a Lead Compound or Wyeth-Ayerst's election to initiate clinical development of a Lead Compound elevating the Lead Compound to Collaboration Product status hereunder.

## ARTICLE SEVEN DEVELOPMENT, MANUFACTURING AND COMMERCIALIZATION

- 7.1 Wyeth-Ayerst Development. Wyeth-Ayerst will, directly and/or through Third Parties, use Commercially Reasonable Efforts to complete the preclinical development, conduct, fund and make all decisions regarding the clinical development of Collaboration Products. Wyeth-Ayerst will have complete control, authority and responsibility for the regulatory strategies adopted for the clinical development of all Collaboration Products and will own all Regulatory Filings and Regulatory Approvals relating to any Lead Compound or Collaboration Product.
- 7.2 Progress Reports. After the end of the Research Program, Wyeth-Ayerst, within sixty (60) days after each June 30 and December 31, will provide Neurocrine with a report summarizing the status of Wyeth-Ayerst's clinical development activities during the six (6) month period ending on such June 30 or December 31, as applicable, for Collaboration Products then in active development by Wyeth-Ayerst and summarize the development plans for Collaboration Products for the following six (6) month period, provided, however, that Wyeth-Ayerst's failure to achieve any of the goals or plans set forth in any such summary shall not, in and of itself, constitute a failure by Wyeth-Ayerst to use Commercially Reasonable Efforts to develop Collaboration Products hereunder.
- 7.3 Manufacturing. Wyeth-Ayerst shall use Commercially Reasonable Efforts to manufacture Collaboration Products, directly and/or through contracted Third Parties for sale in those countries of the Territory where such Collaboration Products have received Regulatory Approval.
- 7.4 Commercialization of Collaboration Products. Wyeth-Ayerst in its sole discretion will make all decisions regarding the commercialization and sales and marketing of Collaboration Products and will use Commercially Reasonable Efforts to commercialize Collaboration Products in those countries of the world where such Collaboration Products have received Regulatory Approval. The use of Commercially Reasonable Efforts by any Affiliate or sublicensee of Wyeth-Ayerst to commercialize Collaboration Products in a country shall satisfy Wyeth-Ayerst's obligation to use Commercially Reasonable Efforts to commercialize such Collaboration Product in such country.
- 7.5 Co-Promotion. On a Collaboration Product by Collaboration Product basis

at the time of NDA filing, if Neurocrine can demonstrate to Wyeth-Ayerst's reasonable satisfaction that Neurocrine has commercial presence in a United States or Canadian market segment not covered by Wyeth-Ayerst or, in Wyeth-Ayerst's view, not sufficiently covered and capability to promote such Collaboration Product in such market segment, Wyeth-Ayerst and Neurocrine will discuss[\*\*\*] co-promote such Collaboration Product in the United States and Canada. If the Parties agree that it would be in the commercial best interests of the Parties for Wyeth-Ayerst and Neurocrine to so co-promote such Collaboration Product, the Parties will, [\*\*\*], use good faith efforts to negotiate a co-promotion agreement setting forth the rights and obligations of each Party, including, without limitation, payments to be made by either Party to the other Party and responsibility for marketing and promotional expenses. If, (i) [\*\*\*], Neurocrine either fails to notify Wyeth-Ayerst of its desire to co-promote such Collaboration Product or fails to demonstrate to Wyeth-Ayerst's reasonable satisfaction that Neurocrine has the required commercial presence and capability to promote such Collaboration Product, or (ii) the Parties fail to enter into a co-promotion agreement by the end of the [\*\*\*] period described above in this Section 7.5, Wyeth-Ayerst shall thereafter be free, at its sole election, to enter into a co-promotion agreement with any Third Party with respect to such Collaboration Product.

## ARTICLE EIGHT

8.1 License Fees. Each of the following License Fees will be payable to Neurocrine one-time only within thirty (30) days following confirmation by the Steering Committee that the specified event has occurred.

Event Payment Validation of [\*\*\*] model of Neurodegeneration [\*\*\*] (such model and criteria for validation to be selected and agreed upon by the [\*\*\*] Steering Committee as soon as practicable after the first Steering Committee meeting) Completion of screening of [\*\*\*] compounds selected by the Steering [\*\*\*] Completion of Screening of [\*\*\*] compounds selected by the Steering Committee from the Neurocrine Proprietary Chemical Library, Wyeth-Ayerst Proprietary Chemical Library and/or some other library(ies) selected by the Steering Committee for the first to complete of [\*\*\*] using Neurocrine's novel High Throughput Screening ("HTS") technology, provided, however, that the [\*\*\*] compounds selected by the Steering Committee must all be readily available to Neurocrine in 96 well plates suitable for screening and within a timeframe that will not materially or unreasonably delay Neurocrine's screening efforts delay Neurocrine's screening efforts The later to occur of (i) completion of screening of [\*\*\*] compounds selected by the Steering Committee from the Neurocrine Proprietary Chemical Library, Wyeth-Ayerst Proprietary Chemical Library and/or some other library(ies) selected by the Steering Committee for the second to complete of [\*\*\*] using Neurocrine's HTS technology and (ii) the [\*\*\*] anniversary of the Effective Date [\*\*\*] [\*\*\*] target validation of [\*\*\*] in a model [\*\*\*] (such mode and criteria for validation to be selected and agreed upon by the [\*\*\*] Steering Committee as soon as practicable after the first Steering Committee meeting) [\*\*\*] validation of [\*\*\*] in a model (such model and criteria for validation to be selected and agreed upon by the Steering Committee as soon as practicable after the first Steering Committee meeting) \*] target validation of [\*\*\*] in an appropriate model for [\*\* [\*\*\*] (such model and criteria for validation to be selected and agreed upon by the Steering Committee as soon as practicable after the first Steering Committee meeting)  $[\ ^{***}]$  validation of the  $[\ ^{***}]$  in an appropriate model for  $[\ ^{***}],$  (such model and criteria for validation and disease category to be [\*\*\*] selected and agreed upon by the Steering Committee as soon as practicable after the first Steering Committee meeting)

For the purposes of the foregoing, Neurocrine's HTS for activity against [\*\*\*] will be deemed `complete' when [\*\*\*]compounds selected by the Steering Committee have been screened for activity against [\*\*\*] and Neurocrine has prepared and delivered to Wyeth-Ayerst a final report setting forth the results. Upon the achievement of a Licensee Fee triggering event for [\*\*\*], any License Fees relating to prior triggering events for [\*\*\*] which have not been paid, shall be deemed payable.

8.2 Additional License Fees. The following additional License Fees will be payable to Neurocrine [\*\*\*] only regardless of the number of Collaboration Products and the number of indications for each Collaboration Product developed and commercialized.

Filing, by Wyeth-Ayerst, of an IND in the United States permitting the clinical study of [***]	[***]
Filing, by Wyeth-Ayerst, of an IND in the United States permitting the clinical study of $[***]$	[***]
Filing, by Wyeth-Ayerst, of an IND in the United States permitting the clinical study of $[***]$	[***]
Filing, by Wyeth-Ayerst, of an IND in the United States permitting the clinical study of $[***]$	[***]
Achievement, by Wyeth-Ayerst, of ICE for the [***]	[***]
Achievement, by Wyeth-Ayerst, of ICE for the [***]	[***]
Achievement, by Wyeth-Ayerst, of ICE for the [***]	[***]
Achievement, by Wyeth-Ayerst, of ICE for the [***]	[***]
<pre>Initiation, by Wyeth-Ayerst, of a Pivotal Trial to study the [***]</pre>	[***]
<pre>Initiation, by Wyeth-Ayerst, of a Pivotal Trial to study the [***]</pre>	[***]
<pre>Initiation, by Wyeth-Ayerst, of a Pivotal Trial to study the [***]</pre>	[***]
<pre>Initiation, by Wyeth-Ayerst, of a Pivotal Trial to study the [***]</pre>	[***]
Filing, by Wyeth-Ayerst, of an NDA in the United States, and acceptance, by the FDA, of such NDA for filing seeking Regulatory Approval in the United States of the [***]	[***]
Filing, by Wyeth-Ayerst, of an NDA in the United States, and acceptance, by the FDA, of such NDA for filing, seeking Regulatory Approval in the United States of the [***]	[***]
Filing, by Wyeth-Ayerst, of an NDA in the United States, and acceptance, by the FDA, of such NDA for filing, seeking Regulatory Approval in the United States of the [***]	[***]
Filing, by Wyeth-Ayerst, of an NDA in the United States and acceptance, by the FDA, of such NDA for filing, seeking Regulatory Approval in the United States of the [***]	[***]
Filing, by Wyeth-Ayerst, of an NDA in Europe (either a centralized filing or filing in at least one (1) of the European Major Market Countries), and acceptance, by the applicable European Regulatory Authorities, of such NDA for filing, seeking Regulatory Approval in Europe (or such European country) of the [***]	[***]
Filing, by Wyeth-Ayerst, of an NDA in Europe (either a centralized filing or filing in at least one (1) of the European Major Market Countries), and acceptance, by the appropriate European Regulatory Authorities, of such NDA for filing seeking Regulatory Approval in Europe (or such European country) of the [***]	[***]
Filing, by Wyeth-Ayerst, of an NDA in Europe (either a centralized filing or filing in at least one (1) of the European Major Market Countries), and acceptance, by the applicable European Regulatory Authorities, of such NDA for filing seeking Regulatory Approval in Europe (or such European country) of the [***]	[***]

Filing, by Wyeth-Ayerst, of an NDA in Europe centralized filing or filing in at least one ( European Major Market Countries), and acceptanc applicable European Regulatory Authorities, of	ì) of the e, by the such NDA	[***]
for filing seeking Regulatory Approval in Europe European country) of the [***]	(or such	
United States Regulatory Approval granted to Wye for the $[***]$	th-Ayerst	[***]
United States Regulatory Approval granted to Wye for the $[***]$	th-Ayerst	[***]
United States Regulatory Approval granted to Wye for the $[***]$	th-Ayerst	[***]
United States Regulatory Approval granted to Wye for the $[***]$	th-Ayerst	[***]
European (either centralized or in at least European Major Market Country) Regulatory granted to Wyeth-Ayerst for the [***]		[***]
European (either centralized or in at least European Major Market Country) Regulatory granted to Wyeth-Ayerst for the [***]		[***]
European (either centralized or in at least European Major Market Country) Regulatory granted to Wyeth-Ayerst for the [***]		[***]
European (either centralized or in at least European Major Market Country) Regulatory granted to Wyeth-Ayerst for the [***]		[***]

Any additional License Fees paid for a Collaboration Product which does not achieve Regulatory Approval shall be fully creditable against Additional License Fees that may be payable for Collaboration Products subsequently developed [\*\*\*]. No additional License Fee shall be payable for the third or any subsequent Collaboration Product to achieve the specified event.

## ARTICLE NINE ROYALTIES

9.1 Royalty Rates. Wyeth-Ayerst will pay to Neurocrine, Royalties, on a Collaboration Product by Collaboration Product basis, which Royalties shall be calculated using the following formula:

[\*\*\*]

where,

A equals [\*\*\*] of Wyeth-Ayerst's worldwide Net Sales of such Collaboration Product, which, during the calendar year in question, are [\*\*\*]

B equals [\*\*\*] of Wyeth-Ayerst's worldwide Net Sales of such Collaboration Product, which, during the calendar year in question, [\*\*\*]; and

C equals [\*\*\*] of Wyeth-Ayerst's worldwide Net Sales of such Collaboration Product, which, during the calendar year in question, are [\*\*\*].

By way of example only, if, during a given year, Wyeth-Ayerst, its Affiliates and sublicensees [\*\*\*] the royalty payable by Wyeth-Ayerst to Neurocrine during such year would be calculated as follows:

[\*\*\*]

Neurocrine acknowledges and agrees that nothing in this Agreement shall be construed as representing an estimate or projection of either (i) the number of Collaboration Products that will or may be successfully developed and/or commercialized estimate or (ii) anticipated sales or the actual value of the Neurocrine Technology, any Lead Compound or any Collaboration Product and that the figures set forth in this Section 9.1 or elsewhere in this Agreement or that have otherwise been discussed by the Parties are merely intended to define Wyeth-Ayerst's royalty obligations to Neurocrine in the event such sales performance is achieved. WYETH-AYERST MAKES NO REPRESENTATION OR WARRANTY, EITHER EXPRESS OR IMPLIED, THAT IT WILL BE ABLE TO SUCCESSFULLY DEVELOP AND/OR COMMERCIALIZE ANY COLLABORATION PRODUCTS OR, IF COMMERCIALIZED, THAT IT WILL ACHIEVE ANY PARTICULAR SALES LEVEL OF SUCH COLLABORATION PRODUCT(S).

- 9.2 Royalty Adjustments. Royalties on a Collaboration Product are subject to reductions and adjustments as a result of certain events as set forth below; provided, however, in no event will Royalties on a Collaboration Product in any country be [\*\*\*] by reason of the adjustments set forth below.
  - (a) Royalty Adjustment for Unpatented Products. If, during a given

calendar quarter, a Collaboration Product is an Unpatented Product in one or more countries, the Royalties will be payable to Neurocrine for the Net Sales of such Collaboration Product in such country(ies) during such calendar quarter at [\*\*\*] of the royalty rate(s) set forth in Section 9.1 above. To calculate the Unpatented Product Royalties, [\*\*\*]. The fact that a Collaboration Product is an Unpatented Product in one country during any calendar quarter shall not result in a reduction of the royalty rate used to calculate the Royalty payable for sales of Collaboration Products in any other country during such calendar quarter.

- (b) Competition. If Competition exists, during a given calendar quarter with respect to a Collaboration Product in a country, the royalty rate(s) used to calculate the Royalties payable to Neurocrine for the sale of such Collaboration Product in such country during such calendar quarter will [\*\*\*] of the royalty rate(s) set forth in Section 9.1 above. To calculate the Royalties when Competition exists in one or more countries, [\*\*\*]. The existence of Competition in one country during any calendar quarter shall not result in a reduction of the royalty rate used to calculate the Royalty payable for sales of Collaboration Products in any other country during such calendar quarter. If at the time of determining any Competition adjustments, applicable IMS International data (or such other data as may be mutually agreed by the Parties) for such time period is unavailable, Wyeth-Ayerst may make a reasonable estimate thereof based on prior available IMS International data (or such other data as may be mutually agreed by the Parties) and calculate the applicable Royalty based on such estimate, and any difference in Royalty payments made by Wyeth-Ayerst based on such estimate and Royalty payments based on actual data, once available, will be accounted for by an adjustment payment by Wyeth-Ayerst at the time the next quarter Royalty payment is made or an adjustment credit against Wyeth-Ayerst's future Royalty obligations, as the case may be.
- 9.3 Term of Royalty. Royalties will be payable on a country by country and Collaboration Product by Collaboration Product basis until the later of (i) the last to expire, in such country, of the Patent Rights included within the Collaboration Technology, [\*\*\*] or (ii) with respect to the sale of such Collaboration Product in countries of the European Union, [\*\*\*] from First Commercial Sale of such Collaboration Product in the European Union and, with respect to the sale of such Collaboration Product in any country outside of the European Union, [\*\*\*] from First Commercial Sale of such Collaboration Product in such country. Upon the expiration of Wyeth-Ayerst's obligation to pay Royalties to Neurocrine hereunder with respect to a Collaboration Product, Wyeth-Ayerst shall have a fully paid, irrevocable, exclusive and unrestricted license under the Collaboration Technology to make, have made, use, sell, offer to sell and import such Collaboration Product.

