NEUROCRINE BIOSCIENCES INC
Form 10-K
February 09, 2012
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UNITED STATES

SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

Form 10-K

(Mark One)

þ **ANNUAL REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934**
For the fiscal year ended December 31, 2011

OR

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

Commission file number: 0-22705

NEUROCRINE BIOSCIENCES, INC.

(Exact name of registrant as specified in its charter)

Delaware	**33-0525145**
(State or other jurisdiction of incorporation or organization)	**(I.R.S. Employer Identification Number)**
12780 El Camino Real, San Diego, CA	**92130**
(Address of principal executive offices)	**(Zip Code)**

Registrant s telephone number, including area code:

(858) 617-7600

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

Title of Each Class	**Name of Each Exchange on Which Registered**
Common Stock, $0.001 par value	The NASDAQ Stock Market

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

Indicate by check mark if the registrant is a well-known seasoned issuer, as defined in Rule 405 of the Securities Act. Yes ¨ No þ

Indicate by check mark if the registrant is not required to file reports pursuant to Section 13 or Section 15(d) of the Act. Yes ¨ No þ

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

Indicate by check mark whether the registrant has submitted electronically and posted on its corporate Web site, if any, every Interactive Data File required to be submitted and posted pursuant to Rule 405 of Regulation S-T (§ 232.405 of this chapter) during the preceding 12 months (or for such shorter period that the registrant was required to submit and post such files). Yes þ No ¨

Indicate by check mark if disclosure of delinquent filers pursuant to Item 405 of Regulation S-K (§ 229.405 of this chapter) is not contained herein, and will not be contained, to the best of 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. þ

Indicate by check mark whether the registrant is a large accelerated filer, an accelerated filer, a non-accelerated filer, or a smaller reporting company. See the definitions of large accelerated filer, accelerated filer and smaller reporting company in Rule 12b-2 of the Exchange Act. (Check one):

Large accelerated filer ¨	Accelerated filer þ	Non-accelerated filer ¨	Smaller reporting company ¨

(Do not check if a smaller reporting company)

Indicate by check mark whether the registrant is a shell company (as defined in Rule 12b-2 of the Act). Yes ¨ No þ

The aggregate market value of the common equity held by non-affiliates of the registrant as of June 30, 2011 totaled approximately $374,004,103 based on the closing price for the registrant s Common Stock on that day as reported by the NASDAQ Stock Market. Such value excludes Common Stock held by executive officers, directors and 10% or greater stockholders as of June 30, 2011. The identification of 10% or

greater stockholders as of June 30, 2011 is based on Schedule 13G and amended Schedule 13G reports publicly filed before June 30, 2011. This calculation does not reflect a determination that such parties are affiliates for any other purposes.

As of January 31, 2012, there were 66,239,495 shares of the registrant s Common Stock outstanding.

DOCUMENTS INCORPORATED BY REFERENCE

Document Description	**10-K Part**
Portions of the registrant s notice of annual meeting of stockholders and proxy statement to be filed pursuant to Regulation 14A within 120 days after registrant s fiscal year end of December 31, 2011 are incorporated by reference into Part III of this report	III

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PART I

FORWARD-LOOKING STATEMENTS

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

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

The cautionary statements made in this report are intended to be applicable to all related forward-looking statements wherever they may appear in this report. We urge you not to place undue reliance on these forward-looking statements, which speak only as of the date of this report. Except as required by law, we assume no obligation to update our forward-looking statements, even if new information becomes available in the future.

ITEM 1. ***BUSINESS***

We were originally incorporated in California in January 1992 and were reincorporated in Delaware in May 1996.

We discover, develop and intend to commercialize drugs for the treatment of neurological and endocrine-related diseases and disorders. Our product candidates address some of the largest pharmaceutical markets in the world, including endometriosis, stress-related disorders, pain, tardive dyskinesia, uterine fibroids, diabetes, insomnia, and other neurological and endocrine-related diseases and disorders. We currently have eleven programs in various stages of research and development, including six programs in clinical development. While we independently develop many of our product candidates, we have entered into collaborations for six of our programs. Our lead clinical development program, elagolix, is a drug candidate for the treatment of endometriosis and uterine fibroids that is partnered with Abbott International Luxembourg S.à r.l. (Abbott).

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Our Product Pipeline

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

Program	Target Indication(s)	Status	Commercial Rights
Product candidates in clinical development:			
Elagolix	Endometriosis	Phase II	Abbott/Neurocrine
Vesicular Monoamine Transporter 2 Inhibitor (VMAT2)	Movement Disorders	Phase II	Neurocrine
CRF_2 Peptide Agonist urocortin 2	Cardiovascular	Phase II	Neurocrine
CRF_1 Antagonist (561679)	Stress-related Disorders	Phase II	GlaxoSmithKline/ Neurocrine
Elagolix	Uterine Fibroids	Phase II	Abbott/Neurocrine
Research programs:			
G Protein-Coupled Receptor 119 (GPR119)	Type II Diabetes	Research	Boehringer Ingelheim/Neurocrine
VMAT2	Schizophrenia	Research	Neurocrine
GnRH Antagonists	Men s and Women s Health, Oncology	Research	Abbott/Neurocrine
Antiepileptic Drugs	Epilepsy, Essential Tremor, Pain	Research	Neurocrine
G Protein-Coupled Receptors	Other Conditions	Research	Neurocrine
Product candidate subject to regulatory review:			
Indiplon	Insomnia	FDA has deemed Approvable	Neurocrine/Dainippon Sumitomo Pharma Co.

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

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

Research indicates identification and evaluation of compound(s) in laboratory and preclinical models.

CRF_1 and CRF_2 refer to two CRF receptor subtypes.

Product Candidates In Clinical Development

Elagolix Gonadotropin-Releasing Hormone (GnRH) Antagonist

GnRH is a peptide that stimulates the secretion of the pituitary hormones that are responsible for sex steroid production and normal reproductive function. Researchers have found that chronic administration of GnRH agonists, after initial stimulation, reversibly shuts down this transmitter pathway and is clinically useful in treating hormone-dependent diseases such as endometriosis and uterine fibroids. Several companies have developed peptide GnRH agonists on this principle, such as Lupron® and Zoladex®. However, since they are peptides, they must be injected via

a depot formulation rather than the preferred oral route of administration. In addition, GnRH agonists can take up to several weeks to exert their desired effect once the initial stimulation has occurred, a factor not seen with the use of GnRH antagonists. More importantly, until the desired effects are

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maximal, GnRH agonists have shown a tendency to exacerbate the condition via a hormonal flare. The ultimate profound suppression effect observed with GnRH agonists is similar to that seen after menopause and can be associated with hot flashes and the loss of bone mineral density.

Orally active, nonpeptide GnRH antagonists potentially offer several advantages over injectable GnRH peptide drugs, including rapid onset of hormone suppression without a hormonal flare. Also, injection site reactions commonly observed in peptide depots are avoided and dosing can be rapidly discontinued if necessary a clinical management option not available with long-acting depot injections. Importantly, by using GnRH antagonists, it may be possible to alter the level of pituitary GnRH suppression thereby titrating circulating estrogen levels. Using this approach, an oral GnRH antagonist may provide patients relief from the painful symptoms of endometriosis while avoiding the need for the active management of bone loss.

Endometriosis. Endometriosis is associated with a multitude of symptoms, some of the most common of which include pain related both to menstruation (dysmenorrhea) and sexual intercourse (dyspareunia) as well as chronic pelvic pain throughout the menstrual cycle, infertility, and menorrhagia, among many others. The wide range of symptoms associated with endometriosis serves to complicate and delay diagnosis due to the significant overlap of symptoms with the disease profiles of other conditions. The World Endometriosis Research Foundation estimates that there are over 170 million women worldwide who suffer from endometriosis. Datamonitor (2009) estimates that there are approximately 7.5 million women in the United States who suffer from the symptoms of endometriosis. We believe that the availability of an oral treatment, lacking the side effect profile of the currently available peptide GnRH agonists, may be a desirable alternative to current pharmaceutical therapies and ultimately encourage a significantly higher treatment rate.

During 2008, we completed the first Phase IIb study of elagolix (PETAL or 603 study) in which 252 patients, with a laparoscopic diagnosis of endometriosis, were treated over the initial 6-month period. This multi-center, randomized, double-blind, double-dummy study consisted of three treatment groups, elagolix 150mg once a day, elagolix 75mg twice daily, and an active control, DMPA-SC. The primary purpose of this study was to assess the impact of six months of treatment of elagolix on bone mineral density as measured by a dual energy x-ray absorptiometry (DXA) scan at the conclusion of treatment and at six and 12 months post treatment. This study also assessed, as secondary endpoints, the impact of treatment on endometriosis symptoms as measured by Composite Pelvic Signs and Symptoms Scale (CPSSS), a monthly recall scale that measures dysmenorrhea, non-menstrual pelvic pain, dyspareunia, pelvic tenderness and induration (all elements of endometriosis pain). Top-line results showed that elagolix met the primary endpoint by having minimal impact on bone mineral density at the conclusion of treatment. This study also showed that elagolix had both a statistical and clinically meaningful reduction in endometriosis symptoms as measured by CPSSS with an 86% responder rate in the 150mg once daily elagolix arm of the study. Additionally, elagolix was shown to be non-inferior to DMPA-SC under the CPSSS. Patient follow up both six and 12 months post treatment showed elagolix did not result in a significant reduction in bone mineral density as measured by DXA, with a mean time of return to ovulation of 24 days for elagolix subjects.