## 9.4 Reports and Payments.

- (a) Cumulative Royalties. The obligation to pay Royalties under this Article Nine shall be imposed only once (i) with respect to any sale of the same unit of Collaboration Product and (ii) with respect to a single unit of Collaboration Product regardless of how many Valid Claims of Patent Rights included in the Collaboration Technology would, but for this Agreement, be infringed by the making, using or selling of such Collaboration Product.
- (b) Statements and Payments. Wyeth-Ayerst shall deliver to Neurocrine within sixty (60) days after the end of each calendar quarter, a report certified by Wyeth-Ayerst as accurate to the best of its ability based on information then available to Wyeth-Ayerst, setting forth for such calendar quarter the following information on a country-by-country and Collaboration Product by Collaboration Product basis: (i) Net Sales of such Collaboration Product in such country, (ii) the basis for any adjustments to the Royalty payable for the sale of such Collaboration Product in such country and (iii) the Royalty due hereunder for the sale of such Collaboration Product in such country. The total Royalty due for the sale of Collaboration Products during such calendar quarter shall be remitted at the time such report is made.
- (c) Taxes and Withholding. All payments under this Agreement will be made without any deduction or withholding for or on account of any tax unless such deduction or withholding is required by applicable law or regulations. If the paying Party is so required to deduct or withhold such Party will (i) promptly notify the other Party of such requirement, (ii) pay to the relevant authorities the full amount required to be deducted or withheld promptly upon the earlier of determining that such deduction or withholding is required or receiving notice that such amount has been assessed against the other Party, (iii) promptly forward to the other Party an official receipt (or certified copy) or other documentation reasonably acceptable to the other Party evidencing such payment to the authorities. In case the other Party can not take a full credit against its tax liability for the withholding tax deducted or withheld by the paying Party, then such other Party may propose a change to the then current arrangement with respect to the flow of moneys under this Agreement in order to reduce or eliminate the extra cost for any Party and the Parties, with no

- obligation as to outcome, shall discuss such proposal in good faith
- (d) Currency. All amounts payable and calculations hereunder shall be in United States dollars. As applicable, Net Sales shall be translated into United States dollars in accordance with Wyeth-Ayerst's customary and usual translation procedures, consistently applied.
- (e) Maintenance of Records; Audit. For a period of three (3) Wyeth-Ayerst shall maintain and shall cause Affiliates and sublicensees to maintain complete and accurate books and records in connection with the sale of Collaboration Products hereunder, as necessary to allow the accurate calculation of Royalties due hereunder including any records required to calculate any Royalty adjustments hereunder. Once per calendar year Neurocrine shall have the right to engage an independent accounting firm acceptable to Wyeth-Ayerst, at Neurocrine's expense, which shall have the right to examine in confidence the relevant Wyeth-Ayerst records as may be reasonably necessary to determine and/or verify the amount of Royalty payments due hereunder. Such examination shall be conducted during Wyeth-Ayerst's normal business hours, after at least fifteen (15) days prior written notice to Wyeth-Ayerst and shall take place at the Wyeth-Ayerst facility(ies) where such records are maintained. Each such examination shall be limited to pertinent books and records for any year ending not more than thirty-six (36) months prior to the date of request. Before permitting such independent accounting firm to have access to such books and records, Wyeth-Ayerst may require such independent accounting firm and its personnel involved in such audit, to sign a confidentiality agreement (in form and substance reasonably acceptable to Wyeth-Ayerst) as to any of Wyeth-Ayerst's, its Affiliates or sublicensees' confidential information which is to be provided to such accounting firm or to which such accounting firm will have access, while conducting the audit under this Section 9.5 (e). The Neurocrine independent accounting firm will prepare and provide to both Neurocrine and Wyeth-Ayerst a written report disclosing only whether the Royalty reports submitted and Royalties paid by Wyeth-Ayerst are correct or incorrect and the specific details concerning any discrepancies. No other information shall be provided to Neurocrine. In the event there was an under-payment by Wyeth-Ayerst hereunder, Wyeth-Ayerst shall promptly (but in no Wyeth-Ayerst hereunder, Wyeth-Ayerst shall promptly (but in no event later than thirty (30) days after Wyeth-Ayerst's receipt of the independent auditor's report so correctly concluding) make payment to Neurocrine of any short-fall. In the event that there was an over-payment by Wyeth-Ayerst hereunder, Neurocrine shall promptly (but in no event later than thirty (30) days after Neurocrine's receipt of the independent auditor's report so correctly concluding) refund to Wyeth-Ayerst the excess amount. In the event any payment by Wyeth-Ayerst shall prove to have been incorrect by more than seven and one-half percent (7.5%) to Neurocrine's detriment seven and one-half percent (7.5%) to Neurocrine's detriment, Wyeth-Ayerst will pay the reasonable fees and costs of Neurocrine's independent auditor for conducting such audit.

### 9.5 Third Party Payments.

- (a) OHSU Agreement. The Parties have agreed to share equally the royalty payments to OHSU required under paragraph 6.02 of the OHSU Agreement (the "Shared Obligation"). All other payments under the OHSU Agreement shall be the responsibility of Neurocrine. Neurocrine shall be responsible for making all payments due under the OHSU License Agreement and, within ten (10) days of making any payment required under paragraph 6.02 of the OHSU Agreement, Neurocrine shall provide to Wyeth-Ayerst documentary evidence that such payment has been made. Within thirty (30) days after Wyeth-Ayerst receives from Neurocrine such documentary evidence, Wyeth-Ayerst shall pay to Neurocrine an amount equal to [\*\*\*] of the payments due to the Oregon Health Sciences University pursuant to [\*\*\*] for Licensed Patent Rights (as defined in the OHSU Agreement) included in the Neurocrine Technology licensed to Wyeth-Ayerst hereunder, provided, however, that any credits that may accrue to Neurocrine by reason of payments by Neurocrine to OHSU pursuant to [\*\*\*] will be considered a credit against Neurocrine's portion of Shared Obligation, and any credits that may accrue pursuant to [\*\*\*] or Wyeth-Ayerst, as the case may be, will be considered a credit against Neurocrine's or Wyeth-Ayerst's, respectively, portion of the Shared Obligation.
- (b) Neurocrine Technology. [\*\*\*] from any Third Party owning or Controlling Patent Rights which would be infringed by [\*\*\*] under this Agreement, a license under such Patent Rights, which license would permit [\*\*\*] will be solely responsible for paying [\*\*\*] of the license fees and royalties that may be payable to any such Third Party for such license(s). In the event [\*\*\*] fails or in unable to negotiate an agreement with such Third Party within [\*\*\*] may negotiate such license on terms reasonably agreed to by [\*\*\*] and in the event [\*\*\*] in obtaining such license on terms agreed to by [\*\*\*] in its good faith business judgment [\*\*\*] amounts payable thereunder. If [\*\*\*] is unable to agree as to whether it is necessary to obtain such a license from a Third Party, the issue shall be referred to [\*\*\*].

- (c) Collaboration Products. Except as set forth in (a) and (b) above, [\*\*\*] determining whether to negotiate an agreement with any Third Party that owns or Controls a Patent Right claiming the manufacture or use of any Collaboration Product. [\*\*\*] from any Third Party owning or Controlling Patent Rights which would be infringed by the development and sale of Lead Compounds and Collaboration Products, a license under such Patent Rights, and in the event [\*\*\*] obtains such a license, [\*\*\*] shall pay [\*\*\*] that may be payable to such Third Party for such license(s).
- (d) Third Party Licenses. Any rights to Third Party Patent Rights licensed by Neurocrine or Wyeth-Ayerst, as the case may be, under paragraphs (b) and (c) above, shall be considered Neurocrine Technology or Wyeth-Ayerst Technology, respectively. In each case, Wyeth-Ayerst and Neurocrine shall use their Commercially Reasonable Efforts to ensure that such licenses provide for the right to sublicense of the Third Party Patent Rights in connection with the license of the Neurocrine Technology and Wyeth-Ayerst Technology upon termination of this Agreement pursuant to Article Twelve. Any sublicenses of Third Party Patent Rights pursuant to Article Twelve shall be subject to the assumption by the Party to whom the rights are sublicensed of all payment and performance obligations in connection with the exercise of the sublicensed rights by such Party.

# ARTICLE TEN CONFIDENTIALITY, PUBLICATION AND PUBLIC ANNOUNCEMENTS

- 10.1 Confidentiality. Except to the extent expressly authorized by this Agreement or otherwise agreed in writing, the Parties agree that, for the term of this Agreement and for [\*\*\*], each Party (the "Receiving Party"), receiving hereunder any information designated hereunder as Confidential Information of the other Party or information of the other Party marked "Confidential" (in either case, the "Disclosing Party"), shall keep such information confidential and shall not publish or otherwise disclose or use for any purpose other than as provided for in this Agreement except, to the extent that it can be established:
  - (a) by the Receiving Party that the Confidential Information was already known to the Receiving Party (other than under an obligation of confidentiality), at the time of disclosure by the Disclosing Party and such Receiving Party has documentary evidence to that effect;
  - (b) by the Receiving Party that the Confidential Information was generally available to the public or otherwise part of the public domain at the time of its disclosure to the Receiving Party;
  - (c) by the Receiving Party that the Confidential Information became generally available to the public or otherwise part of the public domain after its disclosure or development, as the case may be, and other than through any act or omission of a party in breach of this confidentiality obligation;
  - (d) by the Receiving Party that the Confidential Information was disclosed to that Party, other than under an obligation of confidentiality, by a Third Party who had no obligation to the Disclosing Party not to disclose such information to others;
  - (e) by the Receiving Party that the Confidential Information was independently discovered or developed by the Receiving Party without the use of the Confidential Information belonging to the other Party and the Receiving Party has documentary evidence to that effect

### 10.2 Authorized Disclosure.

- (a) Each Party. Each Party may disclose Confidential Information belonging to the other Party to the extent such disclosure is reasonably necessary to:
  - (i) file or prosecute patent applications claiming inventions included within the Collaboration Technology,
  - (ii) prosecute or defend litigation,
  - (iii) exercise rights hereunder provided such
     disclosure is covered by terms of
     confidentiality similar to those set forth
     herein, and
  - (iv) comply with applicable governmental laws and regulations.

In the event a Party shall deem it necessary to disclose pursuant to this Section 10.2 (a), Confidential Information belonging to the other Party, the Disclosing Party shall to the extent possible give reasonable advance notice of such disclosure to the other Party and take reasonable measures to ensure confidential treatment of such information.

- (b) Use. Wyeth-Ayerst shall have the right to use Neurocrine Confidential Information in the conduct of the Research Program and in developing and commercializing Lead Compounds and Collaboration Products. Neurocrine shall have the right to use Wyeth-Ayerst Confidential Information in the conduct of the Research Program and, in the event this Agreement shall be terminated in accordance with Sections 12.3, 12.4, 12.5(a) or 12.6, in the development and commercialization of Lead Compounds and Collaboration Products and Compounds [\*\*\*]. Neurocrine shall also have the right to use that portion of the Wyeth-Ayerst Confidential Information that relates [\*\*\*]. Subject to the license granted in Article Three hereof and the terms of this Article Ten, each Party shall have the right to use the Joint Confidential Information for any purpose.
- 10.3 SEC Filings. The Parties will consult with one another on the terms of this Agreement to be redacted in SEC filings.
- Publications. During the term of the Research Program, each Party will submit to the other Party for review and approval all proposed academic, scientific and medical publications relating to the Research Program, Lead Compounds, Collaboration Products and/or Collaboration Technology for review in connection with preservation of exclusive Patent Rights and/or to determine whether Confidential Information should be modified or deleted. The nonpublishing Party shall have no less than thirty (30) days to review each proposed publication. The review period may be extended for an additional thirty (30) days in the event the nonpublishing Party can demonstrate a reasonable need for such extension including, but not limited to, the preparation and filing of patent applications. By mutual agreement, this period may be further extended. Wyeth-Ayerst and Neurocrine will each comply with standard academic practice regarding authorship of scientific publications and recognition of contribution of other parties in any publications relating to Research Program, Lead Compounds, Collaboration Products and/or Collaboration Technology.
- 10.5 Public Announcements.
  - (a) Coordination. The Parties agree on the importance of coordinating their public announcements respecting this Agreement and the subject matter thereof (other than academic, scientific or medical publications that are subject to the publication provision set forth above). Neurocrine and Wyeth-Ayerst will, from time to time, and at the request of the other Party discuss and agree on the general information content relating to this Agreement, the Research Program, Lead Compounds, Collaboration Products and/or Collaboration Technology which may be publicly disclosed.
  - (b) Announcements. Neither Party will make any public announcement (whether required by law or otherwise) regarding this Agreement, the Research Program, Lead Compounds, Collaboration Products and/or Collaboration Technology (other than academic, scientific or medical publications which are subject to the publication provision set forth above) without giving the other Party the opportunity to review and comment prior to release.

## ARTICLE ELEVEN INDEMNIFICATION

- Indemnification by Wyeth-Ayerst. Wyeth-Ayerst will indemnify, defend and hold harmless Neurocrine, its Affiliates, and each of its and their respective employees, officers, directors and agents (each, a "Neurocrine Indemnified Party") from and against any and all liability, loss, damage, expense (including reasonable attorneys' fees and expenses) and cost (collectively, a "Liability") which the Neurocrine Indemnified Party may be required to pay to one or more Third Parties resulting from or arising out of (i) any claims of any nature (other than claims by Third Parties relating to patent infringement) arising out (y) the conduct of the Research Program or use of Collaboration Technology of by, on behalf of or under authority of, Wyeth-Ayerst (other than by Neurocrine) or (z) research, development and/or commercialization of Lead Compounds and/or Collaboration Products by, on behalf of or under authority of, Wyeth-Ayerst (other than by Neurocrine) and/or (ii) any Wyeth-Ayerst representation or warranty set forth herein being untrue in any material respect when made, except in each case, to the extent caused by the negligence or willful misconduct of Neurocrine or any Neurocrine Indemnified Party. Notwithstanding the foregoing, Wyeth-Ayerst shall have no obligation to defend, indemnify or hold harmless any Neurocrine Indemnified Party from and against any Liability arising out of or resulting from the infringement of a Third Party Patent Right.
- 11.2 Indemnification by Neurocrine. Neurocrine will indemnify, defend and hold harmless Wyeth-Ayerst, its Affiliates, and each of its and their respective employees, officers, directors and agents (each, a "Wyeth-Ayerst Indemnified Party") from and against and all Liability which the Wyeth-Ayerst Indemnified Party may be required to pay to one or more Third Parties arising out of (i) any claims of any nature (other than claims by Third Parties relating to patent infringement) arising out of the conduct of the Research Program by, on behalf of, or under the authority of Neurocrine (other than by Wyeth-Ayerst) and/or (ii) any Neurocrine representation or warranty set forth herein having been untrue in any material respect when made, except in each case, to the extent caused by the negligence or willful misconduct of Wyeth-Ayerst or any Wyeth-Ayerst Indemnified Party. Notwithstanding the foregoing, Neurocrine shall have no obligation to defend, indemnify or

hold harmless any Wyeth-Ayerst Indemnified Party from and against any Liability arising out of or resulting from the infringement of a Third Party Patent Right.

- 11.3 Procedure. Each Party will notify the other in the event it becomes aware of a claim for which indemnification may be sought hereunder. In case any proceeding (including any governmental investigation) shall be instituted involving any Party in respect of which indemnity may be sought pursuant to this Article Eleven, such Party (the "Indemnified Party") shall promptly notify the other Party (the "Indemnifying Party") in writing and the Indemnifying Party and Indemnified Party shall meet to discuss how to respond to any claims that are the subject matter of such proceeding. The Indemnifying Party, upon request of the Indemnified Party, shall retain counsel reasonably satisfactory to the Indemnified Party to represent the Indemnified Party and shall pay the fees and expenses of such counsel related to such proceeding. In any such proceeding, the Indemnified Party shall have the right to retain its own counsel, but the fees and expenses of such counsel shall be at the expense of the Indemnified Party unless (i) the Indemnifying Party and the Indemnified Party shall have mutually agreed to the retention of such counsel or (ii) the named parties to any such proceeding (including any impleaded parties) include both the Indemnifying Party and the Indemnified Party and representation of both parties by the same counsel would be inappropriate due to actual or potential differing interests between them. All such fees and expenses shall be reimbursed as they are incurred. The Indemnifying Party shall not be liable for any settlement of any proceeding effected without its written consent, but if settled with such consent or if there be a final judgment for the plaintiff, the Indemnifying Party agrees to indemnify the Indemnified Party from and against any loss or liability by reason of such settlement or judgment. The Indemnifying Party shall not, without the written consent of the Indemnified Party, effect any settlement of any pending or threatened proceeding in respect of which the Indemnified Party is, or arising out of the same set of facts could have been, a party and indemnity could have been sought hereunder by the Indemnified Party, unless such settlement includes an unconditional release of the Indemnified Party from all liability on claims that are the subject matter of such proceeding.
- Insurance. Each Party further agrees to use its Commercially Reasonable Efforts to obtain and maintain, during the term of this Agreement, Commercial General Liability Insurance, including Products Liability Insurance, with reputable and financially secure insurance carriers to cover its indemnification obligations under Sections 11.1 or 11.2, as applicable, or self-insurance, with limits of not less than [\*\*\*] per occurrence and in the aggregate.

## ARTICLE TWELVE TERM AND TERMINATION

### 12.1 Government Approvals.

- (a) Government Approvals. Each of Neurocrine and Wyeth-Ayerst shall use its good faith efforts to eliminate any concern on the part of any court or government authority regarding the legality of the proposed transaction, including, if required by federal or state antitrust authorities, promptly taking all steps to secure government antitrust clearance, including, without limitation, cooperating in good faith with any government investigation including the prompt production of documents and information demanded by a second request for documents and of witnesses if requested.
- (b) Co-operation. Neurocrine and Wyeth-Ayerst will cooperate and use respectively all reasonable efforts to make all other registrations, filings and applications, to give all notices and to obtain as soon as practicable all governmental or other consents, transfers, approvals, orders, qualifications authorizations, permits and waivers, if any, and to do all other things necessary or desirable for the consummation of the transactions as contemplated hereby. Neither Party shall be required, however, to divest products or assets or materially change its business if doing so is a condition of the transactions contemplated by this Agreement.
- Term. Unless earlier terminated by mutual agreement of the Parties or pursuant to the provisions of this Article Twelve, this Agreement will continue in full force and effect on a country-by country and Collaboration Product by Collaboration Product basis until the obligation to pay Royalties with respect to the sale of such Collaboration Product in such country expires as provided in Section 9.3 hereof.
- Early Termination for [\*\*\*]. In the event that at any time after the [\*\*\*] anniversary of the Effective Date, the Steering Committee shall determine that [\*\*\*] as set forth in Exhibit B Parts 1(a), 1(b), 2(a) and 2(b), has been demonstrated for [\*\*\*] (or, if this Agreement has already been terminated with respect to [\*\*\*] pursuant to Section 12.4, the [\*\*\*] subject to this Agreement), Wyeth-Ayerst may elect to terminate this Agreement upon [\*\*\*] months prior written notice to Neurocrine. Upon such termination, Wyeth-Ayerst will have no further funding obligation for the Research Program. In the event this Agreement shall be terminated pursuant to this Section 12.3, all licenses granted by Neurocrine to Wyeth-Ayerst hereunder will revert to Neurocrine and:
  - (i) Wyeth-Ayerst will disclose to Neurocrine all material

Research Program research and pre-clinical data on Hits generated prior to the date of termination provided such data are reasonably available to Wyeth-Ayerst and Neurocrine shall have the right to use such data, at its own risk and expense, in its development of Compounds (other than Wyeth-Ayerst Compounds) which [\*\*\*]

- (ii) Wyeth-Ayerst will grant to Neurocrine a perpetual, irrevocable, exclusive, royalty-free, fully-paid, worldwide license under the Wyeth-Ayerst Technology and Wyeth-Ayerst's interest in the Joint Technology to make, have made, use, import, market, offer for sale and sell in the Field of Use, Compounds (other than Wyeth-Ayerst Compounds) which [\*\*\*]
- (iii) Wyeth-Ayerst shall remain free to develop and commercialize any Wyeth-Ayerst Compound, provided, however, that such Compound is not developed for any indication in [\*\*\*] and the continued identification, development and commercialization of such Compound does not utilize Neurocrine Technology.
- Termination of Collaboration Product Development and Commercialization. Subject to satisfaction of Wyeth-Ayerst's minimum Research Program Funding commitment (i.e., [\*\*\*] of Research Program Funding), in the event that Wyeth-Ayerst shall elect at any time to discontinue all activities relating to the development and commercialization of all Collaboration Products which [\*\*\*] or shall elect to discontinue use of Commercially Reasonable Efforts in the development and commercialization of all Collaboration Products which [\*\*\*] Wyeth-Ayerst shall provide written notice to Neurocrine setting forth Wyeth-Ayerst's election to terminate this Agreement with respect to [\*\*\*] and upon Neurocrine's receipt of such notice this Agreement with respect to [\*\*\*], will terminate. In the event this Agreement shall be terminated with respect to a Neurocrine Transporter pursuant to this Section 12.4:
  - (i) Wyeth-Ayerst will disclose to Neurocrine all material Research Program research, pre-clinical and clinical data generated prior to the date of termination on Hits, Lead Compounds and Collaboration Products relating to the terminated Neurocrine Transporter(s), provided such data are reasonably available to Wyeth-Ayerst and Neurocrine shall have the right to use such data, at its own risk and expense, in its development of Compounds [\*\*\*] which [\*\*\*]
  - (ii) Wyeth-Ayerst will assign (or, if the filing [\*\*\*] grant a right of cross reference) to Neurocrine all Regulatory Filings relating to Compounds designated as Lead Compounds and/or Collaboration Products prior to the date of termination of this Agreement (other than Lead Compounds and/or Collaboration Products which are [\*\*\*] in so far as such Regulatory Filings relate to [\*\*\*];
  - (iii) Wyeth-Ayerst will grant to Neurocrine a perpetual, irrevocable, exclusive, royalty-free, fully-paid, worldwide license under the [\*\*\*] to make, have made, use, sell and import in the Field of Use, Compounds including Compounds designated as Lead Compounds and Collaboration Products prior to the date of termination of this Agreement (but excluding [\*\*\*] only [\*\*\*] in which [\*\*\*]
  - (iv) Wyeth-Ayerst will enter into good faith negotiations with Neurocrine regarding the grant to Neurocrine of the licenses as set forth in (A), (B) and (C) below, to allow Neurocrine to continue to develop and commercialize, [\*\*\*] designated as Lead Compounds or Collaboration Products prior to the date of termination of this Agreement:
    - (A) an exclusive, worldwide license under the [\*\*\*] to make, have made, use, import, offer for sale and sell in the Field of Use [\*\*\*] which are [\*\*\*], such license to be on commercially reasonable terms and conditions mutually agreed by the Parties including, without limitation, provision of payments intended to reflect both Parties' investment and opportunity in such Compounds and royalties on net sales of such [\*\*\*] the Royalties payable by Wyeth-Ayerst to Neurocrine hereunder and other terms and conditions which Wyeth-Ayerst believes are reasonable necessary or desirable to protect Wyeth-Ayerst's research, development and commercialization activities for [\*\*\*];
    - (B) an exclusive, worldwide license under the [\*\*\*] to make, have made, use, import, offer for sale and sell in the Field of Use only [\*\*\*] in which [\*\*\*], such licenses to be on commercially reasonable terms and conditions mutually agreed by the Parties

including, without limitation, provision of payments intended to reflect both Parties' investment and opportunity in such Compounds and royalties on net sales of such [\*\*\*] the Royalties payable by Wyeth-Ayerst to Neurocrine hereunder and other terms and conditions which Wyeth-Ayerst believes are reasonable necessary or desirable to protect Wyeth-Ayerst's research, development and commercialization activities for [\*\*\*];

- (C) an exclusive, worldwide license under the [\*\*\*] to make, have made, use, import, offer for sale and sell in the Field of Use only [\*\*\*] in which [\*\*\*], such licenses to be on commercially reasonable terms and conditions mutually agreed by the Parties including, without limitation, provision of payments intended to reflect both Parties' investment and opportunity in such Compounds and royalties on net sales of such [\*\*\*] Royalties payable by Wyeth-Ayerst to Neurocrine hereunder and other terms and conditions which Wyeth-Ayerst believes are reasonable necessary or desirable to protect Wyeth-Ayerst's research, development and commercialization activities [\*\*\*]
- (D) upon the grant of the licenses set forth in (A), (B) and/or (C) above, Wyeth-Ayerst will assign (or, if the filing [\*\*\*] grant a right of cross reference) to Neurocrine all Regulatory Filings on [\*\*\*] that are the subject of the license in so far as such Regulatory Filings relate [\*\*\*] which [\*\*\*]
- (v) Wyeth-Ayerst shall remain free to develop and/or sublicense any [\*\*\*] to Third Parties, provided, however, in no event will Wyeth-Ayerst commercialize or sublicense Third Parties to commercialize [\*\*\*] designated as Lead Compounds or Collaboration Products prior to the date of termination of this Agreement (a) for [\*\*\*] and (b) if the identification or continued development and commercialization of such Compound utilizes Neurocrine Technology.

Notwithstanding the foregoing, Wyeth-Ayerst shall have no obligation to negotiate or grant any of the licenses set forth in (iv) (A), (B), or (C) above with respect to [\*\*\*].

### 12.5 Default.

- (a) Wyeth-Ayerst. Upon the Default by Wyeth-Ayerst under this Agreement, Neurocrine may notify Wyeth-Ayerst of such Default and require that Wyeth-Ayerst cure such Default within [\*\*\*], provided, however, that if such Default is not susceptible of cure within [\*\*\*] period and Wyeth-Ayerst uses its Commercially Reasonable Efforts to cure such default, such [\*\*\*] period shall be extended to [\*\*\*]. In the event Wyeth-Ayerst shall not have cured the Default at the end of the period specified in the preceding sentence, Neurocrine may upon written notice to Wyeth-Ayerst terminate this Agreement and upon such termination:
  - (i) all licenses granted by Neurocrine to Wyeth-Ayerst herein will revert to Neurocrine:
  - (ii) Wyeth-Ayerst will satisfy its minimum Research Funding commitment hereunder [\*\*\*] to the extent not previously satisfied;
  - (iii) Wyeth-Ayerst will disclose to Neurocrine all material Research Program research, pre-clinical and clinical data on Hits, Lead Compounds and Collaboration Products generated prior to the date of termination of this Agreement, provided such data are reasonably available to Wyeth-Ayerst and Neurocrine thereafter shall have the right to use such data, at its own risk and expense, to develop Compounds [\*\*\*] which [\*\*\*];
  - (iv) Wyeth-Ayerst will assign (or, if the filing
     [\*\*\*] grant a right of cross reference) to
     Neurocrine all Regulatory Filings relating
     to Compounds designated as Lead Compounds
     and/or Collaboration Products prior to the
     date of termination of the Agreement (other
     than Lead Compounds and/or Collaboration
     Products that are [\*\*\*] in so far as such
     Regulatory Filings relate [\*\*\*] in which
     [\*\*\*];
  - (v) Wyeth-Ayerst will grant to Neurocrine a

perpetual, irrevocable, exclusive, royalty-free, fully-paid, worldwide license under [\*\*\*] to make, have made, use, import, market, offer for sale and sell in the Field of Use, Compounds including Compounds designated as Lead Compounds and/or Collaboration Products prior to the date of termination of this Agreement [\*\*\*] only [\*\*\*] in which [\*\*\*];