Toward the conclusion of the 603 study, the U.S. Food and Drug Administration (FDA) requested that the endpoints for dysmenorrhea and non-menstrual pelvic pain be assessed on a daily basis rather than utilizing the CPSSS monthly recall scale. In addition, the FDA also provided modified wording to assess the dysmenorrhea and non-menstrual pelvic pain scores on a daily basis. Given these new independent co-primary endpoints, we conducted two additional Phase IIb trials of elagol*ix* to evaluate these modified endpoints as proposed by the FDA, to fully explore the elagolix dose range utilizing both 150mg and 250mg doses. These two trials were designed to assess elagolix for an initial three months, with the non-elagolix treatment arms re-randomized after three months into treatment groups of either 150mg or 250mg of elagolix once daily for an additional three months.

The first additional Phase IIb trial (Lilac PETAL or 702 study) consisted of three arms, elagolix 150mg once daily, elagolix 250mg once daily, and placebo. We randomized 155 subjects with a laparoscopic diagnosis of

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endometriosis in this trial. The three-month placebo controlled portion of the 702 study showed that elagoli*x* provided endometriosis sufferers with clinical improvement of symptoms, coupled with an excellent safety and tolerability profile. However, the FDA-proposed non-menstrual pelvic pain daily scale had a low baseline score and was relatively insensitive to treatment effects. There were no treatment related serious adverse events in the 702 study and the two most common adverse events were headache and nausea, which were typically mild and transient and consistent with our previous studies.

The second additional Phase IIb trial (Tulip PETAL or 703 study) consisted of four arms, elagolix 150mg once daily, elagolix 250mg once daily, Prostap® SR 3.75mg (leuprorelin), and placebo. We enrolled 174 subjects with a laparoscopic diagnosis of endometriosis in this trial. The three-month placebo controlled portion of the 703 study confirmed that elagolix and leuprorelin are associated with reductions in dysmenorrhea and non-menstrual pelvic pain daily scores when compared to placebo. However, the FDA proposed non-menstrual pelvic pain daily scale numeric changes and dynamic range were both small. Although the adverse events reported in the 703 study as occurring more often with elagolix than with placebo were nausea and headache ($\leq$12%), consistent with previous clinical studies of elagolix, these events were generally mild or moderate, transient and not generally associated with study discontinuation. There were no treatment related serious adverse events.

In August 2009, we held a Type C meeting with the FDA to discuss the non-menstrual pelvic pain scale as proposed by the FDA and used in the 702 and 703 studies. Based on this meeting, we modified the wording of the non-menstrual pain and dysmenorrhea daily scale and launched a new clinical trial, the Daisy PETAL Study (901 study). This double-blind placebo-controlled clinical trial was designed to provide an assessment of the modified scale over an eight- week treatment period of 150mg elagolix, followed by sixteen weeks of open-label treatment. This trial commenced in September 2009 and randomized approximately 130 subjects. In May 2010, we announced the results of this trial which showed the symptoms of dysmenorrhea and non-menstrual pelvic pain, as measured by the modified daily scale, both improved significantly in the elagolix treated arms ($p<0.001$ and <0.01, respectively). Daily dysmenorrhea pain scores were a 2.1 at baseline (0-3 scale) with a 1.13 reduction in the elagolix arm compared to a 0.37 reduction in the placebo arm at eight weeks. Daily non-menstrual pelvic pain scores were a 1.4 at baseline (0-3 scale) with a 0.47 reduction in the elagolix arm compared to a 0.19 reduction in the placebo arm at eight weeks. There were no treatment related serious adverse events in the 901 study and the two most common adverse events were headache and nausea, which were typically mild and transient and consistent with our previous studies.

In June 2010, we entered into a worldwide collaboration with Abbott International Luxembourg S.à r.l. (Abbott) to develop and commercialize elagolix and all next-generation non-peptide GnRH antagonists for women s and men s health indications. We completed the final transfer of the Investigational New Drug (IND) application for elagolix to Abbott during the fourth quarter of 2010. Abbott now has primary responsibility for all regulatory interactions with the FDA related to elagolix and the next-generation GnRH antagonists covered by the collaboration.

We and Abbott held an end of Phase II meeting with the FDA in March 2011, and several Type C meetings during 2011. Abbott is currently pursuing a Special Protocol Assessment (SPA) with the FDA, the purpose of which would be to agree with the FDA on the design of the pivotal Phase III program for elagolix in endometriosis. Subject to finalizing the SPA, we expect elagolix to enter Phase III clinical trials for endometriosis in the first half of 2012.

Uterine Fibroids. Uterine Fibroids are benign hormonally responsive tumors that form in the wall of the uterus. They are the most common solid tumor in women with a prevalence rate of at least 25% (American College of Obstetricians and Gynecologists). While many women do not have symptoms, depending on the size, location and number, uterine fibroids can cause pelvic pain, reproductive problems, and severe bleeding that can lead to anemia. Due to the severity of symptoms, treatment sometimes requires surgery, including the removal of the uterus. In fact, uterine fibroids is a leading indication for hysterectomy in the United, with

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approximately 250,000 hysterectomies performed each year related to uterine fibroids (Whiteman *et al AJOG* 2008, *198,* e1). We believe that a safe and effective oral therapy would be a preferred treatment regimen rather than surgical intervention.

During 2011, Abbott initiated a randomized, double-blind, placebo controlled, Phase II study of 300 women to assess the safety and efficacy of elagolix in the treatment of uterine fibroids. The primary endpoint in this study is an assessment of blood loss after three months of treatment with elagolix. The study is a dose ranging study designed to evaluate various doses of elagolix compared to placebo. Additional efficacy endpoints being evaluated are change in uterine volume, fibroid volume, and change in menstrual patterns. This study is expected to be completed in late 2012.

Vesicular Monoamine Transporter 2 Inhibitor (VMAT2)

VMAT2 is a protein concentrated in the human brain that is essential for the transmission of nerve impulses between neurons. VMAT2 is primarily responsible for re-packaging and transporting monoamines (dopamine, norepinephrine, serotonin, and histamine) among nerve cells. Specifically, dopamine enables neurotransmission among nerve cells that are involved in voluntary and involuntary motor control.

We have identified a highly selective VMAT2 inhibitor (NBI-98854) that is effective in preclinical testing in regulating the levels of dopamine release during nerve communication, while at the same time having minimal impact on the other monoamines thereby reducing the likelihood of off target side effects.

During 2009, a Phase I single ascending dose clinical trial of NBI-98854 was completed in healthy male volunteers in Canada under an approved Clinical Trial Application with Health Canada. This trial showed NBI-98854 to be generally safe and well tolerated. There were no serious adverse events, clinically significant drug-related laboratory abnormalities or clinically significant electrocardiogram (ECG) findings. The characteristics of NBI-98854 met the pre-specified pharmacokinetic requirements for the trial: dose proportionality, low maximum concentration with adequate area-under-curve for drug exposure, low variability, and a half-life which supports once per day dosing.

During 2010, we completed a multiple, repeated dose Phase I study of NBI-98854 in healthy male volunteers. This trial also showed NBI-98854 to be generally safe and well tolerated, and again displayed the desired pharmacokinetic requirements. There were no serious adverse events, clinically significant drug-related laboratory abnormalities or clinically significant ECG findings.

Based on the successful completion of this second Phase I study, we initiated a Phase IIa open label dose exploration study of NBI-98854 in six patients with tardive dyskinesia in late 2010. This study was designed to assess, over a twelve-day dosing period, the efficacy, safety and tolerability of NBI-98854 in schizophrenia patients who have moderate to severe tardive dyskinesia. The impact on the dyskinesia was assessed utilizing the Abnormal Involuntary Movement Scale (AIMS). The study inclusion criteria included a baseline total score of at least nine on the first seven physical components of AIMS, with at least two body regions receiving scores of moderate (3) or severe (4). For the study the mean baseline score was 14.3 (AIMS total items 1-7, possible total score of 28). The dosing regimen consisted of three, four-day periods of NBI-98854, at increasing doses of 12.5mg, 25mg, and 50mg administered once daily. After discontinuation of NBI-98854, a seven-day washout period was followed by a final assessment. After the twelve days of dosing, the mean AIMS score decreased to 8.4, a reduction of 41.3%. Reduction in abnormal involuntary movements was shown across multiple assessment points. After the seven-day washout period, most patients AIMS scores returned to their baseline levels. The adverse events reported during administration of NBI-98854 were transient and mild or moderate including one subject with dizziness and one with restlessness. One subject became anxious and agitated seven days after study medication due to the patient s return to baseline-intensity dyskinesia.

Upon successful completion of this open-label Phase IIa study, we filed an IND with the FDA to permit the initiation of larger Phase II studies in patients with tardive dyskinesia in the United States.