- (vi) Wyeth-Ayerst will grant to Neurocrine an exclusive, worldwide license under [\*\*\*] to make, have made, use, import, market, offer for sale and sell in the Field of Use only [\*\*\*] in which [\*\*\*] which have been designated as Lead Compounds and/or Collaboration Products prior to the date of termination of this Agreement, such license to be on commercially reasonable terms and conditions to be mutually agreed by the Parties including provision of payments intended to reflect both Parties' investment and opportunity in such Compounds and royalties on net sales of [\*\*\*] Royalties payable by Wyeth-Ayerst to Neurocrine hereunder provided, however, that Wyeth-Ayerst shall have no obligation to negotiate or grant any license with respect to any [\*\*\*]
- (vii) upon the grant of the licenses set forth in
   (vi) above, Wyeth-Ayerst will assign (or, if
   the filing is not [\*\*\*] in which [\*\*\*] grant
   a right of cross reference) to Neurocrine
   all Regulatory Filings on the Wyeth-Ayerst
   Compounds that are the subject of the
   license in so far as such Regulatory Filings
   relates [\*\*\*] in which [\*\*\*]; and
- (viii) Wyeth-Ayerst shall remain free to develop and/or sublicense [\*\*\*] provided, however, in no event will Wyeth-Ayerst commercialize or sublicense Third Parties to commercialize any [\*\*\*] designated as Lead Compounds or Collaboration Products prior to the date of termination of this Agreement (a) for [\*\*\*] in which [\*\*\*] and (b) if the identification, continued development and commercialization of such Compound utilizes Neurocrine Technology.
- (b) Neurocrine. Upon the Default by Neurocrine under this Agreement, Wyeth-Ayerst may notify Neurocrine of such Default and require that Neurocrine cure such Default within [\*\*\*], provided, however, that if such Default is not susceptible of cure within such [\*\*\*] period and Neurocrine uses its Commercially Reasonable Efforts to cure such default, such [\*\*\*] period shall be extended to [\*\*\*]. In the event Neurocrine shall not have cured the Default within the period specified in the preceding sentence, Wyeth-Ayerst may upon written notice to Neurocrine elect to terminate this Agreement and upon such termination:
  - (i) Neurocrine will grant to Wyeth-Ayerst a perpetual, irrevocable, non-exclusive, royalty-free, fully paid, worldwide license under the Neurocrine Transporter Technology to make, have made, use, import, market, offer for sale and sell in the Field of Use, Compounds (other than Neurocrine Compounds) which [\*\*\*]
  - (ii) Neurocrine will grant to Wyeth-Ayerst a perpetual, irrevocable, exclusive, royalty-free, fully paid, worldwide license under the Neurocrine Technology and Neurocrine's interest in the Joint Technology to make, have made, use, import, market, offer for sale and sell in the Field of Use, Compounds (other than Neurocrine Compounds), only [\*\*\*] in which [\*\*\*]
  - (iii) Neurocrine will grant to Wyeth-Ayerst an exclusive, royalty-free, worldwide license under the Neurocrine Technology and Neurocrine's interest in the Joint Technology to develop, make, have made, use, import, market, offer for sale and sell in the Field of Use, Neurocrine Compounds which have been designated as Lead Compounds and/or Collaboration Products prior to the date of termination of this Agreement only [\*\*\*].
- 12.6 Bankruptcy. Each party may, in addition to any other remedies available to it by law or in equity, exercise the rights set forth below by written notice to the other Party (the "Insolvent Party"), in the event the Insolvent Party shall have become insolvent or bankrupt, or shall

have made an assignment for the benefit of its creditors, or there shall have been appointed a trustee or receiver of the Insolvent Party or for all or a substantial part of its property, or any case or proceeding shall have been commenced or other action taken by or against the Insolvent Party in bankruptcy or seeking reorganization, readjustment of its debts or any other relief under any bankruptcy, insolvency, reorganization or other similar act or law of any jurisdiction now or hereafter in effect, or there shall have been issued a warrant of attachment, execution, distraint or similar process against any substantial part of the property of the Insolvent Party, and any such event shall have continued for sixty (60) days undismissed, unbonded and undischarged. All rights and licenses granted under or pursuant to this Agreement by Neurocrine and Wyeth-Ayerst are, and shall otherwise be deemed to be, for purposes of Section 365 (n) of the U.S. Bankruptcy Code, licenses of rights to "intellectual property" as defined under Section 101 of the U.S. Bankruptcy Code. The Parties agree that the Parties as licensees of such rights under this Agreement, shall retain and may fully exercise all of their rights and elections under the U.S. Bankruptcy Code. The Parties further agree that, in the event of the commencement of a bankruptcy proceeding by or against either Party under the U.S. Bankruptcy Code, the other Party shall be entitled to a complete duplicate of (or complete access to, as appropriate) any such intellectual property and all embodiments of such intellectual property, and same, if not already in the their possession, shall be promptly delivered to them (i) upon any such commencement of a bankruptcy proceeding upon its written request therefor, unless the Party subject to such proceeding elects to continue to perform all of their obligations under this Agreement or (ii) if not delivered under (i) above, upon the rejection of this Agreement by or on behalf of the Party subject to such proceeding upon written request therefor by the other Party.

- (a) Neurocrine. In the event Neurocrine shall be an Insolvent Party, Wyeth-Ayerst:
  - (i) may terminate the Research Program; and/or
  - (ii) keep this Agreement in full force and effect and retain all licenses granted by Neurocrine to Wyeth-Ayerst herein to make, have made, use, import, market, offer for sale and sell Lead Compounds and Collaboration Products in the Field of Use, subject to the payment to Neurocrine of the License Fees and Royalties set forth above.
- (b) Wyeth-Ayerst. In the event Wyeth-Ayerst shall be an Insolvent Party, Neurocrine may, to the extent permitted by applicable law, terminate this Agreement and all licenses granted by Neurocrine to Wyeth-Ayerst herein will revert to Neurocrine and:
  - (i) Wyeth-Ayerst will disclose to Neurocrine all material Research Program research, pre-clinical and clinical data on Hits, Lead Compounds and Collaboration Products generated prior to the date of termination provided such data are reasonably available to Wyeth-Ayerst and Neurocrine thereafter shall have the right to use such data, at its own risk and expense, to develop Compounds [\*\*\*] which [\*\*\*]
  - (ii) Wyeth-Ayerst will assign (or, if the filing is not [\*\*\*] in which [\*\*\*] grant a right of cross reference) to Neurocrine all Regulatory Filings relating to Lead Compounds and/or Collaboration Products (other than Lead Compounds and/or Collaboration Products [\*\*\*]) in so far as such Regulatory Filings relate [\*\*\*] in which [\*\*\*];
  - (iii) Wyeth-Ayerst will grant to Neurocrine a perpetual, irrevocable, exclusive, royalty-free, fully-paid, worldwide license [\*\*\*] to make, have made, use, import, market, offer for sale and sell in the Field of Use, Compounds ([\*\*\*]) which [\*\*\*];
  - (iv) Wyeth-Ayerst will grant to Neurocrine, a perpetual, irrevocable, exclusive, royalty free, fully-paid, worldwide license [\*\*\*] to make, have made, use, import, market, offer for sale and sell in the Field of Use, Neurocrine Compounds designated as Lead Compounds and/or Collaboration Products prior to the date of termination of this Agreement for [\*\*\*] in which [\*\*\*];
  - (v) Wyeth-Ayerst will grant to Neurocrine an exclusive, worldwide license under [\*\*\*] to make, have made, use, import, market, offer for sale and sell in the Field of Use, [\*\*\*] which have been designated as Lead Compounds and/or Collaboration Products prior to the date of termination of this Agreement for [\*\*\*] in which [\*\*\*], such license to be on commercially reasonable terms and conditions mutually agreed by the Parties including provision of payments intended to reflect both Parties' investment and opportunity in such Compounds and royalties on net sales of such [\*\*\*] Royalties and License Fees payable by Wyeth-Ayerst to Neurocrine hereunder and upon the grant of such license, Wyeth-Ayerst will assign to

Neurocrine all Regulatory Filings on [\*\*\*] which have been designated as Lead Compounds and/or Collaboration Products prior to the date of termination of this Agreement.

- 12.7 Acquisition. Upon the Acquisition of Neurocrine by a Third Party (a) such that Neurocrine [\*\*\*], (b) such that Neurocrine [\*\*\*], or (c) who is [\*\*\*], Wyeth-Ayerst shall have the right at any time on or before [\*\*\*] following such the completion of such Acquisition to elect one or more of the following:
  - (a) terminate the Research Program;
  - (b) terminate this Agreement; or
  - (c) keep this Agreement in full force and effect and retain all licenses granted by Neurocrine to Wyeth-Ayerst herein to make, have made, use, sell and import Lead Compounds and Collaboration Products, in the Field of Use, subject to the payment to Neurocrine of the License Fees and Royalties set forth above.
- 12.8 Liabilities. Termination of this Agreement shall not release either Party from any obligation or liability which shall have accrued at the time of termination, or preclude either Party from pursuing all rights at law and in equity with respect to any Default under this Agreement. Notwithstanding the foregoing, neither Party will be liable for punitive, exemplary or consequential damages incurred by the other Party arising out of any Default under this Agreement.
- Disclaimer. WITH RESPECT TO ANY DATA, INFORMATION OR INTELLECTUAL PROPERTY THAT EITHER PARTY BECOMES OBLIGATED TO TRANSFER TO THE OTHER UNDER THIS ARTICLE TWELVE, THE TRANSFERING PARTY MAKES NO REPRESENTATIONS AND EXPRESSLY DISCLAIMS AND MAKES NO WARRANTIES OF ANY KIND, WRITTEN OR ORAL, EXPRESS OR IMPLIED, INCLUDING, WITHOUT LIMITATION ANY WARRANTIES OF MERCHANTABILITY OR FITNESS FOR A PARTICULAR PURPOSE, OR THAT ANY SUCH INFORMATION, DATA OR INTELLECTUAL PROPERTY IS ACCURATE OR COMPLETE OR CAN BE USED BY THE RECEIVING PARTY WITHOUT INFRINGING THE INTELLECTUAL PROPERTY RIGHTS OF ANY THIRD PARTY.

## ARTICLE THIRTEEN INTELLECTUAL PROPERTY

- Inventions. Each Party shall own Patent Rights claiming inventions made by its employees or agents in the performance of such Party's obligations under this Agreement (respectively, "Neurocrine Inventions" and "Wyeth-Ayerst Inventions") and both Parties shall jointly own inventions made jointly by employees or agents of both Parties in the performance of their obligations hereunder ("Joint Inventions"). Inventorship shall be determined in accordance with United States laws of inventorship.
- 13.2 Patent Prosecution.
  - (a) Wyeth-Ayerst Inventions and Collaboration Products.
    Wyeth-Ayerst, at its expense, shall use Commercially
    Reasonable Efforts to prepare, file, prosecute, and maintain
    worldwide (i) Patent Rights relating to Wyeth-Ayerst
    Inventions and (ii) Patent Rights claiming Lead Compounds
    and/or Collaboration Products exclusively licensed to
    Wyeth-Ayerst hereunder.
  - (b) OHSU Licensed Patent Rights. Consistent with the terms and conditions of the OHSU Agreement, OHSU shall be responsible for preparation, filing, prosecution and maintenance of Patent Rights relating to the Licensed Patent Rights (as defined in the OSHU Agreement) included in the Collaboration Technology. Wyeth-Ayerst and Neurocrine will [\*\*\*] after the Effective Date in connection with the preparation, filing, prosecution and maintenance of such Patent Rights. Wyeth-Ayerst shall pay to Neurocrine its share of such expenses within thirty (30) days after Wyeth-Ayerst's receipt from Neurocrine of an invoice therefor, which invoice shall be accompanied by supporting documentation showing, in reasonable detail, the expenses so incurred.
  - (c) Neurocrine Inventions. Neurocrine, [\*\*\*], will use Commercially Reasonable Efforts to prepare, file, prosecute, and maintain worldwide Patent Rights relating to Neurocrine Inventions.
  - (d) Joint Inventions. Wyeth-Ayerst, [\*\*\*], shall use Commercially Reasonable Efforts to prepare, file, prosecute, and maintain worldwide Patent Rights relating to Joint Inventions.
- 13.3 Enforcement of Patent Rights.
  - (a) Wyeth-Ayerst Inventions. Wyeth-Ayerst shall have the sole right but not the obligation, in its own name and at its own expense, to enforce Patent Rights relating to Wyeth-Ayerst Inventions or Wyeth-Ayerst Technology against any Third Party suspected of infringing a claim of such a Patent Right.
  - (b) Neurocrine Inventions and Joint Inventions. Wyeth-Ayerst shall have the first right, but not the obligation, in its own name, to enforce Patent Rights relating to Neurocrine Inventions and

Joint Inventions, against any Third Party suspected of infringing a claim of such a Patent Right. In the event Wyeth-Ayerst shall not elect to enforce any Patent Right relating to a Neurocrine Invention or Joint Invention, Neurocrine shall have the right to do so. The Party electing to enforce such Patent Rights (the "Enforcing Party") shall have exclusive control over the conduct of any such proceedings, including the right to settle or compromise such proceedings consistent with Wyeth-Ayerst's licenses hereunder, provided, however, that the Enforcing Party may not settle or compromise any such action in a manner which diminishes the Patent Rights relating to any Neurocrine Inventions without Neurocrine's consent or Joint Inventions without the consent of both Parties or which would impose any financial obligation on the other Party without such other Party's consent. The expenses of any proceeding the Enforcing Party initiates, including lawyers' fees and costs, shall be borne by the Enforcing Party, provided, however, that the other Party (the "Non-enforcing Party") may elect to pay [\*\*\*] of all such expenses. The Non-enforcing Party will cooperate fully with the Enforcing Party in such action upon request by the Enforcing Party. In the event the Non-enforcing Party has not elected [\*\*\*], any award or recovery paid to the Enforcing Party by a Third Party as a result of such patent infringement proceedings (whether by way of settlement or otherwise) shall first be applied toward reimbursement of legal fees, costs and expenses incurred by the Enforcing Party, and from the remainder, if any, Wyeth-Ayerst in the event Wyeth-Ayerst shall be the Enforcing Party shall pay to Neurocrine (or Neurocrine shall retain in the event Neurocrine shall be the Enforcing Party) an amount equal to the applicable Royalty rate set forth in Article Nine as applied to the remainder as rate set forth in Article Nine as applied to the remainder as though such remainder were added to Net Sales in the year in which the recovery is made. In the event the Non-enforcing Party [\*\*\*], such award or recovery paid to the Enforcing Party shall first be applied toward reimbursement of legal fees, costs and expenses incurred by the Parties (in proportion to expenses incurred), and the remainder, if any, shall be divided equally between the Parties.

- (c) OHSU Licensed Patent Rights. Wyeth-Ayerst, as Neurocrine's exclusive sublicensee of certain Patent Rights included in the OHSU Licensed Patent Rights (as defined in the OHSU Agreement), shall have with respect to patent enforcement of Patent Rights exclusively licensed to Wyeth-Ayerst hereunder, the rights of an exclusive sublicensee under Article Eleven of the OHSU Agreement.
- (d) Neurocrine Technology. Neurocrine shall have the sole right but not the obligation, in its own name and at its own expense, to enforce Patent Rights relating to Neurocrine Technology (other than Neurocrine Inventions and OHSU Licensed Patent Rights (as defined in the OHSU Agreement)) against any Third Party suspected of infringing a claim of such a Patent Right.