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In September 2011, we began a second Phase II study in tardive dyskinesia patients. This 32 patient placebo controlled, double-blind, randomized, cross-over study, uses a within-subject comparison for safety and efficacy evaluation. Patients are randomized to either 12.5mg or 50mg doses of NBI-98854 for a two week dosing period, and also have a two week placebo dosing period. The primary efficacy endpoint of the study will be a comparison of placebo versus active AIMS scores at the end of the two dosing periods. Data from this study will be used to guide the dosing selection for larger Phase IIb studies in tardive dyskinesia patients that are expected to begin in 2012.

Tardive dyskinesia (TD) is defined by hyperkinetic involuntary movements which arise after months or years of treatment with dopamine receptor antagonist therapeutics (DRBA), e.g. antipsychotics for schizophrenia, bipolar disorder, and depression, and metoclopramide for nausea and vomiting and gastric emptying in patients with gastroparesis. Features of the disorder may include grimacing, tongue protrusion, lip smacking, puckering and pursing of the lips, and rapid eye blinking. Rapid movements of the extremities may also occur. The impact on daily function and the quality of life for individuals suffering from TD can be substantial. While the prevalence rates of TD can vary greatly in accordance with the population being studied, it is estimated that nearly 500,000 individuals are affected by TD in the United States alone (Kantar Health).

To address the unmet medical needs of patients suffering from TD. Neurocrine is developing NBI-98854. NBI-98854 is a potent, highly selective, VMAT2 inhibitor that is effective in regulating pre-synaptic release of dopamine, while at the same time having minimal impact on the other monoamines, e.g. norepinephrine and serotonin. This selectivity may reduce the likelihood of off target side effects. Additionally, Neurocrine has designed this novel compound to provide low, sustained, plasma and brain concentrations of the active drug to minimize the potential side effects associated with excessive dopamine depletion. With these features, NBI-98854 should be well tolerated in patients. NBI-98854 has been evaluated in several Phase I studies and a two Phase II studies to assess its safety, tolerability and efficacy and to establish a treatment regimen to be used in future clinical trials. Neurocrine believes that the potential efficacy and safety profile of NBI-98854 will address many of the shortcomings of current off-label treatments. Finally, NBI-98854 may well be useful in other disorders, such as Huntington s chorea, schizophrenia, Tourette s Syndrome, and tardive dystonia.

CRF_2 Receptor Peptide Agonist (Urocortin 2)

Congestive heart failure (CHF) is a condition where the heart cannot pump enough blood to supply all of the body s organs. It is a result of narrowing of the arteries combined with high blood pressure, which results in increased respiration as well as edema from water retention. In the case of acute symptomology, CHF patients will eventually experience a rapid deterioration and require urgent treatment in the hospital. According to 2011 data from the American Heart Association, over 6 million people experience CHF and about 670,000 new cases are diagnosed each year in the United States. CHF becomes more prevalent with age and the number of cases is expected to grow as the overall age of the population increases. Current treatment options include a cocktail of drugs consisting of diuretics to remove excess water, beta blockers and digitalis to improve heart muscle contraction, and/or ACE inhibitors, Angiotensin Receptor Blockers, and vasodilators to expand blood vessels. According to the American Heart Association (2012), there are approximately one million hospital discharges each year in the United States for CHF.

Urocortin 2 is an endogenous peptide ligand of the CRF_2 receptor present in the cardiovascular system, notably the heart and cerebral arterial system. Urocortin 2 plays a role in the control of the hormonal, cardiovascular, gastrointestinal, and behavioral responses to stress, and has an array of effects on the cardiovascular system and metabolism. Based on preclinical efficacy and safety data, together with its known role in human physiology, we believe that urocortin 2 may have positive hemodynamic effects on cardiac output and blood pressure which may benefit patients with acute CHF.

We completed a Phase II placebo controlled dose-escalation study in 2005 to evaluate the safety, pharmacokinetics and pharmacodynamics of two dose levels of urocortin 2 in patients with stable CHF. Results

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of this study demonstrated a dose-related increase in cardiac output of up to 50% with only a modest increase (6%) in heart rate. We completed an additional Phase II study evaluating urocortin 2 over four-hour infusions in patients with stable CHF in the first half of 2006. The treatments were generally well tolerated without serious adverse events, abnormalities in electrocardiograms or significant changes in renal function. Positive hemodynamic effects were noted in virtually all patients with increases in cardiac output ranging from 6% to 54%.

We have also completed the necessary preclinical work to allow for periods of infusion of urocortin 2 up to 14 days. This substantially completes all of the preclinical toxicology work required by the FDA. Further development of urocortin 2 for CHF and other acute care cardiovascular diseases is highly dependent upon partnering of this program.

During 2009, The Christchurch Cardioendocrine Research Group at University of Otago, Christchurch School of Medicine and Health Sciences, New Zealand, began a pilot study of urocortin 2 in at least 50 patients with Acute Decompensated Heart Failure through a grant from the Health Research Council of New Zealand. In this blinded study, standard-of-care treatment (i.e., diuretics and vasodilators) are compared to standard of care treatment plus a four hour infusion of urocortin 2; enrollment of subjects is was completed in December 2011. A subset of 15 subjects also underwent right heart catheterization for more detailed evaluation of their cardiac status and response to treatment. We anticipate having the results of this study in the first quarter of 2012.

Additional urocortin 2 studies are being conducted by the Centre for Cardiovascular Sciences at The University of Edinburgh through a British Heart Foundation grant. A total of nine studies are to be conducted in both healthy volunteers and patients with stable CHF to determine the impact of urocortin 2 infusions on biomarkers of cardiovascular function and dysfunction. These studies began in 2010, and are expected to take several years to complete.

Corticotropin-Releasing Factor (CRF) Receptor$_1$ Antagonist

Researchers have identified what they believe to be the central mediator of the body s stress responses or stress-induced disorders. This mediator is a brain chemical known as CRF. CRF is overproduced in clinically depressed patients and may be dysregulated in individuals with anxiety disorders. Current research indicates that clinically depressed patients and patients with anxiety experience dysfunction of the hypothalamic-pituitary-adrenal axis, the system that manages the body s overall response to stress. This amplifies production of CRF, and induces the physical effects that are associated with stress that can lead to stress-related disorders such as posttraumatic stress disorder and acute stress disorder. According to Datamonitor (2008), there are approximately 7.8 million post-traumatic stress disorder sufferers in the United States. We believe the novelty and specificity of the CRF mechanism of action and the prospect of improving upon selective serotonin reuptake inhibitor therapy represents a market opportunity both to better serve patients and expand the overall treatment of stress-related disorders.

We have a strategic position in the CRF field through our intellectual property portfolio and relationship with experts in the neuropsychiatric field. We have further characterized the CRF receptor system and have identified additional members of the CRF receptor family. We have patent rights on two receptor subtypes termed CRF_1 and CRF_2, and we have pending patent applications on small molecule organic compounds modulating the CRF receptors.

In July 2001, we announced a worldwide collaboration with GlaxoSmithKline (GSK), to develop and commercialize CRF antagonists for psychiatric, neurological and gastrointestinal diseases. Under the terms of this agreement, GSK sponsored and we jointly conducted a research program and collaborated in the development of our current lead compounds, as well as novel back-up candidates and second generation compounds identified through the collaborative research. The sponsored research portion of the collaboration was completed in 2005.

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GSK advanced one of the lead CRF_1 receptor antagonist compounds, 561679, into a Phase II depression study during 2008. This multicenter randomized, double-blind, placebo-controlled trial was designed to assess the safety and efficacy of 561679 in approximately 150 women with Major Depressive Disorder over six weeks of treatment. The primary endpoint was a change from baseline in the Bech melancholia scale at Week 6 and a key secondary endpoint was a change from baseline in the HAMD-17 scale at Week 6. Results of the statistical analysis using the intent-to-treat population revealed no benefit of 561679 compared to placebo on either scale.

Emory University of Atlanta and Mt. Sinai Medical Center in New York, in conjunction with GSK, through a grant from the National Institute of Mental Health, has been conducting a Phase II clinical trial evaluating 561679 in women with post-traumatic stress disorder. This randomized, double-blind, placebo-controlled trial is expected to enroll approximately 150 patients for a six-week treatment period. This study began in late 2009 and is expected to take several years to complete. Additionally, the National Institute on Alcohol Abuse and Alcoholism, in conjunction with GSK, is planning to initiate a Phase II clinical trial evaluating 561679 in stress-induced craving in alcoholic women with high anxiety. This randomized, double-blind, placebo-controlled trial is expected to enroll 50 patients for a four-week treatment period. This study is expected to take several years to complete.

Research Programs

Our research and development focus is on addressing diseases and disorders of the central nervous and endocrine systems, which include therapeutic categories ranging from diabetes to stress-related disorders and neurodegenerative diseases. Central nervous system and endocrinology drug therapies are among the largest therapeutic categories, accounting for $100 billion in worldwide drug sales according to MedAdNews (2011).