### 13.4 Infringement Defense.

- (a) Wyeth-Ayerst. Wyeth-Ayerst shall have the right, but not the obligation, to defend and control any suit against any of Wyeth-Ayerst, Wyeth-Ayerst's Affiliates or sublicensees, alleging infringement of any patent or other intellectual property right of a Third Party arising out of the manufacture, use, sale, offer to sell or importation of a Collaboration Product by Wyeth-Ayerst, Wyeth-Ayerst's Affiliates or sublicensees. Wyeth-Ayerst shall be responsible for the costs and expenses, including lawyer's fees and costs, associated with any suit or action, Wyeth-Ayerst and Neurocrine will consult with one another and cooperate in the defense of any such action. If Wyeth-Ayerst finds it necessary or desirable to join Neurocrine as a party to any such action, Neurocrine will execute all papers and perform such acts as shall be reasonably required, at Wyeth-Ayerst expense. In the event the patent claim of any Third Party is held in a final and unappealable order of a court to be valid and infringed, or if Wyeth-Ayerst enters into a settlement of such proceedings, Wyeth-Ayerst shall pay the full amount of any damages and/or settlement amounts due to such Third Party, provided, however, [\*\*\*].
- (b) OHSU Licensed Patent Rights. Wyeth-Ayerst, as Neurocrine's exclusive sublicensee of certain Patent Rights included in the OHSU Licensed Patent Rights (as defined in the OHSU Agreement), shall have with respect to infringement defense relating to Licensed Patent Rights (as defined in the OHSU Agreement) exclusively licensed to Wyeth-Ayerst hereunder, the rights of an exclusive sublicensee under Article Eleven of the OHSU Agreement.
- Cooperation Between the Parties. The Parties recognize that the designation of a Compound as a Lead Compound or Collaboration Product may impact the designation of the Party responsible for such invention under this Article Thirteen. The Parties anticipate that patent applications may be filed on Compounds prior to designation of the Compound as Lead Compound or Collaboration Product, and agree to co-operate in deciding how to allocate responsibilities and expenses in the event designation of a Compound as Lead Compound or Collaboration Product impacts responsibilities under this Article Thirteen. In

addition, the Parties agree to cooperate with each other in the preparation, filing, prosecuting, maintenance, defense and enforcement of Patent Rights included in Collaboration Technology licensed hereunder. In any action taken in the prosecution of, or in the defense of an action by a Third Party related to patent invalidity or non-patentability of any patent application or patent claiming Collaboration Technology licensed hereunder, neither Party shall admit the invalidity or non-patentability of any Patent Right or take any other action that may diminish Patent Rights within Collaboration Technology licensed hereunder without the other Party's prior written consent. Wyeth-Ayerst agrees to provide Neurocrine with sufficient time to review, comment and consult on all patent applications and patents and all correspondence to and from the various patent offices, including, but not limited to, proposed responses, interferences and oppositions, claiming Neurocrine Inventions, Joint Inventions and Wyeth-Ayerst Inventions. The Parties agree to cooperate with each other and to use best efforts to ensure the cooperation of any of their respective personnel and licensee(s) or licensor(s) as might reasonably be requested in any such matters. be requested in any such matters, and shall sign any necessary legal papers and provide the prosecuting party with data or other information in support thereof. The Parties will confer on what action to take with respect to the defense of infringement proceedings naming both Wyeth-Ayerst and Neurocrine or in proceedings to enforce patents claiming Collaboration Technology licensed hereunder against a Third Party. If the Parties cannot agree on the course of action to be taken in the filing, prosecution, maintenance, or enforcement of any Joint Invention or Wyeth-Ayerst Invention, Wyeth-Ayerst's decisions shall control. If the Parties cannot agree on the course of action to be taken in the filing, prosecution, maintenance, or enforcement of Neurocrine Invention, Neurocrine's decisions shall control.

#### ARTICLE FOURTEEN **MISCELLANEOUS**

Disputes. If the Parties are unable to resolve a dispute among them informally, Wyeth-Ayerst and Neurocrine, by written notice to the other, may have such dispute referred to their respective executive 14.1 officers designated for attempted resolution by good faith negotiations:

> For Wyeth-Ayerst: President of Wyeth-Ayerst Research for development issues

President Wyeth-Ayerst Global Pharmaceuticals

for commercialization issues

President and Chief Executive Officer For Neurocrine:

Any such dispute shall be submitted to the above-designated executive officers no later than thirty (30) days following such request by either Wyeth-Ayerst or Neurocrine. In the event the designated executive officers are not able to resolve any such dispute within [\*\*\*] after submission of the dispute to such executive officers, Wyeth-Ayerst or Neurocrine, as the case may be, may pursue what ever measures are legally available to them to resolve such dispute. All negotiations pursuant to this Section 14.1 shall be treated as compromise and settlement negotiations. Nothing said or disclosed, nor any document produced, in the course of such negotiations which is not otherwise independently discoverable shall be offered or received as evidence or used for impeachment or for any other purpose in any current or future arbitration or litigation.

- Assignment. Neither this Agreement nor any interest hereunder shall be assignable by either Party without the prior written consent of the other Party, except for assignment by operation of law in connection with a merger of a Party with or into another Person. This Agreement shall be binding upon the successors and permitted assigns of the Parties and the name of a Party appearing herein shall be deemed to include the names of such Party's successors and permitted assigns to the extent necessary to carry out the intent of this Agreement. Any assignment not in accordance with this Section 14.2 shall be void. 14.2 assignment not in accordance with this Section 14.2 shall be void.
- 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 14.3 of the Agreement.
- Force Majeure. No Party shall be liable to the other Party for loss or 14.4 damages or shall have any right to terminate this Agreement for any default or delay attributable to any Force Majeure, if the Party affected shall give prompt notice of any such cause to the other Party. The Party giving such notice shall thereupon be excused from such of its obligations hereunder as it is thereby disabled from performing for so long as it is so disabled, provided, however, that such affected Party commences and continues to use its Commercially Reasonable Efforts to cure such cause.
- 14.5 Correspondence and Notices.
  - (a) Ordinary Notices. Correspondence, reports, documentation, and any other communication in writing between the Parties in the any other communication in writing between the Parties in the course of ordinary implementation of this Agreement shall be delivered by hand, sent by facsimile transmission (receipt verified), or by airmail to the employee or representative of the other Party who is designated by such other Party to receive such written communication.

(b) Extraordinary Notices. Extraordinary notices and other communications hereunder (including, without limitation, any notice of force majeure, breach, termination, change of address, exercise of rights to negotiate additional agreements, etc.) shall be in writing and shall be deemed given if delivered personally or by facsimile transmission (receipt verified), mailed by registered or certified mail (return receipt requested), postage prepaid, or sent by nationally recognized express courier service, to the Parties at the following addresses (or at such other address for a Party as shall be specified by like notice, provided, however, that notices of a change of address shall be effective only upon receipt thereof):

All correspondence to Wyeth-Ayerst shall be addressed as follows:

Wyeth-Ayerst Laboratories 555 East Lancaster Avenue St. Davids, Pennsylvania 19087

Attn: Senior Vice President, Global Business Development

Fax: (610) 688-9498

with a copy to: American Home Products Corporation 5 Giralda Farms Madison, New Jersey 07940

Madison, New Jersey 07940 Attn: Senior Vice President and General Counsel

Fax: (973) 660-7156

All correspondence to Neurocrine shall be addressed as follows:

Neurocrine Biosciences, Inc. 10555 Science Park Road San Diego, California 9211-1102 Attn: Director Product Licensing Fax: 619-658-7602

> with a copy to: Neurocrine Biosciences, Inc. 10555 Science Park Road San Diego, California 9211-1102 Attn: Corporate Secretary Fax: 619-658-7605

- 14.6 Amendment. No amendment, modification or supplement of any provision of this Agreement shall be valid or effective unless made in writing and signed by a duly authorized officer of each Party.
- 14.7 Waiver. No provision of the Agreement shall be waived by any act, omission or knowledge of a Party or its agents or employees except by an instrument in writing expressly waiving such provision and signed by a duly authorized officer of the waiving Party.
- 14.8 Counterparts. This Agreement may be executed in any number of counterparts, each of which need not contain the signature of more than one Party but all such counterparts taken together shall constitute one and the same agreement.
- 14.9 Descriptive Headings. The descriptive headings of this Agreement are for convenience only, and shall be of no force or effect in construing or interpreting any of the provisions of this Agreement.
- 14.10 Governing Law. This Agreement shall be governed by and interpreted in accordance with the substantive laws of the State of Delaware (without regard to conflict of law principles) and the Parties hereby submit to the exclusive jurisdiction of the federal courts of the state of California.
- 14.11 Severability. In the event that any clause or portion thereof in this Agreement is for any reason held to be invalid, illegal or unenforceable, the same shall not affect any other portion of this Agreement, as it is the intent of the Parties that this Agreement shall be construed in such fashion as to maintain its existence, validity and enforceability to the greatest extent possible. In any such event, this Agreement shall be construed as if such clause of portion thereof had never been contained in this Agreement, and there shall be deemed substituted therefor such provision as will most nearly carry out the intent of the Parties as expressed in this Agreement to the fullest extent permitted by applicable law unless doing so would have the effect of materially altering the right and obligations of the Parties in which event this Agreement shall terminate and all the rights and obligations granted to the Parties hereunder shall cease and be of no further force and effect.
- 14.12 Entire Agreement of the Parties. This Agreement constitutes and contains the complete, final and exclusive understanding and agreement of the Parties and cancels and supersedes any and all prior negotiations, correspondence, understandings and agreements including, without limitation, the Prior Agreement, whether oral or written, among the Parties respecting the subject matter hereof and thereof.
- 14.13 Independent Contractors. The relationship between Wyeth-Ayerst and Neurocrine created by this Agreement is one of independent contractors and neither Party shall have the power or authority to bind or obligate

the other except as expressly set forth in this Agreement.

- 14.14 No Trademark Rights. Expect as otherwise provided herein, no right, express or implied, is granted by this Agreement to use in any manner the name "Neurocrine Biosciences" "Wyeth-Ayerst," or any other trade name or trademark of the other Party or its Affiliates in connection with the performance of this Agreement.
- 14.15 Accrued Rights; Surviving Obligations. Unless explicitly provided otherwise in this Agreement, termination, relinquishment or expiration of the Agreement for any reason shall be without prejudice to any rights which shall have accrued to the benefit to any Party prior to such termination, relinquishment or expiration, including damages arising from any breach hereunder. Such termination, relinquishment or expiration shall not relieve any Party from obligations which are expressly indicated to survive termination or expiration of the Agreement, including, without limitation, those obligations set forth in Articles Ten, Eleven and Twelve and Sections 5.8, 5.9, 9.4, 14.1 and 14.5 hereof.
- 14.16 Export. Notwithstanding anything to the contrary set forth herein, all obligations of Neurocrine and Wyeth-Ayerst are subject to prior compliance with United States and foreign export regulations and such other United States and foreign laws and regulations as may be applicable and to obtaining all necessary approvals required by applicable agencies of the governments of the United States and foreign jurisdictions. Neurocrine and Wyeth-Ayerst will co-operate with one another and provide assistance to one another as reasonably necessary to obtain any required approvals.

IN WITNESS WHEREOF, duly authorized representatives of the Parties have duly executed this Agreement to be effective as of the Effective Date.

AMERICAN HOME PRODUCTS CORPORATION, acting through its WYETH-AYERST LABORATORIES DIVISION

NEUROCRINE BIOSCIENCES, INC.

By /s/ Egon Berg By: /s/ Gary Lyons
Name: Egon Berg Name: Gary Lyons
Title: Vice President & Title: President &

Associate General Counsel Chief Executive Officer

Date: 03/02/98 Date: 03/02/98

EXHIBIT A
TRANSPORTERS
[\*\*\*]

EXHIBIT B LEAD COMPOUND [\*\*\*]

EXHIBIT C
PATENT RIGHTS
[\*\*\*]

EXHIBIT D
OHSU AGREEMENT
[\*\*\*]

EXHIBIT E
THIRD PARTY PATENTS
[\*\*\*]

EXHIBIT F
OTHER NEUROCRINE OBLIGATIONS
[\*\*\*]

### EMPLOYMENT AGREEMENT

THIS AGREEMENT, dated as of October 1, 1998, is made by and between NEUROCRINE BIOSCIENCES. INC., a Delaware corporation (hereinafter the "Company"), and Margaret Valeur-Jensen (hereinafter "Executive").

#### RECITALS

WHEREAS, the Company and Executive wish to set forth in this Agreement the terms and conditions under which Executive is to be employed by the Company on and after the date hereof; and

NOW, THEREFORE, the Company and Executive, in consideration of the mutual promises set forth herein, agree as follows:

#### ARTICLE 1

#### TERM OF AGREEMENT

- 1.1 Commencement Date. Executive's fulltime employment with the Company under this Agreement shall commence as of January 4, 1999 ("Commencement Date") and this Agreement shall expire after a period of three (3) years from the Commencement Date, unless terminated earlier pursuant to Article 6. It is understood the Executive shall be available to the Company on a part-time basis during the period October 1, 1998 to December 31, 1998.
- 1.2 Renewal. The term of this Agreement shall be automatically renewed for successive, additional three (3) year terms unless either party delivers written notice to the other at least ninety (90) days prior to the expiration date of this Agreement of an intention to terminate this Agreement or to renew it for a term of less than three (3) years but not less than (1) year. If the term of this Agreement is renewed for a term of less than three (3) years, then thereafter the term of this Agreement shall be automatically renewed for successive, additional identical terms unless either party delivers a written notice to the other at least ninety (90) days prior to a terminate date of this Agreement of an intention to terminate this Agreement or to renew it for a different term of not less than one (1) year.