G Protein-Coupled Receptor 119 (GPR119)

Type II diabetes is growing at epidemic proportions world-wide. This disease is characterized by reduced ability to secrete and respond to insulin. Drugs which can enhance the secretion of insulin in response to rising blood glucose levels can improve blood glucose control without increased risk of hypoglycemia. Nearly 25 million suffer from diabetes in the United States alone with a worldwide prevalence in excess of 300 million. Recent estimates put the total direct and indirect costs of diabetes at $174 billion.

GPR119 has been identified as a novel target for the treatment of Type II diabetes. GPR119 is expressed predominantly in the pancreas and gastrointestinal tract. The activation of GPR119 receptors located in the gastrointestinal tract stimulates incretins, resulting in increased insulin production, while activation of GPR119 receptors located on pancreatic islet beta cells can stimulate insulin secretion directly.

In June 2010, we entered into a worldwide collaboration with Boehringer Ingelheim International GmBH (Boehringer Ingelheim) to research and develop small molecule GPR119 agonists for the treatment of Type II diabetes and other indications. We will work jointly with Boehringer Ingelheim to identify and advance candidates into preclinical development. Boehringer Ingelheim will then be responsible for the global development and commercialization of potential GPR119 agonist products.

VMAT2

VMAT2 inhibition results in the modulation of dopamine pathways which may also be useful for patients suffering from schizophrenia. Approximately 2.2 million people in the Unites States suffer from schizophrenia at an estimated annual cost of $62 billion. Our discovery efforts around VMAT2 inhibitors also focuses on developing novel therapies for schizophrenia sufferers.

GnRH Antagonists

As previously mentioned, GnRH antagonists may be useful in treating certain hormone dependent diseases. Our discovery work in nonpeptide GnRH antagonists continues to focus on endometriosis, uterine fibroids and oncology indications as we continue to explore additional drug candidates with our collaboration partner Abbott.

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Antiepileptic Drugs

Antiepileptic drugs are utilized in the treatment of epileptic seizures by suppressing the rapid firing of neurons that initiate a seizure. Antiepileptics also have additional effects within the central nervous system that have proven beneficial in bipolar disease, neuropathic pain and essential tremor. According to Datamonitor, in 2008, worldwide sales of anticonvulsants totaled approximately $13 billion.

G Protein-Coupled Receptors (GPCR)

GPCR are the largest known gene superfamily of the human genome. Greater than thirty percent of all marketed prescription drugs act on GPCR; which makes this class of proteins the historically most successful therapeutic target family. However, only a small fraction of the GPCR gene superfamily has been exploited. Next generation therapies derived from GPCR will be discovered through the understanding of the complex relationships of drug/receptor interactions and their subsequent impact on efficacy, downstream signaling networks and regulation.

Our GPCR research platform has met this requirement by integrating drug discovery research efforts with a suite of assays and assay systems and automated analytical techniques. This process provides a profile of GPCR pharmacological receptor/ligand interactions capable of predicting in vivo efficacy allowing for rapid discovery of initial leads and advancement into preclinical and clinical development. Importantly, this design cycle is not limited to GPCR targets, but can be utilized for other proteins that play a role in human disease where current treatments or therapies are either inadequate or nonexistent.

Product Candidate Subject to Regulatory Review

Indiplon

Indiplon is a non-benzodiazepine $GABA_A$ receptor agonist for the treatment of insomnia which acts via the same mechanism as the currently marketed non-benzodiazepine therapeutics. We obtained the rights to indiplon through an exclusive worldwide sublicense agreement that we entered into with DOV Pharmaceutical, Inc. (DOV) in June 1998.

Based on the results of preclinical studies and Phase I, Phase II and Phase III clinical trials on indiplon, as well as a non-clinical data package related to indiplon manufacturing, formulation and commercial product development, we assembled and filed NDAs with the FDA for both indiplon capsules and indiplon tablets. On May 15, 2006, we received two complete responses from the FDA regarding our indiplon capsule and tablet NDAs. These responses indicated that indiplon 5mg and 10mg capsules were approvable (2006 FDA Approvable Letter) and that the 15mg tablets were not approvable.

We resubmitted our NDA for indiplon 5mg and 10mg capsules seeking clearance to market indiplon capsules for the treatment of insomnia. In December 2007, we received an action letter from the FDA stating the indiplon 5mg and 10mg capsules were approvable (2007 FDA Approvable Letter). The 2007 FDA Approvable Letter acknowledged that the resubmitted NDA had addressed the issues raised in the 2006 FDA Approvable Letter, but set forth new requirements. The new requirements set forth in the 2007 FDA Approvable Letter are the following: (i) an objective/subjective clinical trial in the elderly, (ii) a safety study assessing the rates of adverse events occurring with indiplon when compared to a marketed product, and (iii) a preclinical study to evaluate indiplon administration during the third trimester of pregnancy.

After receipt of the 2007 FDA Approvable Letter, we ceased all indiplon clinical development activities in the United States as well as all pre-commercialization activities. We continue to evaluate various alternatives for the indiplon program.

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Our Business Strategy

Our goal is to become the leading biopharmaceutical company focused on neurological and endocrine-related diseases and disorders. The following are the key elements of our business strategy:

Continuing to Advance and Build Our Product Portfolio Focused on Neurological and Endocrine-Related Diseases and Disorders. We believe that by continuing to advance and build our product pipeline, we can mitigate some of the clinical development risks associated with drug development. We currently have eleven programs in various stages of research and development, including six programs in clinical development. We take a portfolio approach to managing our pipeline that balances the size of the market opportunities with clear and defined clinical and regulatory paths to approval. We do this to ensure that we focus our internal development resources on innovative therapies with improved probabilities of technical and commercial success.

Identifying Novel Drugs to Address Unmet Market Opportunities. We seek to identify and validate novel drugs on characterized targets for internal development or collaboration. For example, GnRH antagonists, compounds designed to reduce the secretions of sex steroids, may represent the first novel non-peptide, non-injectible means of treatment of endometriosis. The creativity and productivity of our discovery research group will continue to be a critical component for our continued success. Research and development costs were $31.0 million, $31.2 million and $33.7 million for the years ended December 31, 2011, 2010 and 2009, respectively.

Selectively Establishing Corporate Collaborations with Global Pharmaceutical Companies to Assist in the Development of Our Products and Mitigate Financial Risk while Retaining Significant Commercial Upside. We leverage the development, regulatory and commercialization expertise of our corporate collaborators to accelerate the development of certain of our potential products, while typically retaining co-promotional rights, and at times commercial rights, in North America. We intend to further leverage our resources by selectively entering into additional strategic alliances to enhance our internal development and commercialization capabilities by licensing our technology.

Acquiring Rights to Complementary Drug Candidates and Technologies. We plan to continue to selectively acquire rights to products in various stages of development to take advantage of our drug development capabilities.

Our Corporate Collaborations and Strategic Alliances

One of our business strategies is to utilize strategic alliances to enhance our development and commercialization capabilities. The following is a summary of our significant collaborations/alliances:

Abbott International Luxembourg S.à r.l. (Abbott). In June 2010, we announced an exclusive worldwide collaboration with Abbott to develop and commercialize elagolix and all next-generation gonadotropin-releasing hormone (GnRH) antagonists (collectively, GnRH Compounds) for women s and men s health. Under the terms of our agreement with Abbott, we and Abbott will work jointly to advance GnRH Compounds towards commercialization. Abbott made an upfront payment of $75 million and agreed to make additional development and regulatory event based payments of up to $480 million and up to an additional $50 million in commercial event based payments. Under the terms of the agreement, Abbott is responsible for all development, marketing and commercialization costs. We will receive funding for certain internal collaboration expenses which includes reimbursement from Abbott for internal and external expenses related to the GnRH Compounds, which reimbursement includes up to approximately $24 million in personnel funding through the end of 2012. We will be entitled to a percentage of worldwide sales of GnRH Compounds for the longer of ten years or the life of the related patent rights. Under the terms of our agreement with Abbott, the collaboration effort between the parties to advance GnRH compounds towards commercialization is governed by a joint development committee with representatives from both Neurocrine and Abbott; provided, however, that final decision making authority rests with Abbott. Abbott may terminate the collaboration at its discretion upon 180 days written notice to us. In such event, we would be entitled to specified payments for ongoing clinical development and related activities and all GnRH Compound product rights would revert to us. Since the inception of the agreement, we have recorded revenues of $46.0 million related to the amortization of up-front license fees, $30.0 million in milestone revenue,

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$10.0 million of which was related to advancing elagolix into Phase II clinical trials for uterine fibroids and $20.0 million of which was related to the outcome of an elagolix pre-Phase III meeting with the FDA for endometriosis, and $19.2 million in sponsored development revenue consisting of reimbursement of internal and external expenses. In addition, at December 31, 2011, we had $29.0 million of deferred revenue related to the Abbott agreement, which is being amortized over the estimated remaining term of the collaborative development period.