#### ARTICLE 2

#### **EMPLOYMENT DUTIES**

- 2.1 Title/Responsibilities. Executive hereby accepts employment with the Company pursuant to the terms and conditions hereof. Executive agrees to serve the Company in the position of Vice President General Counsel and Corporate Secretary. Executive shall have the powers and duties commensurate with such position, including but not limited to hiring personnel necessary to carry out the responsibilities for such position as set forth in the annual business plan approved by the Board of Directors.
- 2.2 Full Time Attention. Executive shall devote her best efforts and her full business time and attention to the performance of the services customarily incident to such office and to such other services as the President or Board may reasonably request.
- 2.3 Other Activities. Except upon the prior written consent of the President & Chief Executive Officer, Executive shall not during the period of employment engage, directly or indirectly, in any other business activity (whether or not pursued for pecuniary advantage) that is or may be competitive with, or that might place her in a competing position to that of the Company or any other corporation or entity that directly or indirectly controls, is controlled by, or is under common control with the Company (an "Affiliated Company"), provided that Executive may own less than two percent of the outstanding securities of any such publicly traded competing corporation. It is understood Executive will enter into a Consulting Agreement with the Executive's former employer, Amgen, Inc. Prior to execution of such Agreement, the Executive must receive approval from the President & Chief Executive Officer, approval which will not be unreasonably withheld.

### ARTICLE 3

### COMPENSATION

- 3.1 Base Salary. Executive shall receive a Base Salary at an annual rate of two hundred twelve thousand dollars (\$212,000), payable semi-monthly in equal installments in accordance with the Company's normal payroll practices. The Company's Board of Directors shall provide Executive with annual performance reviews, and, thereafter, Executive shall be entitled to such increase in Base Salary as the Board of Directors may from time to time establish in its sole discretion. During the period October 1, 1998 to December 31, 1998, Executive shall receive a Salary of \$5,000 for services performed for or on behalf of the Company on the Company's premises.
- 3.2 Incentive Bonus. In addition to any other bonus Executive shall be awarded by the Company's Board of Directors, the Company shall pay Executive a bonus payment of up to fifty thousand dollars (\$50,000) annually based upon achievement by the Company against six to eight impact goals approved by the Board of Directors annually. Such goals shall be set forth in writing by the Board within ninety (90) days after the start of the Company's fiscal year and a copy shall be delivered to Executive within fifteen (15) days thereafter. The Board of Directors shall, in their sole discretion, determine whether such impact goals have been obtained.
  - 3.3 Equity. The Executive will receive a nonqualified stock option to

purchase one hundred fifteen thousand (115,000) shares of the Company's common stock with an exercise price of \$5.0625 per share, representing the Company's market price at the time of Board approval. Such option shall vest over a four-year period with 25% of such vesting occurring on December 31, 1999 and 1/48 per month thereafter in accordance with the terms of the Company's 1992 Incentive Stock Incentive Plan, as amended.

3.3 Withholdings. All compensation and benefits payable to Executive hereunder and the Agreement shall be subject to all federal, state, local and other withholdings and similar taxes and payments required by applicable law.

#### ARTICLE 4

#### EXPENSE ALLOWANCES AND FRINGE BENEFITS

- 4.1 Vacation. Executive shall be entitled to the greater of three (3) weeks of annual paid vacation or the amount of annual paid vacation to which Executive may become entitled under the terms of Company's vacation policy for employees during the term of this Agreement.
- 4.2 Benefits. During the term of this Agreement, the Company shall also provide Executive with the usual health insurance benefits it generally provides to its other senior management employees. As Executive becomes eligible in accordance with criteria to be adopted by the Company, the Company shall provide Executive with the right to participate in and to receive benefit from life, accident, disability, medical, pension, bonus, stock, profit-sharing and savings plans and similar benefits made available generally to employees of the Company as such plans and benefits may be adopted by the Company. The amount and extent of benefits to which Executive is entitled shall be governed by the specific benefit plan as it may be amended from time to time.
- 4.3 Relocation. The Company will pay for reasonable relocation expenses consisting of (i) out of pocket expenses directly related to selling your existing home, including customary real estate commissions and associated costs; (ii) reasonable house hunting expenses, temporary living expenses through March 1999 and duplicate mortgage payments, if required, through June 1999; (iii) customary closing costs and fees, including up to one and one half points (1.5%) of the mortgage financing amount related to the purchase of a new home; (iv) reasonable and customary moving expenses of household goods and personal property (including temporary storage) to San Diego, CA; (v) up to \$10,000 in other miscellaneous documented expenses. Relocation costs associated with items (i) through (iv) above will be tax equalized.
- 4.4 Loss on Sale: In the event that you sell your home to a bona fide purchaser in good faith at a gross price before deducting direct selling expenses or commissions (the "Sales Price"), less than your purchase price plus the cost of improvements (the "Purchase Price"), the Company will lend you the lesser of the difference between the Sales Price and Purchase Price or \$50,000, with such loan to be evidenced by a promissory note due and payable in the event of (a) the sale of stock options by the Employee (to the extent of the proceeds received by Employee in such sale), or (b) ninety (90) days following termination of your employment with the Company or (c) sale of your San Diego house. Fifty percent (50%) of the total amount of such loan shall be forgiven by the Company over a four (4) year period in four (4) equal installments on each of the first through fourth anniversary dates of the commencement of your full-time employment with the Company, provided that you are still employed by the Company on such date.

### ARTICLE 5

## CONFIDENTIALITY

- 5.1 Proprietary Information. Executive represents and warrants that he has previously executed and delivered to the Company the Company's standard Proprietary Information and Inventions Agreement in form acceptable to the Company's counsel.
- 5.2 Return of Property. All documents, records, apparatus, equipment and other physical property which is furnished to or obtained by Executive in the course of her employment with the Company shall be and remain the sole property of the Company. Executive agrees that, upon the termination of her employment, he shall return all such property (whether or not it pertains to Proprietary Information as defined in the Proprietary Information and Inventions Agreement), and agrees not to make or retain copies, reproductions or summaries of any such property.

# ARTICLE 6

## TERMINATION

- 6.1 By Death. The period of employment shall terminate automatically upon the death of Executive. In such event, the Company shall pay to Executive's beneficiaries or her estate, as the case may be, any accrued Base Salary, any bonus compensation to the extent earned, any vested deferred compensation (other than pension plan or profit-sharing plan benefits which will be paid in accordance with the applicable plan), any benefits under any plans of the Company in which Executive is a participant to the full extent of Executive's rights under such plans, any accrued vacation pay and any appropriate business expenses incurred by Executive in connection with her duties hereunder, all to the date of termination (collectively Accrued Compensation), but no other compensation or reimbursement of any kind, including, without limitation, severance compensation, and thereafter, the Company's obligations hereunder shall terminate.
- 6.2 By Disability. If Executive is prevented from properly performing her duties hereunder by reason of any physical or mental incapacity for a period of 120 consecutive days, or for 180 days in the aggregate in any 365-day period, then, to the extent permitted by law, the Company may terminate the employment

of Executive at such time. In such event, the Company shall pay to Executive all Accrued Compensation, and shall continue to pay to Executive the Base Salary until such time (but not more than 90 days following termination), as Executive shall become entitled to receive disability insurance payments under the disability insurance policy maintained by the Company, but no other compensation or reimbursement of any kind, including without limitation, severance compensation, and thereafter the Company's obligations hereunder shall terminate. Nothing in this Section shall affect Executive's rights under any disability plan in which he is a participant.

- 6.3 By Company for Cause. The Company may terminate the Executive's employment for Cause (as defined below) without liability at any time with or without advance notice to Executive. The Company shall pay Executive all Accrued Compensation, but no other compensation or reimbursement of any kind, including without limitation, severance compensation, and thereafter the Company's obligations hereunder shall terminate. Termination shall be for "Cause" in the event of the occurrence of any of the following: (a) any intentional action or intentional failure to act by Executive which was performed in bad faith and to the material detriment of the Company; (b) Executive intentionally refuses or intentionally fails to act in accordance with any lawful and proper direction or order of the Board; (c) Executive willfully and habitually neglects the duties of employment; or (d) Executive is convicted of a felony crime involving moral turpitude, provided that in the event that an of the foregoing events is capable of being cured, the Company shall provide written notice to Executive describing the nature of such event and Executive shall thereafter have ten (10) business days to cure such event.
- 6.4 Termination Without Cause. At any time, the Company may terminate the employment of Executive without liability other than as set forth below, for any reason not specified in Section 6.3 above, by giving thirty (30) days advance written notice to Executive. If the Company elects to terminate Executive pursuant to this Section 6.4, (a) the Company shall pay to Executive all Accrued Compensation (b) the Company shall continue to pay to Executive as provided herein Executive's Base Salary over the period equal to nine (9) months from the date of such termination as severance compensation, (c) if Executive's employment terminates in the second half of the Company's fiscal year, the Company shall make a lump sum payment to Executive in an amount equal to a pro rata portion of the Executive's annual actual cash incentive bonus for Company's fiscal year preceding the year of termination based on the number of completed months of Executive's employment in the fiscal year divided by nine (9); (d) the vesting of all outstanding stock options held by Executive shall be accelerated so that the amount of shares vested under such option shall equal that number of shares which would have been vested if the Executive had continued to render services to the Company for nine (9) continuous months after the date of her termination of employment; and (e) the Company shall pay all costs which the Company would otherwise have incurred to maintain all of Executive's health and welfare, and retirement benefits (either on the same or substantially equivalent terms and conditions) if the Executive had continued to render services to the Company for nine (9) continuous months after the date of her termination of employment. The Company shall have no further obligations to Executive other than those set forth in the preceding sentence. During the period when such Base Salary severance compensation is being paid to Executive, Executive shall not (i) engage, directly or indirectly, in providing services to any other business program or project that is competitive to a program or project being conducted by the Company or any Affiliated Company at the time of such employment termination (provided that Executive may own less than two percent (2%) of the outstanding securities of any publicly traded corporation), or (ii) hire, solicit, or attempt to solicit on behalf of himself or any other party or any employee or exclusive consultant of the Company. If the Company terminates this Agreement or the employment of Executive with the Company other than pursuant to Section 6.1, 6.2 or 6.3, then this section 6.4 shall apply.
- 6.5 Constructive Termination A Constructive Termination shall be deemed to be a termination of employment of Executive without cause pursuant to Section 6.4 For Purposes of this Agreement, a "Constructive Termination" means that the Executive voluntarily terminates her employment after any of the following are undertaken without Executive's express written consent:
  - (a) the assignment to Executive of any duties or responsibilities which result in any diminution or adverse change of Executive's position, status or circumstances of employment; or any removal of Executive from or any failure to re-elect Executive to any of such positions, except in connection with the termination of her employment for death, disability, retirement, fraud, misappropriation, embezzlement (or any other occurrence which constitutes "Cause" under section 6.3) or any other voluntary termination of employment by Executive other than a Constructive Termination;
  - (b) a reduction by the Company in Executive's annual Base Salary by greater than five percent (5%);
  - (c) a relocation of Executive or the Company's principal executive offices if Executive's principal office is at such offices, to a location more than forty (40) miles from the location at which Executive is then performing her duties, except for an opportunity to relocate which is accepted by Executive in writing;
  - (d) any  $\,$  material  $\,$  breach by the Company of any  $\,$  provision  $\,$  of this Agreement; or
  - (e) any failure by the Company to obtain the assumption of this Agreement by any successor or assign of the Company.
- 6.6 Termination Following Change in Control In the event of a non-renewal of this Agreement, a termination without Cause or a Constructive Termination within eighteen (18) months following a Change in Control, Executive shall receive the same benefits package as Executive would have received upon a termination without Cause (except that the payment of Base Salary shall be made

in the form of a lump sum) and in addition, the vesting of all outstanding stock options held by Executive shall be accelerated so that the options are immediately exercisable in full.

- 6.7 Change in Control. For purposes of this Agreement, a "Change in Control" shall have occurred if at any time during the term of Executive's employment hereunder, any of the following events shall occur:
  - (a) The Company is merged, or consolidated. or reorganized into or with another corporation or other legal person, and as a result of such merger, consolidation or reorganization less than 50% of the combined voting power of the then-outstanding securities of such corporation or person immediately after such transaction are held in the aggregate by the holders of voting securities of the Company immediately prior to such transaction;
  - (b) The Company sells all or substantially all of its assets or any other corporation or other legal person and thereafter, less than 50% of the combined voting power of the then-outstanding voting securities of the acquiring or consolidated entity are held in the aggregate by the holders of voting securities of the Company immediately prior to such sale;
  - (c) There is a report filed after the date of this Agreement on Schedule 13 D or schedule 14 D-1 (or any successor schedule, form or report), each as promulgated pursuant to the Securities Exchange Act of 1934 (the "Exchange Act") disclosing that any person (as the term "person" is used in Section 13(d)(3) or Section 14(d)(2) of the exchange Act) has become the beneficial owner (as the term beneficial owner is defined under Rule 13d-3 or any successor rule or regulation promulgated under the Exchange Act) representing 50% or more of the combined voting power of the then-outstanding voting securities of the Company;
  - (d) The Company shall file a report or proxy statement with the Securities and Exchange Commission pursuant to the Exchange Act disclosing in response to item 1 of Form 8-X thereunder or Item 5(f) of Schedule 14 A thereunder (or any successor schedule, form or report or item therein) that the change in control of the Company has or may have occurred or will or may occur in the future pursuant to any then-existing contract or transaction; or
  - (e) During any period of two consecutive years, individuals who at the beginning of any such period constitute the directors of the Company cease for any reason to constitute at least a majority thereof unless the election to the nomination for election by the Company's shareholders of each director of the Company first elected during such period was approved by a vote of at least two-thirds of the directors of the Company then still in office who were directors of the Company at the beginning of such period.
- 6.8 Termination by Executive. At any time, Executive may terminate her employment by giving thirty (30) days advance written notice to the Company. The Company shall pay Executive all Accrued Compensation, but no other compensation or reimbursement of any kind, including without limitation, severance compensation, and thereafter the Company's obligations hereunder shall terminate.
- 6.9 Mitigation Except as otherwise specifically provided herein, Executive shall not be required to mitigate the amount of any payment provided under this Agreement by seeking other employment or self-employment, nor shall the amount of any payment provided for under this Agreement be reduced by any compensation earned by Executive as a result of employment by another employer or through self-employment or by retirement benefits after the date of Executive's termination of employment from the Company.
- 6.10 Coordination If upon termination of employment, Executive becomes entitled to rights under other plans, contracts or arrangements entered into by the Company, this Agreement shall be coordinated with such other arrangements so that Executive's rights under this Agreement are not reduced, and that any payments under this Agreement offset the same types of payments otherwise provided under such other arrangements, but do not otherwise reduce any payments or benefits under such other arrangements to which Executive becomes entitled.

### ARTICLE 7

# GENERAL PROVISIONS

- 7.1 Governing law. The validity, interpretation, construction and performance of this Agreement and the rights of the parties thereunder shall be interpreted and enforced under California law without reference to principles of conflicts of laws. The parties expressly agree that inasmuch as the Company's headquarters and principal place of business are located in California, it is appropriate that California law govern this Agreement.
  - ${\it 7.2 Assignment; Successors Binding Agreement.}\\$
  - $7.2.1\,$  Executive may not assign, pledge or encumber her interest in this Agreement or any part thereof.
  - 7.2.2 The Company will require any successor (whether direct or indirect, by purchase, merger, consolidation or otherwise) to all or substantially all of the business and/or assets of the Company, by operation of law or by agreement in form and substance reasonably satisfactory to Executive, to assume and agree to perform this Agreement in the same manner and to the same extent that the Company would be required to perform it if no such succession had taken place.