Boehringer Ingelheim International GmbH (Boehringer Ingelheim). In June 2010, we announced a worldwide collaboration with Boehringer Ingelheim to research, develop and commercialize small molecule GPR119 agonists for the treatment of Type II diabetes and other indications. Under the terms of the agreement, we and Boehringer Ingelheim are working jointly to identify and advance GPR119 agonist candidates into preclinical development. Boehringer Ingelheim will then be responsible for the global development and commercialization of potential GPR119 agonist products. We received a $10 million upfront payment and we are currently receiving research funding to support discovery efforts. We are eligible to receive up to approximately $3 million in additional preclinical milestone payments and payments of up to approximately $223 million in clinical development and commercial event based payments. We will be entitled to a percentage of any future worldwide sales of GPR119 agonists resulting from the collaboration. Under the terms of the agreement, the collaboration effort between the parties to identify and advance GPR119 agonist candidates into preclinical development is governed by a steering committee with representatives from both Neurocrine and Boehringer Ingelheim; provided, however, that the final decision making authority rests with Boehringer Ingelheim. Boehringer Ingelheim may terminate the agreement at its discretion upon prior written notice to us. In such event, we may be entitled to specified payments and product rights would revert to us. Since the inception of the agreement, we have recorded revenues of $7.7 million related to amortization of up-front license fees and $2.1 million in sponsored research. At December 31, 2011, we had $2.3 million of deferred license fees that will be amortized over the estimated remaining term of the collaborative research period of the agreement.

Dainippon Sumitomo Pharma Co. Ltd. (DSP). In October 2007, we announced an exclusive license agreement with DSP to develop and commercialize indiplon in Japan. Under the terms of the agreement, DSP made an up-front payment to us of $20 million and is responsible for all future development, marketing and commercialization costs of indiplon in Japan. We will be eligible to receive additional event based payments upon specified future events related to the development and commercialization of indiplon in Japan. Should all event based payments be achieved, we may be entitled to additional payments totaling up to $115 million. We are also entitled to royalties from DSP on future sales of indiplon in Japan. As of December 31, 2011, we had recorded revenues of $12.2 million in license fees from DSP over the life of the agreement.

GlaxoSmithKline (GSK). In July 2001, we announced a worldwide collaboration with an affiliate of GSK to develop and commercialize CRF antagonists for psychiatric, neurological and gastrointestinal diseases. Under the terms of this agreement, we and GSK conducted a collaborative research program and collaborate in the development of our current lead compounds, as well as novel back-up candidates and second generation compounds identified through the collaborative research. The sponsored research portion of this collaboration agreement concluded in 2005. In addition, we will be eligible to receive event based payments as compounds progress through the research and development process, royalties on future product sales and co-promotion rights in the U.S. in some circumstances. GSK may terminate the agreement at its discretion upon 90 days prior written notice to us. In such event, we may be entitled to specified payments and all product rights would revert to us.

Intellectual Property

We seek to protect our lead compounds, compound libraries, expressed proteins, synthetic organic processes, formulations, assays, cloned targets, screening technology and other technologies by filing, or by causing to be filed on our behalf, patent applications in the United States and abroad. Additionally, we have licensed from institutions such as The Salk Institute, DOV, Research Development Foundation and others the rights to issued United States patents, pending United States patent applications, and issued and pending foreign filings. We face the risk that one or more of the above patent applications may be denied. We also face the risk that issued patents that we own or license may be challenged or circumvented or may otherwise not provide protection for any commercially viable products we develop.

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The technologies we use in our research, as well as the drug targets we select, may infringe the patents or violate the proprietary rights of third parties. If this occurs, we may be required to obtain licenses to patents or proprietary rights of others in order to continue with the commercialization of our products.

In addition to the granted and potential patent protection, the United States, the European Union and Japan all provide data and marketing exclusivity for new medicinal compounds. If this protection is available, no competitor may use the original applicant s data as the basis of a generic marketing application during the period of data and marketing exclusivity. This period of exclusivity is generally five years in the United States, six years in Japan and ten years in the European Union, measured from the date of FDA, or corresponding foreign, approval.

Elagolix, our small molecule GnRH antagonist currently in clinical trials for the treatment of endometriosis, is covered by six issued U.S. patents relating to composition of matter, pharmaceutical compositions, and methods of use. U.S. Patent Nos. 6,872,728, 7,179,815 and 7,462,625 are due to expire in 2021 (not including potential patent term extensions of up to five years) while U.S. Patent Nos. 7,056,927, 7,176,211 and 7,419,983 are due to expire in 2024 (not including potential patent term extensions of up to five years).

Our highly selective VMAT2 inhibitor NBI-98854 is currently in clinical trials for the treatment of tardive dyskinesia and is covered by U.S. Patent number 8,039,627 which expires in 2029 (not including a potential patent term extension of up to five years). We have also received a Notice of Allowance in the European Union related to NBI-98854.

Urocortin 2 is an endogenous peptide ligand of the CRF_2 receptor which may be useful in the treatment of congestive heart failure based on preclinical efficacy and safety data. This peptide is covered by U.S. Patent Nos. 7,223,846 and 7,638,607, which are both due to expire in 2021 (not including potential patent term extensions of up to five years).

Our CRF antagonist 561679 is currently in clinical trials for the treatment of stress-related disorders and is subject to a pending patent application. Our CRF antagonist program is subject to a collaboration agreement with GSK who controls patent prosecution and strategy for the program.

Indiplon is our non-benzodiazepine $GABA_A$ receptor agonist for the treatment of insomnia. The compound is covered by U.S. Patent No. 6,399,621 which is due to expire in 2020 (not including a potential patent term extension of up to five years).

Manufacturing and Distribution

We currently rely on, and expect to continue to rely on, contract manufacturers to produce sufficient quantities of our product candidates for use in our preclinical and anticipated clinical trials. In addition, we intend to rely on third parties to manufacture any products that we may commercialize in the future. We have established an internal pharmaceutical development group to develop manufacturing methods for our product candidates, to optimize manufacturing processes, and to select and transfer these manufacturing technologies to our suppliers. We contract with multiple manufacturers to ensure adequate product supply and to mitigate risk.

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

We currently have no distribution capabilities. In order to independently commercialize any of our product candidates, we must either internally develop distribution capabilities or make arrangements with third parties to perform these services.

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Marketing and Sales

We currently have limited experience in marketing or selling pharmaceutical products. Under our collaboration agreement with GSK, we may have the opportunity to co-promote any products resulting from the collaboration in the United States. To market any of our other products independently would require us to develop a sales force with technical expertise along with establishing commercial infrastructure and capabilities.

Government Regulation

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

Preclinical studies generally are conducted in laboratory animals to evaluate the potential safety and efficacy of a product. Drug developers submit the results of preclinical studies to the FDA as a part of an IND application before clinical trials can begin in humans. Typically, clinical evaluation involves a time consuming and costly three-phase process.

Phase I	Clinical trials are conducted with a small number of subjects to determine the early safety profile, maximum tolerated dose and pharmacological properties of the product in human volunteers.
Phase II	Clinical trials are conducted with groups of patients afflicted with a specific disease in order to determine preliminary efficacy, optimal dosages and expanded evidence of safety.
Phase III	Large-scale, multi-center, comparative clinical trials are conducted with patients afflicted with a specific disease in order to determine safety and efficacy as primary support for regulatory approval by the FDA to market a product candidate for a specific disease.

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

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

If the FDA approves the NDA, the drug becomes available for physicians to prescribe in the United States. After approval, the drug developer must submit periodic reports to the FDA, including descriptions of any adverse reactions reported. The FDA may request additional studies, known as Phase IV, to evaluate long-term effects. The FDA may also require a Risk Evaluation and Mitigation Strategy (REMS) safety plan upon approval.

We will also have to complete an approval process similar to that in the United States in virtually every foreign target market for our products in order to commercialize our product candidates in those countries. The

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approval procedure and the time required for approval vary from country to country and may involve additional testing. Foreign approvals may not be granted on a timely basis, or at all. In addition, regulatory approval of prices is required in most countries other than the United States. The resulting prices may not be sufficient to generate an acceptable return to us or our corporate collaborators.

Competition

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

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

Developments by others may render our product candidates or technologies obsolete or noncompetitive. We are performing research on or developing products for the treatment of several disorders including endometriosis, stress-related disorders, pain, tardive dyskinesia, uterine fibroids, diabetes, insomnia, and other neurological and endocrine-related diseases and disorders.

Lupron Depot®, marketed by Abbott Laboratories, and Synarel® and Depo-Provera®, marketed by Pfizer, are products that have been approved for the treatment of endometriosis, infertility, and central precocious puberty. These drugs, and any generic alternatives, may compete with any small molecule non-peptide GnRH antagonists we develop for these indications.

We, in conjunction with our collaborative partner Abbott, are developing elagolix for the treatment of uterine fibroids. There are no current pharmaceutical therapies approved in the United States for the chronic treatment of uterine fibroids. Lupron Depot® is approved for short-term use to improve the outcome of uterine fibroid surgery. However, approximately 250,000 hysterectomies are performed annually in the United States as a direct result of uterine fibroids, as well as myomectomies (surgery) to remove the fibroids. Our oral small molecule pharmaceutical agent, elagolix, would compete directly with these current invasive standards of care.