- 7.2.3 This Agreement shall inure to the benefit of and be enforceable by Executive's personal or legal representatives, executors, administrators, successors, heirs, distributee, devisees and legatees. If Executive should die while any amount is at such time payable to her hereunder, all such amounts, unless otherwise provided herein, shall be paid in accordance with the terms of this Agreement to Executive's devisee, legates or other designee or, if there be no such designee, to her estate.
- 7.3 Certain Reduction of Payments In the event that any payment or benefit received or to be received by Executive under this Agreement would result in all or a portion of such payment to be subject to the excise tax on "golden parachute payments" under Section 4999 of the Internal Revenue Code of 1986, as amended (the "Code"), then Executive's payment shall be either (a) the full payment or (b) such lesser amount which would result in no portion of the payment being subject to excise tax under Section 4999 of the Code, whichever of the foregoing amounts, taking into account the applicable Federal, state and local employment taxes, income taxes, and the excise tax imposed by Section 4999 of the Code, results in the receipt by Executive on an after-tax basis, of the greatest amount of the payment notwithstanding that all or some portion of the payment may be taxable under Section 4999 of the Code.
- 7.4 Notice. For the purposes of this Agreement, notices and all other communications provided for in this Agreement shall be in writing and shall be deemed to have been duly given when delivered or mailed by certified or registered mail, return receipt requested, postage prepaid, addressed to the respective addresses set forth below or to such other address as either party may have furnished to the other in writing in accordance herewith, except that notice of change of address shall be effective only upon receipt.

To the Company:

Neurocrine Biosciences, Inc. 10555 Science Center Drive San Diego, CA 92121 Attn.: President & Chief Executive Officer

To Executive:

Ms. Margaret Valeur-Jensen 4507 South Lane Del Mar, CA 92014

- 7.5 Modification; Waiver; Entire Agreement. No provisions of this Agreement may be modified, waived or discharged unless such waiver, modification or discharge is agreed to in writing signed by Executive and such officer as may be specifically designated by the Board of the Company. No waiver by either party hereto at any time of any breach by the other party of, or compliance with, any condition or provision of this Agreement to be performed by such other party shall be deemed a waiver of similar or dissimilar provisions or conditions at the same or any prior or subsequent time. No agreements or representations, oral or otherwise, express or implied, with respect to the subject matter hereof have been made by either party which are not expressly set forth in this Agreement.
- 7.6 Validity. The invalidity or unenforceability of any provision of this Agreement shall not affect the validity or enforceability of any other provision of this Agreement, which shall remain in full force and effect.
- 7.7 Controlling Document. Except to the extent described in Section 6.10, in case of conflict between any of the terms and condition of this Agreement and the document herein referred to, the terms and conditions of this Agreement shall control.
- 7.8 Executive Acknowledgment. Executive acknowledges (a) that he has consulted with or has had the opportunity to consult with independent counsel of her own choice concerning this Agreement, and has been advised to do so by the Company, and (b) that he has read and understands the Agreement, is fully aware of its legal effect, and has entered into it freely based on her own judgment.

### 7.9 Remedies

- 7.9.1 Injunctive Relief. The parties agree that the services to be rendered by Executive hereunder are of a unique nature and that in the event of any breach or threatened breach of any of the covenants contained herein, the damage or imminent damage to the value and the goodwill of the Company's business will be irreparable and extremely difficult to estimate, making any remedy at law or in damages inadequate. Accordingly, the parties agree that the Company shall be entitled to injunctive relief against Executive in the event of any breach or threatened breach of any such provisions by Executive, in addition to any other relief (including damage) available to the Company under this Agreement or under law.
- 7.9.2 Exclusive. Both parties agree that the remedy specified in Section 7.9.1 above is not exclusive of any other remedy for the breach by Executive of the terms hereof.
- 7.10 Counterparts. This Agreement may be executed in one or more counterparts, all of which taken together shall constitute one and the same Agreement.
- 7.11 Prevailing Party Expenses. In the event that any action or proceeding is commenced to enforce the provisions of the Agreement, the court adjudicating such action or proceeding shall award to the prevailing party all costs and expenses thereof, including, but not limited to, all reasonable attorneys' fees, court costs, and all other related expenses.

Executed by the parties as of the day and year first above written.

EXECUTIVE

NEUROCRINE BIOSCIENCES, INC

By: /s/Margaret Valeur-Jensen Margaret Valeur-Jensen By: /s/Gary A. Lyons Gary A. Lyons President & Chief Executive Officer

#### EMPLOYMENT AGREEMENT

THIS AGREEMENT, dated as of January 1, 1998, is made by and between NEUROCRINE BIOSCIENCES. INC., a Delaware corporation (hereinafter the "Company"), and BRUCE CAMPBELL, Ph.D. (hereinafter "Executive").

### RECITALS

WHEREAS, the Company and Executive wish to set forth in this Agreement the terms and conditions under which Executive is to be employed by the Company on and after the date hereof; and

NOW, THEREFORE, the Company and Executive, in consideration of the mutual promises set forth herein, agree as follows:

#### ARTICLE 1

#### TERM OF AGREEMENT

- 1.1 Commencement Date. Executive's fulltime employment with the Company under this Agreement shall commence as of January 1, 1998 ("Commencement Date") and this Agreement shall expire after a period of three (3) years from the Commencement Date, unless terminated earlier pursuant to Article 6.
- 1.2 Renewal. The term of this Agreement shall be automatically renewed for successive, additional three (3) year terms unless either party delivers written notice to the other at least ninety (90) days prior to the expiration date of this Agreement of an intention to terminate this Agreement or to renew it for a term of less than three (3) years but not less than (1) year. If the term of this Agreement is renewed for a term of less than three (3) years, then thereafter the term of this Agreement shall be automatically renewed for successive, additional identical terms unless either party delivers a written notice to the other at least ninety (90) days prior to a terminate date of this Agreement of an intention to terminate this Agreement or to renew it for a different term of not less than one (1) year.

#### ARTICLE 2

#### EMPLOYMENT DUTIES

- 2.1 Title/Responsibilities. Executive hereby accepts employment with the Company pursuant to the terms and conditions hereof. Executive agrees to serve the Company in the position of Vice President Development. Executive shall have the powers and duties commensurate with such position, including but not limited to hiring personnel necessary to carry out the responsibilities for such position as set forth in the annual business plan approved by the Board of Directors.
- 2.2 Full Time Attention. Executive shall devote his best efforts and his full business time and attention to the performance of the services customarily incident to such office and to such other services as the President or Board may reasonably request.
- 2.3 Other Activities. Except upon the prior written consent of the President & Chief Executive Officer, Executive shall not during the period of employment engage, directly or indirectly, in any other business activity (whether or not pursued for pecuniary advantage) that is or may be competitive with, or that might place him in a competing position to that of the Company or any other corporation or entity that directly or indirectly controls, is controlled by, or is under common control with the Company (an "Affiliated Company"), provided that Executive may own less than two percent (2%) of the outstanding securities of any such publicly traded competing corporation.

### ARTICLE 3

### COMPENSATION

- 3.1 Base Salary. Executive shall receive a Base Salary at an annual rate of two hundred thousand dollars (200,000), payable semi-monthly in equal installments in accordance with the Company's normal payroll practices. The Company's Board of Directors shall provide Executive with annual performance reviews, and, thereafter, Executive shall be entitled to such increase in Base Salary as the Board of Directors may from time to time establish in its sole discretion. In addition, upon signing this Agreement, Executive will receive an initial bonus of twenty thousand dollars (\$20,000).
- 3.2 Incentive Bonus. In addition to any other bonus Executive shall be awarded by the Company's Board of Directors, the Company shall pay Executive a bonus payment of up to fifty thousand dollars (\$50,000) annually based upon achievement by the Company against six to eight impact goals approved by the Board of Directors annually. Such goals shall be set forth in writing by the Board within ninety (90) days after the start of the Company's fiscal year and a copy shall be delivered to Executive within fifteen (15) days thereafter. The Board of Directors shall, in their sole discretion, determine whether such impact goals have been obtained.
- 3.3 Equity. Executive has previously entered into a Consulting Agreement ("Consulting Agreement") with the Company dated September 9, 1997. Pursuant to the Consulting Agreement, Executive has received a stock option to purchase one hundred twenty-five thousand (125,000) shares of the Company's common stock with an exercise price of six dollars and ninety-one cents (\$6.91) per share, representing the Company's market price at the time of Board approval. Such option shall continue to vest in accordance with the Consulting Agreement and in accordance with the terms of the Company's 1992 Incentive Stock Incentive Plan, as amended. Upon execution of this Agreement, the Consulting Agreement will terminate.

3.3 Withholdings. All compensation and benefits payable to Executive hereunder and the Agreement shall be subject to all federal, state, local and other withholdings and similar taxes and payments required by applicable law.

#### ARTICLE 4

### EXPENSE ALLOWANCES AND FRINGE BENEFITS

- 4.1 Vacation. Executive shall be entitled to the greater of three (3) weeks of annual paid vacation or the amount of annual paid vacation to which Executive may become entitled under the terms of Company's vacation policy for employees during the term of this Agreement.
- 4.2 Benefits. During the term of this Agreement, the Company shall also provide Executive with the usual health insurance benefits it generally provides to its other senior management employees. As Executive becomes eligible in accordance with criteria to be adopted by the Company, the Company shall provide Executive with the right to participate in and to receive benefit from life, accident, disability, medical, pension, bonus, stock, profit-sharing and savings plans and similar benefits made available generally to employees of the Company as such plans and benefits may be adopted by the Company. The amount and extent of benefits to which Executive is entitled shall be governed by the specific benefit plan as it may be amended from time to time.
- 4.3 Relocation to San Diego, CA. The Executive shall be reimbursed for reasonable and customary relocation expenses as follows:
  - (a) out of pocket expenses related to selling Executive's existing home in the United Kingdom, including customary real estate commissions not to exceed one percent (1%) of selling price and associated costs;
  - (b) reasonable house hunting and up to sixty (60) days temporary living expenses;
  - (c) customary closing costs associated with the purchase of a new home including up to one and one-half points of the mortgage financing amount related to the purchase of a new home;
  - (d) reasonable and customary moving expenses of household goods and personal property (including temporary storage of up the three (3) months) to San Diego, CA;
  - (e) up to twenty thousand dollars (\$20,000) for miscellaneous documented relocation expenses, payable upon the purchase or rental of a home in San Diego, CA.

The Company will reimburse the Executive for the incremental increase in federal and state income taxes associated with the payment of expenses associated with items (a) through (d) above. In addition, the Company will retain at Company expense, for the benefit of Executive, a tax specialist who will provide tax guidance associated with the Executive's relocation to the United States for the three tax periods immediately following Executive's relocation to the United States.

- 4.4 Relocation Loan: In connection with the purchase of a home in the San Diego area, the Company will provide to Executive a loan of up to two hundred and fifty thousand dollars (\$250,000) representing the excess over the purchase price of a home in San Diego over five hundred thousand dollars (\$500,000). Such loan will, at the option of the Company, be secured by a second mortgage deed on the home purchased by Executive. The principal balance of the loan will bear interest at a rate of one percent per annum (1.0% p.a.) and principal and interest will be payable upon the first to occur of (i) sale of the home, (ii) six (6) months following voluntary or involuntary termination of Executive's employment with the Company, (iii) the exercise, pledge or sale of all or part of the stock options granted by Company to Executive or (iv) December 31, 1999.
- 4.5 Relocation to the Untied Kingdom: Upon termination of Executive's employment with the Company, the Company will reimburse Executive for costs associated with relocation back to the United Kingdom including (i) the lesser of customary closing costs and fees (not to exceed six percent (6%) of the selling price) related to the sale by Executive of the first home in San Diego owned by Executive during the term of this Agreement or customary closing costs and fees (not to exceed six percent (6%) of the selling price) related to the sale of Executive's home in San Diego on the date of termination of this Agreement, (ii) documented reasonable and customary moving expenses of household goods and personal property not to exceed in the aggregate ten thousand dollars (\$10,000). The foregoing provision shall not apply in the event (i) at the time of relocation, Executive has accepted employment with another company or it is Executive's intention to do so within a period of six (6) months, (ii) Executive has not completed four (4) full years of employment at the Company (other than by reason of the failure of the Company to renew the term of this Agreement) or (iii) termination of Executive's employment with the Company is for Cause as defined in paragraph 6.3 below.
- 4.6 Other Relocation Expenses. The Company will provide to the Executive's wife, mother and mother-in-law, one round trip coach ticket to and from San Diego and London. The Company will arrange for a Business Class upgrade for these tickets.
- 4.7 Business Expense Reimbursement. During the term of this Agreement, Executive shall be entitled to receive proper reimbursement for all reasonable out-of-pocket expenses incurred by him (in accordance with the policies and procedures established by the Company for its senior executive officers) in performing services hereunder. Executive agrees to furnish to the Company adequate records and other documentary evidence of such expense for which Executive seeks reimbursement. Such expenses shall be reimbursed and accounted for under the policies and procedure established by the Company and the Audit

#### ARTICLE 5

#### CONFIDENTIALITY

- 5.1 Proprietary Information. Executive represents and warrants that he has previously executed and delivered to the Company the Company's standard Proprietary Information and Inventions Agreement in form acceptable to the Company's counsel.
- 5.2 Return of Property. All documents, records, apparatus, equipment and other physical property which is furnished to or obtained by Executive in the course of his employment with the Company shall be and remain the sole property of the Company. Executive agrees that, upon the termination of his employment, he shall return all such property (whether or not it pertains to Proprietary Information as defined in the Proprietary Information and Inventions Agreement), and agrees not to make or retain copies, reproductions or summaries of any such property.