Our VMAT2 inhibitor is designed for the treatment of movement disorders, specifically tardive dyskinesia. At present there are no approved drug therapies for tardive dyskinesia; however, treatment regimens consist of utilizing various atypical antipsychotic medications (e.g., Clozapine), benzodiazepines (off-label) or botulinum toxin injections to treat the movements associated with tardive dyskinesia. Other potential indications for our VMAT2 inhibitor are Tourette s syndrome, Huntington s disease and tardive dystonia. Currently, Xenazine®, marketed by Lundbeck, is approved for the chorea associated with Huntington s disease. Generic neuroleptic medications (pimozide and haloperidol) are generally utilized to control the tics associated with Tourette s syndrome.

A potential indication currently being explored for our small molecule CRF antagonists is the area of post-traumatic stress disorders, for which there are no current approved drug therapies. However, clinicians utilize anxiolytics and anti-depressants such as Cymbalta®, marketed by Eli Lilly, Xanax®, marketed by Pfizer, Lexapro®, marketed by Forest Laboratories, Zoloft®, marketed by Pfizer, Paxil®, marketed by GSK and Pristiq®, marketed by Pfizer, among others, as well as any generic alternatives for each of these products.

In the area of insomnia, competitive products include Ambien®, Sonata®, Lunesta®, Intermezzo®, and Rozerem®, which are currently marketed by Sanofi-Aventis, King Pharmaceuticals, Inc., Sunovion Pharmaceuticals, Inc., Transcept Pharmaceuticals, Inc. and Takeda Pharmaceutical Company, respectively. During 2006, Sanofi-Aventis launched a controlled-release formulation of Ambien® called Ambien CR® and during 2007 generic Ambien®, or zolpidem, also entered the insomnia market.

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If one or more of these products or programs are successful, it may reduce or eliminate the market for our products.

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

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

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

Employees

As of December 31, 2011, we had approximately 71 full-time employees, of which 15 hold Ph.D., M.D. or equivalent degrees, and 12 others hold an M.S., M.B.A., or equivalent degrees. Of these full-time employees, 53 were engaged in, or directly support, research and development activities, and 18 were in general and administrative positions. None of our employees are represented by a collective bargaining arrangement, and we believe our relationship with our employees is good. In addition, we rely on a number of consultants to assist us in formulating our research and development strategies.

Insurance

We maintain product liability insurance for our clinical trials. We intend to expand our insurance coverage to include the sale of commercial products if marketing approval is obtained for products in development. However, insurance coverage is becoming increasingly expensive, and we may not be able to maintain insurance coverage at a reasonable cost or in sufficient amounts to protect us against losses due to liability. In addition, we may not be able to obtain commercially reasonable product liability insurance for any products approved for marketing.

Available Information

Our Annual Reports on Form 10-K, Quarterly Reports on Form 10-Q, Current Reports on Form 8-K and amendments to reports filed pursuant to Sections 13(a) and 15(d) of the Securities Exchange Act of 1934, as amended, are available free of charge on our website at *www.neurocrine.com*, as soon as reasonably practicable after such reports are available on the Securities and Exchange Commission website at *www.sec.gov*.

Additionally, copies of our annual report will be made available, free of charge, upon written request.

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ITEM 1A. ***RISK FACTORS***

The following information sets forth risk factors that could cause our actual results to differ materially from those contained in forward-looking statements we have made in this Annual Report on Form 10-K and those we may make from time to time. If any of the following risks actually occur, our business, operating results, prospects or financial condition could be harmed. Additional risks not presently known to us, or that we currently deem immaterial, may also affect our business operations.

Risks Related to Our Company

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

Before obtaining regulatory approval for the sale of any of our potential products, we must subject these product candidates to extensive preclinical and clinical testing to demonstrate their safety and efficacy for humans. Clinical trials are expensive, time-consuming and may take years to complete.

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

- the U.S. Food and Drug Administration (FDA) or similar foreign regulatory authority may not approve an Investigational New Drug (IND) or foreign equivalent filings required to initiate human clinical studies for our drug candidates or may require additional time consuming preclinical studies prior to such approval;
- the product candidate may not prove to be effective or as effective as other competing product candidates;
- we may discover that a product candidate may cause harmful side effects;
- the results may not replicate the results of earlier, smaller trials;
- the FDA or similar foreign regulatory authorities may require use of new or experimental endpoints that may prove insensitive to treatment effects;
- we or the FDA or similar foreign regulatory authorities may suspend the trials;
- the results may not be statistically significant;
- patient recruitment may be slower than expected;
- patients may drop out of the trials; and
- regulatory requirements may change.

These risks and uncertainties impact all of our clinical programs. Specifically, with respect to our gonadotropin-releasing hormone (GnRH) program with Abbott International Luxembourg S.à r.l. (Abbott), any of the clinical, regulatory or operational events described above could delay timelines for the completion of our Phase III endometriosis program or our Phase II uterine fibroids program, prevent the completion of

these programs and/or prevent the ultimate filings for regulatory approvals. Similarly, our VMAT2 inhibitor program and urocortin 2 programs may be delayed if any of the events above lead to delayed enrollment in, or completion of, the Phase II clinical trials of our lead candidates in those programs. Specifically, our VMAT2 inhibitor program will be delayed if the results of the Phase II study with our lead candidate (NBI-98854) do not support advancing the lead candidate to later stage clinical trials or if toxicology studies required by the FDA are not acceptable to the FDA. With respect to our lead Corticotropin Releasing Factor (CRF1) receptor antagonist, 561679, while academic collaborative clinical trials are ongoing to evaluate its effects in post-traumatic stress disorder, anxiety and alcoholism, the top-line efficacy and safety results from a Phase II clinical trial utilizing 561679 in patients experiencing a major depressive episode revealed no benefit of 561679 compared with

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placebo. Uncertainty regarding future development of indiplon is described below under the risk factor entitled *There is uncertainty regarding future development of our product candidate, indiplon, which may never receive regulatory approval or be commercialized.*

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. Any failure or substantial delay in completing clinical trials for our product candidates may severely harm our business.

We depend on continuing our current collaborations and developing additional collaborations to develop and commercialize our product candidates.

Our strategy for fully developing and commercializing our products is dependent upon maintaining our current arrangements and establishing new arrangements with research collaborators, corporate collaborators and others. We have active collaboration agreements with Abbott, Boehringer Ingelheim International GmbH, GlaxoSmithKline and Dainippon Sumitomo Pharma Co. Ltd. and previously have had collaborations with Pfizer, Wyeth, Johnson & Johnson, Novartis, Taisho and Eli Lilly and Company. We historically have been dependent upon these corporate collaborators to provide adequate funding for a number of our programs, and our collaboration agreements with Abbott and Boehringer Ingelheim provide for, among other things, significant future payments should certain development, regulatory and commercial milestones be achieved. Under these arrangements, our corporate collaborators are typically responsible for:

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

Because we expect to continue to rely heavily on our current corporate collaborators and to enter into new collaborations in the future, the development and commercialization of our programs would be substantially delayed, and our ability to receive future funding would be substantially impaired if one or more of our current or future collaborators:

- failed to select a compound that we have discovered for subsequent development into marketable products;
- failed to gain the requisite regulatory approvals of these products;
- did not successfully commercialize products that we originate;
- did not conduct its collaborative activities in a timely manner;
- did not devote sufficient time and resources to our partnered programs or potential products;
- terminated its alliance with us;
- developed, either alone or with others, products that may compete with our products;

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

merged with a third party that wants to terminate the collaboration.

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

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

All of our product candidates are in research, clinical development or subject to review by the FDA. Only a small number of research and development programs ultimately result in commercially successful drugs. Potential products that appear to be promising at early stages of development may not reach the market for a number of reasons. These reasons include the possibilities that the potential products may:

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

If any of our products encounters any of these potential problems, we may never successfully market that product.

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

We may require additional funding to continue our research and product development programs, to conduct preclinical studies and clinical trials, for operating expenses and to pursue regulatory approvals for product candidates, for the costs involved in filing and prosecuting patent applications and enforcing or defending patent claims, if any, product in-licensing and any possible acquisitions, and we may require additional funding to establish manufacturing and marketing capabilities in the future. We believe that our existing capital resources, together with investment income, and future payments due under our strategic alliances, will be sufficient to satisfy our current and projected funding requirements for at least the next 12 months. However, these resources might be insufficient to conduct research and development programs to the full extent currently planned. If we cannot obtain adequate funds, we may be required to curtail significantly one or more of our research and development programs or obtain funds through additional arrangements with corporate collaborators or others that may require us to relinquish rights to some of our technologies or product candidates.

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

- continued scientific progress in our research and development programs;
- the magnitude of our research and development programs;
- progress with preclinical testing and clinical trials;
- the time and costs involved in obtaining regulatory approvals;

the costs involved in filing and pursuing patent applications, enforcing patent claims, or engaging in interference proceedings or other patent litigation;

competing technological and market developments;

the establishment of additional strategic alliances;

the cost of commercialization activities and arrangements, including manufacturing of our product candidates; and

the cost of product in-licensing and any possible acquisitions.