#### ARTICLE 6

### TERMINATION

- 6.1 By Death. The period of employment shall terminate automatically upon the death of Executive. In such event, the Company shall pay to Executive's beneficiaries or his estate, as the case may be, any accrued Base Salary, any bonus compensation to the extent earned, any vested deferred compensation (other than pension plan or profit-sharing plan benefits which will be paid in accordance with the applicable plan), any benefits under any plans of the Company in which Executive is a participant to the full extent of Executive's rights under such plans, any accrued vacation pay and any appropriate business expenses incurred by Executive in connection with his duties hereunder, all to the date of termination (collectively Accrued Compensation), but no other compensation or reimbursement of any kind, including, without limitation, severance compensation, and thereafter, the Company's obligations hereunder shall terminate.
- 6.2 By Disability. If Executive is prevented from properly performing his duties hereunder by reason of any physical or mental incapacity for a period of 120 consecutive days, or for 180 days in the aggregate in any 365-day period, then, to the extent permitted by law, the Company may terminate the employment of Executive at such time. In such event, the Company shall pay to Executive all Accrued Compensation, and shall continue to pay to Executive the Base Salary until such time (but not more than 90 days following termination), as Executive shall become entitled to receive disability insurance payments under the disability insurance policy maintained by the Company, but no other compensation or reimbursement of any kind, including without limitation, severance compensation, and thereafter the Company's obligations hereunder shall terminate. Nothing in this Section shall affect Executive's rights under any disability plan in which he is a participant.
- 6.3 By Company for Cause. The Company may terminate the Executive's employment for Cause (as defined below) without liability at any time with or without advance notice to Executive. The Company shall pay Executive all Accrued Compensation, but no other compensation or reimbursement of any kind, including without limitation, severance compensation, and thereafter the Company's obligations hereunder shall terminate. Termination shall be for "Cause" in the event of the occurrence of any of the following: (a) any intentional action or intentional failure to act by Executive which was performed in bad faith and to the material detriment of the Company; (b) Executive intentionally refuses or intentionally fails to act in accordance with any lawful and proper direction or order of the Board; (c) Executive willfully and habitually neglects the duties of employment; or (d) Executive is convicted of a felony crime involving moral turpitude, provided that in the event that an of the foregoing events is capable of being cured, the Company shall provide written notice to Executive describing the nature of such event and Executive shall thereafter have ten (10) business days to cure such event.
- 6.4 Termination Without Cause. At any time, the Company may terminate the employment of Executive without liability other than as set forth below, for any reason not specified in Section 6.3 above, by giving thirty (30) days advance written notice to Executive. If the Company elects to terminate Executive pursuant to this Section 6.4, (a) the Company shall pay to Executive all Accrued Compensation (b) the Company shall continue to pay to Executive as provided herein Executive's Base Salary over the period equal to nine (9) months from the date of such termination as severance compensation, (c) if Executive's employment terminates in the second half of the Company's fiscal year, the Company shall make a lump sum payment to Executive in an amount equal to a pro rata portion of the Executive's annual actual cash incentive bonus for Company's fiscal year preceding the year of termination based on the number of completed months of Executive's employment in the fiscal year divided by nine (9); (d) the vesting of all outstanding stock options held by Executive shall be accelerated so that the amount of shares vested under such option shall equal that number of shares which would have been vested if the Executive had continued to render services to the Company for nine (9) continuous months after the date of his termination of employment; and (e) the Company shall pay all costs which the Company would otherwise have incurred to maintain all of Executive's health and welfare, and retirement benefits (either on the same or substantially equivalent terms and conditions) if the Executive had continued to render services to the Company for nine (9) continuous months after the date of his termination of employment. The Company shall have no further obligations to Executive shall not (i) engage, directly or indirectly, in providing services to any other business program or project that is competitive to a program or project being conducted by the Company or any Affiliated Company at the time of such employment termination (pr

outstanding securities of any publicly traded corporation), or (ii) hire, solicit, or attempt to solicit on behalf of himself or any other party or any employee or exclusive consultant of the Company. If the Company terminates this Agreement or the employment of Executive with the Company other than pursuant to Section 6.1, 6.2 or 6.3, then this section 6.4 shall apply.

6.5 Constructive Termination A Constructive Termination shall be deemed to be a termination of employment of Executive without cause pursuant to Section 6.4 For Purposes of this Agreement, a "Constructive Termination" means that the Executive voluntarily terminates his employment after any of the following are undertaken without Executive's express written consent:

- (a) the assignment to Executive of any duties or responsibilities which result in any diminution or adverse change of Executive's position, status or circumstances of employment; or any removal of Executive from or any failure to re-elect Executive to any of such positions, except in connection with the termination of his employment for death, disability, retirement, fraud, misappropriation, embezzlement (or any other occurrence which constitutes "Cause" under section 6.3) or any other voluntary termination of employment by Executive other than a Constructive Termination;
- (b) a reduction by the Company in Executive's annual Base Salary by greater than five percent (5%);
- (c) a relocation of Executive or the Company's principal executive offices if Executive's principal office is at such offices, to a location more than forty (40) miles from the location at which Executive is then performing his duties, except for an opportunity to relocate which is accepted by Executive in writing;
- (d) any material breach by the Company of any provision of this Agreement; or
- (e) any failure by the Company to obtain the assumption of this Agreement by any successor or assign of the Company.
- 6.6 Termination Following Change in Control In the event of a non-renewal of this Agreement, a termination without Cause or a Constructive Termination within eighteen (18) months following a Change in Control, Executive shall receive the same benefits package as Executive would have received upon a termination without Cause (except that the payment of Base Salary shall be made in the form of a lump sum) and in addition, the vesting of all outstanding stock options held by Executive shall be accelerated so that the options are immediately exercisable in full.
- 6.7 Change in Control. For purposes of this Agreement, a "Change in Control" shall have occurred if at any time during the term of Executive's employment hereunder, any of the following events shall occur:
  - (a) The Company is merged, or consolidated. or reorganized into or with another corporation or other legal person, and as a result of such merger, consolidation or reorganization less than 50% of the combined voting power of the then-outstanding securities of such corporation or person immediately after such transaction are held in the aggregate by the holders of voting securities of the Company immediately prior to such transaction;
  - (b) The Company sells all or substantially all of its assets or any other corporation or other legal person and thereafter, less than 50% of the combined voting power of the then-outstanding voting securities of the acquiring or consolidated entity are held in the aggregate by the holders of voting securities of the Company immediately prior to such sale;
  - (c) There is a report filed after the date of this Agreement on Schedule 13 D or schedule 14 D-1 (or any successor schedule, form or report), each as promulgated pursuant to the Securities Exchange Act of 1934 (the "Exchange Act") disclosing that any person (as the term "person" is used in Section 13(d)(3) or Section 14(d)(2) of the exchange Act) has become the beneficial owner (as the term beneficial owner is defined under Rule 13d-3 or any successor rule or regulation promulgated under the Exchange Act) representing 50% or more of the combined voting power of the then-outstanding voting securities of the Company;
  - (d) The Company shall file a report or proxy statement with the Securities and Exchange Commission pursuant to the Exchange Act disclosing in response to item 1 of Form 8-X thereunder or Item 5(f) of Schedule 14 A thereunder (or any successor schedule, form or report or item therein) that the change in control of the Company has or may have occurred or will or may occur in the future pursuant to any then-existing contract or transaction; or
  - (e) During any period of two consecutive years, individuals who at the beginning of any such period constitute the directors of the Company cease for any reason to constitute at least a majority thereof unless the election to the nomination for election by the Company's shareholders of each director of the Company first elected during such period was approved by a vote of at least two-thirds of the directors of the Company then still in office who were directors of the Company at the beginning of such period.
- 6.8 Termination by Executive. At any time, Executive may terminate his employment by giving thirty (30) days advance written notice to the Company. The Company shall pay Executive all Accrued Compensation, but no other compensation or reimbursement of any kind, including without limitation, severance compensation, and thereafter the Company's obligations hereunder shall

- 6.9 Mitigation Except as otherwise specifically provided herein, Executive shall not be required to mitigate the amount of any payment provided under this Agreement by seeking other employment or self-employment, nor shall the amount of any payment provided for under this Agreement be reduced by any compensation earned by Executive as a result of employment by another employer or through self-employment or by retirement benefits after the date of Executive's termination of employment from the Company.
- 6.10 Coordination If upon termination of employment, Executive becomes entitled to rights under other plans, contracts or arrangements entered into by the Company, this Agreement shall be coordinated with such other arrangements so that Executive's rights under this Agreement are not reduced, and that any payments under this Agreement offset the same types of payments otherwise provided under such other arrangements, but do not otherwise reduce any payments or benefits under such other arrangements to which Executive becomes entitled.

#### ARTICLE 7

#### GENERAL PROVISIONS

- 7.1 Governing law. The validity, interpretation, construction and performance of this Agreement and the rights of the parties thereunder shall be interpreted and enforced under California law without reference to principles of conflicts of laws. The parties expressly agree that inasmuch as the Company's headquarters and principal place of business are located in California, it is appropriate that California law govern this Agreement.
  - 7.2 Assignment; Successors Binding Agreement.
  - $7.2.1\,$  Executive may not assign, pledge or encumber his interest in this Agreement or any part thereof.
  - 7.2.2 The Company will require any successor (whether direct or indirect, by purchase, merger, consolidation or otherwise) to all or substantially all of the business and/or assets of the Company, by operation of law or by agreement in form and substance reasonably satisfactory to Executive, to assume and agree to perform this Agreement in the same manner and to the same extent that the Company would be required to perform it if no such succession had taken place.
  - 7.2.3 This Agreement shall inure to the benefit of and be enforceable by Executive's personal or legal representatives, executors, administrators, successors, heirs, distributee, devisees and legatees. If Executive should die while any amount is at such time payable to his hereunder, all such amounts, unless otherwise provided herein, shall be paid in accordance with the terms of this Agreement to Executive's devisee, legates or other designee or, if there be no such designee, to his estate.
- 7.3 Certain Reduction of Payments In the event that any payment or benefit received or to be received by Executive under this Agreement would result in all or a portion of such payment to be subject to the excise tax on "golden parachute payments" under Section 4999 of the Internal Revenue Code of 1986, as amended (the "Code"), then Executive's payment shall be either (a) the full payment or (b) such lesser amount which would result in no portion of the payment being subject to excise tax under Section 4999 of the Code, whichever of the foregoing amounts, taking into account the applicable Federal, state and local employment taxes, income taxes, and the excise tax imposed by Section 4999 of the Code, results in the receipt by Executive on an after-tax basis, of the greatest amount of the payment notwithstanding that all or some portion of the payment may be taxable under Section 4999 of the Code.
- 7.4 Notice. For the purposes of this Agreement, notices and all other communications provided for in this Agreement shall be in writing and shall be deemed to have been duly given when delivered or mailed by certified or registered mail, return receipt requested, postage prepaid, addressed to the respective addresses set forth below or to such other address as either party may have furnished to the other in writing in accordance herewith, except that notice of change of address shall be effective only upon receipt.

To the Company:

Neurocrine Biosciences, Inc. 10555 Science Center Drive San Diego, CA 92121 Attn.: President & Chief Executive Officer

To Executive:

Ms. Margaret Valeur-Jensen 4507 South Lane Del Mar, CA 92014

- 7.5 Modification; Waiver; Entire Agreement. No provisions of this Agreement may be modified, waived or discharged unless such waiver, modification or discharge is agreed to in writing signed by Executive and such officer as may be specifically designated by the Board of the Company. No waiver by either party hereto at any time of any breach by the other party of, or compliance with, any condition or provision of this Agreement to be performed by such other party shall be deemed a waiver of similar or dissimilar provisions or conditions at the same or any prior or subsequent time. No agreements or representations, oral or otherwise, express or implied, with respect to the subject matter hereof have been made by either party which are not expressly set forth in this Agreement.
  - 7.6 Validity. The invalidity or unenforceability of any provision of

this Agreement shall not affect the validity or enforceability of any other provision of this Agreement, which shall remain in full force and effect.

- 7.7 Controlling Document. Except to the extent described in Section 6.10, in case of conflict between any of the terms and condition of this Agreement and the document herein referred to, the terms and conditions of this Agreement shall control.
- 7.8 Executive Acknowledgment. Executive acknowledges (a) that he has consulted with or has had the opportunity to consult with independent counsel of his own choice concerning this Agreement, and has been advised to do so by the Company, and (b) that he has read and understands the Agreement, is fully aware of its legal effect, and has entered into it freely based on his own judgment.

#### 7.9 Remedies

- 7.9.1 Injunctive Relief. The parties agree that the services to be rendered by Executive hereunder are of a unique nature and that in the event of any breach or threatened breach of any of the covenants contained herein, the damage or imminent damage to the value and the goodwill of the Company's business will be irreparable and extremely difficult to estimate, making any remedy at law or in damages inadequate. Accordingly, the parties agree that the Company shall be entitled to injunctive relief against Executive in the event of any breach or threatened breach of any such provisions by Executive, in addition to any other relief (including damage) available to the Company under this Agreement or under law.
- 7.9.2 Exclusive. Both parties agree that the remedy specified in Section 7.9.1 above is not exclusive of any other remedy for the breach by Executive of the terms hereof.
- $7.10\,$  Counterparts. This Agreement may be executed in one or more counterparts, all of which taken together shall constitute one and the same Agreement.
- 7.11 Prevailing Party Expenses. In the event that any action or proceeding is commenced to enforce the provisions of the Agreement, the court adjudicating such action or proceeding shall award to the prevailing party all costs and expenses thereof, including, but not limited to, all reasonable attorneys' fees, court costs, and all other related expenses.

Executed by the parties as of the day and year first above written.

**EXECUTIVE** 

NEUROCRINE BIOSCIENCES, INC

By: /s/Bruce Campbell, Ph.D. Bruce Campbell, Ph.D. By: /s/Gary A. Lyons Gary A. Lyons President & Chief Executive Officer NEUROCRINE BIOSCIENCES, INC.

Subsidiary State of Incorporation or Formation
Northwest NeuroLogic, Inc. Oregon

Ownership 100%

# CONSENT OF ERNST & YOUNG LLP, INDEPENDENT AUDITORS

We consent to the incorporation by reference in the Registration Statement (Form S-8 No. 333-5787) pertaining to the Neurocrine Biosciences, Inc. Amended 1992 Incentive Stock Plan, the Neurocrine Biosciences, Inc. Amended 1996 Director Option Plan and the Northwest NeuroLogic, Inc. Restated 1997 Incentive Stock Plan of our report dated January 26, 1999, except for Note 13 for which the date is March 2, 1999, with respect to the consolidated financial statements of Neurocrine Biosciences, Inc. included in its Annual Report on Form 10-K for the year ended December 31, 1998.

ERNST & YOUNG LLP

San Diego, California January 26, 1999, except for Note 13, as to which the date is March 2, 1999 12-MOS DEC-31-1998 JAN-01-1998 DEC-31-1998 11,708 50,962 1,407 0 0 65,633 15,073 4,174 80,529 5,569 0 0 0 19 71,939 80,529 0 16,037 0 33,307 7,188 0 151 (19,954) 1 0 0 0 (19,955) (1.10) (1.10)