We intend to seek additional funding through strategic alliances, and may seek additional funding through public or private sales of our securities, including equity securities. For example, we have an effective shelf registration statement on file with the Securities and Exchange Commission (SEC) which allows us to issue

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shares of our common stock from time to time for an aggregate initial offering price of up to $125 million, and we have a Committed Equity Financing Facility (CEFF) with Kingsbridge Capital Limited (Kingsbridge) covering the potential sale of shares of our common stock for up to $75 million in gross proceeds. As of January 31, 2012, we have used approximately $88 million under the shelf registration statement and have approximately $37 million still available. In addition, we have previously financed capital purchases and may continue to pursue opportunities to obtain additional debt financing in the future. In the past few years, the credit markets and the financial services industry have experienced a period of unprecedented turmoil and upheaval characterized by the bankruptcy, failure, collapse or sale of various financial institutions and an unprecedented level of intervention from the United States federal government. These events have generally made equity and debt financing more difficult to obtain. Accordingly, additional equity or debt financing might not be available on reasonable terms, if at all. Any additional equity financings, including funds raised under the CEFF, will be dilutive to our stockholders and any additional debt financings may involve operating covenants that restrict our business.

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

Since our inception, we have incurred significant net losses and negative cash flow from operations. As a result of historical operating losses, we had an accumulated deficit of $724.7 million as of December 31, 2011. While we were profitable for the year ended December 31, 2011, we did not generate positive cash flow from operations in 2011. We do not expect to remain profitable, nor do we expect to become cash flow positive, for the foreseeable future.

We have not yet obtained regulatory approvals of any products and, consequently, have not generated revenues from the sale of products. Even if we succeed in developing and commercializing one or more of our drugs, we may not be profitable. We also expect to continue to incur significant operating and capital expenditures as we:

- seek regulatory approvals for our product candidates;
- develop, formulate, manufacture and commercialize our product candidates;
- in-license or acquire new product development opportunities;
- implement additional internal systems and infrastructure; and
- hire additional clinical, scientific and marketing personnel.

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

The CEFF that we entered into with Kingsbridge may not be available to us if we elect to make a draw down, may require us to make additional blackout or other payments to Kingsbridge, could cause our stock price to decline and may result in dilution to our stockholders.

The CEFF entitles us to sell and obligates Kingsbridge to purchase, from time to time until September 15, 2012, newly issued shares of our common stock up to the lesser of an aggregate of approximately 7.8 million shares or $75 million, subject to certain conditions and restrictions. Kingsbridge will not be obligated to purchase shares under the CEFF unless certain conditions are met, which include a minimum price for our common stock;

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the accuracy of representations and warranties made to Kingsbridge; compliance with laws; effectiveness of the registration statement filed by us with the SEC with respect to the CEFF; and the continued listing of our stock on the NASDAQ Global Select Market or other specified markets. In addition, Kingsbridge is permitted to terminate the CEFF if it obtains actual knowledge that a material and adverse event has occurred affecting our business, operations, properties or financial condition. If we are unable to access funds through the CEFF, or if the CEFF is terminated by Kingsbridge, we may be unable to access capital on favorable terms or at all.

We are entitled, in certain circumstances, to deliver a blackout notice to Kingsbridge to suspend the registration statement filed by us with the SEC with respect to the CEFF and prohibit Kingsbridge from selling shares. If we deliver a blackout notice in the 15 calendar days following the settlement of a draw down, or if the registration statement is not effective in circumstances not permitted by the registration rights agreement, then we must make a payment to Kingsbridge, calculated on the basis of the number of shares held by Kingsbridge acquired by way of the most recent drawdown prior to the blackout notice and actually held by Kingsbridge multiplied by the change in the market price of our common stock during the period in which the use of the registration statement is suspended. If the trading price of our common stock declines during a suspension of the registration statement, the blackout or other payment could be significant.

Should we sell shares to Kingsbridge under the CEFF, or issue shares in lieu of a blackout payment, it will have a dilutive effect on the holdings of our current stockholders, and may result in downward pressure on the price of our common stock. If we draw down under the CEFF, we will issue shares to Kingsbridge at a discount of up to 10 percent from the volume weighted average price of our common stock. If we draw down amounts under the CEFF when our share price is decreasing, we will need to issue more shares to raise the same amount than if our stock price was higher. Issuances in the face of a declining share price will have an even greater dilutive effect than if our share price were stable or increasing, and may further decrease our share price.

There is uncertainty regarding future development of our product candidate, indiplon, which may never receive regulatory approval or be commercialized.

In December 2007, we received an action letter from the FDA stating that indiplon 5mg and 10mg capsules are approvable (2007 FDA Approvable Letter). The 2007 FDA Approvable Letter acknowledged that our resubmitted NDA for indiplon 5mg and 10mg capsules had addressed the issues raised in a previous approvable letter, but set forth new requirements. The new requirements set forth in the 2007 FDA Approvable Letter are the following: (i) an objective/subjective clinical trial in the elderly, (ii) a safety study assessing the rates of adverse events occurring with indiplon when compared to a marketed product and (iii) a preclinical study to evaluate indiplon administration during the third trimester of pregnancy. After receipt of the 2007 FDA Approvable Letter, we ceased all indiplon clinical development activities in the United States as well as all pre-commercialization activities. We met with the FDA in July 2008 to discuss the 2007 FDA Approvable Letter. We have not received the final minutes of this meeting. We continue to evaluate various alternatives for the indiplon program.

The process of preparing and resubmitting the NDA for indiplon would require significant resources and could be time consuming and subject to unanticipated delays and cost. As a result of the 2007 FDA Approvable Letter, there is a significant amount of uncertainty regarding the future development of indiplon. Should the NDA be refiled, the FDA could again refuse to approve the NDA, or could still require additional data analysis or clinical trials, which would require substantial expenditures by us and would further delay the approval process. Even if our indiplon NDA is approved, the FDA may determine that our data do not support elements of the labeling we have requested. In such a case, the labeling actually granted by the FDA could limit the commercial success of the product. The FDA could require Phase IV, or post-marketing, trials to study the long-term effects of indiplon and could withdraw its approval based on the results of those trials. The FDA could also require a Risk Evaluation and Mitigation Strategy program for indiplon that could limit the commercial success of the product. We face the risk that for any of the reasons described above, as well as other reasons set forth herein, indiplon may never be approved by the FDA or commercialized anywhere in the world.

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The price of our common stock is volatile.

The market prices for securities of biotechnology and pharmaceutical companies historically have been highly volatile, and the market has from time to time experienced significant price and volume fluctuations that are unrelated to the operating performance of particular companies. Over the course of the last 12 months, the price of our common stock has ranged from approximately $5.00 per share to approximately $9.00 per share. The market price of our common stock may fluctuate in response to many factors, including:

- the results of our clinical trials;
- developments concerning new and existing collaboration agreements;
- announcements of technological innovations or new therapeutic products by us or others;
- general economic and market conditions;
- developments in patent or other proprietary rights;
- developments related to the FDA;
- future sales of our common stock by us or our stockholders (or Kingsbridge, if we elect to draw down under our CEFF with Kingsbridge);
- comments by securities analysts;
- fluctuations in our operating results;
- government regulation;
- health care reimbursement;
- failure of any of our product candidates, if approved, to achieve commercial success; and
- public concern as to the safety of our drugs.

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

Our quarterly revenues, expenses and operating results have fluctuated in the past and are likely to fluctuate significantly in the future. Our revenues are unpredictable and may fluctuate, among other reasons, due to our achievement of product development objectives and milestones, clinical trial enrollment and expenses, research and development expenses and the timing and nature of contract manufacturing and contract

research payments. A high portion of our costs are predetermined on an annual basis, due in part to our significant research and development costs. Thus, small declines in revenue could disproportionately affect operating results in a quarter. Because of these factors, our operating results in one or more future quarters may fail to meet the expectations of securities analysts or investors, which could cause our stock price to decline.

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

We are dependent on licenses from third parties for some of our key technologies. These licenses typically subject us to various commercialization, reporting and other obligations. If we fail to comply with these obligations, we could lose important rights. For example, we have licensed indiplon from DOV Pharmaceuticals, Inc. In addition, we license some of the core technologies used in our research and development activities and collaborations from third parties, including the CRF receptor we license from The Salk Institute and use in our CRF_1 program, urocortin 2 which we license from Research Development Foundation, and the GnRH receptor we license from Mount Sinai School of Medicine and use in our elagolix program. If we were to default on our obligations under any of our licenses, we could lose some or all of our rights to develop, market and sell products covered by these licenses. Likewise, if we were to lose our rights under a license to use proprietary research tools, it could adversely affect our existing collaborations or adversely affect our ability to form new

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collaborations. We also face the risk that our licensors could, for a number of reasons, lose patent protection or lose their rights to the technologies we have licensed, thereby impairing or extinguishing our rights under our licenses with them.

We have limited marketing experience, sales force or distribution capabilities, and if our products are approved, we may not be able to commercialize them successfully.

Although we do not currently have any marketable products, our ability to produce revenues ultimately depends on our ability to sell our products if and when they are approved by the FDA. We currently have limited experience in marketing and selling pharmaceutical products. If we fail to establish successful marketing and sales capabilities or fail to enter into successful marketing arrangements with third parties, our product revenues will suffer.

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

the timing of receipt of marketing approvals;

the safety and efficacy of the products;

the success of existing products addressing our target markets or the emergence of equivalent or superior products; and

the cost-effectiveness of the products.

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

Compliance with changing regulation of corporate governance and public disclosure may result in additional expenses.

Changing laws, regulations and standards relating to corporate governance and public disclosure, including the Sarbanes-Oxley Act of 2002, new SEC regulations and NASDAQ rules, are creating uncertainty for companies such as ours. These laws, regulations and standards are subject to varying interpretations in some cases due to their lack of specificity, and as a result, their application in practice may evolve over time as new guidance is provided by regulatory and governing bodies, which could result in continuing uncertainty regarding compliance matters and higher costs necessitated by ongoing revisions to disclosure and governance practices. We are committed to maintaining high standards of corporate governance and public disclosure. As a result, our efforts to comply with evolving laws, regulations and standards have resulted in, and are likely to continue to result in, increased general and administrative expenses and management time related to compliance activities. In particular, our efforts to comply with Section 404 of the Sarbanes-Oxley Act of 2002 and the related regulations regarding our required assessment of our internal controls over financial reporting requires, and we expect to continue to require, the commitment of significant financial and managerial resources. If we fail to comply with these laws, regulations and standards, our reputation may be harmed and we might be subject to sanctions or investigation by regulatory authorities, such as the SEC. Any such action could adversely affect our financial results and the market price of our common stock.

Risks Related to Our Industry

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

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

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

Health care reform measures could adversely affect our business.

The business and financial condition of pharmaceutical and biotechnology companies are affected by the efforts of governmental and third-party payers to contain or reduce the costs of health care. In the United States,

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comprehensive health care reform legislation was enacted by the Federal government and we expect that there will continue to be a number of federal and state proposals to implement government control over the pricing of prescription pharmaceuticals. In addition, increasing emphasis on reducing the cost of health care in the United States will continue to put pressure on the rate of adoption and pricing of prescription pharmaceuticals. Moreover, in some foreign jurisdictions, pricing of prescription pharmaceuticals is already subject to government control. We are currently unable to predict what additional legislation or regulation, if any, relating to the health care industry or third-party coverage and reimbursement may be enacted in the future or what effect the recently enacted Federal healthcare reform legislation or any such additional legislation or regulation would have on our business. The pendency or approval of such proposals or reforms could result in a decrease in our stock price or limit our ability to raise capital or to enter into collaboration agreements for the further development and commercialization of our programs and products.

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

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

Competition may also arise from, among other things:

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

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

We are performing research on or developing products for the treatment of several disorders including endometriosis, stress-related disorders, pain, diabetes, insomnia, and other neurological and endocrine-related diseases and disorders, and there are a number of competitors to products in our research pipeline. If one or more of our competitors products or programs are successful, the market for our products may be reduced or eliminated.

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

- capital resources;
- research and development resources, including personnel and technology;
- regulatory experience;
- preclinical study and clinical testing experience;
- manufacturing and marketing experience; and

production facilities.

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

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

obtain patent protection for our products;

preserve our trade secrets;

prevent third parties from infringing upon our proprietary rights; and

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

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

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

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

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

We cannot assure you that third parties will not assert patent or other intellectual property infringement claims against us or our collaborators with respect to technologies used in potential products. If a patent infringement suit were brought against us or our collaborators, we or our collaborators could be forced to stop or delay developing, manufacturing or selling potential products that are claimed to infringe a third party s intellectual property unless that party grants us or our collaborators rights to use its intellectual property. In such cases, we could be required to obtain licenses to patents or proprietary rights of others in order to continue to commercialize our products. However, we may not be able to obtain any licenses required under any patents or proprietary rights of third parties on acceptable terms, or at all. Even if our collaborators or we were able to obtain rights to the third party s intellectual property, these rights may be non-exclusive, thereby giving our competitors access to the same intellectual property. Ultimately, we may be unable to commercialize some of our potential products or may have to cease some of our business operations as a result of patent infringement claims, which could severely harm our business.

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

The use of any of our potential products in clinical trials, and the sale of any approved products, may expose us to liability claims. These claims might be made directly by consumers, health care providers, pharmaceutical companies or others selling our products. We have obtained limited product liability insurance coverage for our clinical trials in the amount of $10 million per occurrence and $10 million in the aggregate. However, our

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insurance may not reimburse us or may not be sufficient to reimburse us for any expenses or losses we may suffer. Moreover, insurance coverage is becoming increasingly expensive, and we may not be able to maintain insurance coverage at a reasonable cost or in sufficient amounts to protect us against losses due to liability. We intend to expand our insurance coverage to include the sale of commercial products if we obtain marketing approval for product candidates in development, but we may be unable to obtain commercially reasonable product liability insurance for any products approved for marketing. On occasion, juries have awarded large judgments in class action lawsuits based on drugs that had unanticipated side effects. A successful product liability claim or series of claims brought against us would decrease our cash reserves and could cause our stock price to fall.

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

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

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ITEM 1B. ***UNRESOLVED STAFF COMMENTS***

None.

ITEM 2. ***PROPERTIES***

We lease our corporate headquarters which consists of approximately 140,000 square feet of laboratory and office space located at 12780 El Camino Real in San Diego, California. The lease expires in December 2019, however we have options to extend the term of the lease for up to two consecutive ten year periods.

We believe that our property and equipment are generally well maintained and in good operating condition.

ITEM 3. ***LEGAL PROCEEDINGS***

We are not currently a party to any material legal proceedings.

ITEM 4. ***REMOVED AND RESERVED***

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PART II

ITEM 5. ***MARKET FOR REGISTRANT S COMMON EQUITY, RELATED STOCKHOLDER MATTERS AND ISSUER PURCHASES OF EQUITY SECURITIES***

Our common stock is traded on the NASDAQ Global Select Market under the symbol NBIX. The following table sets forth for the periods indicated the high and low sale price for our common stock. These prices do not include retail markups, markdowns or commissions.

	High	Low
Year Ended December 31, 2011		
1st Quarter	$ 8.40	$ 6.41
2nd Quarter	8.60	6.77
3rd Quarter	8.44	5.49
4th Quarter	8.75	5.42
Year Ended December 31, 2010		
1st Quarter	$ 2.85	$ 2.12
2nd Quarter	6.23	2.30
3rd Quarter	6.64	4.98
4th Quarter	9.30	5.80

As of January 31, 2012, there were approximately 68 stockholders of record of our common stock. We have not paid any cash dividends on our common stock since inception and do not anticipate paying cash dividends in the foreseeable future.

Information about our equity compensation plans is incorporated herein by reference to Item 12 of Part III of this Annual Report on Form 10-K.

Recent Sales of Unregistered Securities

There were no unregistered sales of equity securities during fiscal 2011.

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Stock Performance Graph and Cumulative Total Return

The graph below shows the cumulative total stockholder return assuming the investment of $100 on December 31, 2006 (and the reinvestment of dividends thereafter) in each of (i) Neurocrine Biosciences, Inc. s common stock, (ii) the NASDAQ Composite Index and (iii) the NASDAQ Biotechnology Index. The comparisons in the graph below are based upon historical data and are not indicative of, or intended to forecast, future performance of our common stock or Indexes.

* **$100 INVESTED ON 12/31/06 IN STOCK OR INDEX INCLUDING REINVESTMENT OF DIVIDENDS AT FISCAL YEARS ENDING DECEMBER 31.**

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ITEM 6. ***SELECTED FINANCIAL DATA***

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

	2011	2010	2009	2008	2007
	(In thousands, except for income (loss) per share data)				
STATEMENT OF OPERATIONS DATA					
Revenues:					
Sponsored research and development	$ 10,462	$ 10,938	$ 34	$ 47	$ 139
Milestones and license fees	66,951	22,563	2,919	3,919	986
Grant income and other revenues				9	99
Total revenues	77,413	33,501	2,953	3,975	1,224
Operating expenses:					
Research and development	30,951	31,151	33,722	55,544	77,108
General and administrative	12,458	13,273	14,360	17,936	35,434
Cease-use expense	82	2,799	5,984	15,742	
Restructuring expenses			2,557	2,051	6,924
Asset impairment					94,000
Total operating expenses	43,491	47,223	56,623	91,273	213,466
Income (loss) from operations	33,922	(13,722)	(53,670)	(87,298)	(212,242)
Other income and (expense):					
Gain on sale/disposal of assets	3,195	3,161	3,626	3,570	129
Other income (expense), net	454	2,593	(994)	(4,885)	4,814
Total other income and (expense)	3,649	5,754	2,632	(1,315)	4,943
Net income (loss)	$ 37,571	$ (7,968)	$ (51,038)	$ (88,613)	$ (207,299)
Net income (loss) per common share:					
Basic	$ 0.68	$ (0.15)	$ (1.30)	$ (2.30)	$ (5.45)
Diluted	$ 0.67	$ (0.15)	$ (1.30)	$ (2.30)	$ (5.45)
Shares used in calculation of net income (loss) per common share:					
Basic	55,176	52,820	39,137	38,449	38,009
Diluted	56,347	52,820	39,137	38,449	38,009
BALANCE SHEET DATA					
Cash, cash equivalents and short-term investments	$ 129,103	$ 126,865	$ 53,464	$ 80,473	$ 179,385
Working capital	85,366	80,274	35,426	55,329	153,041
Total assets	138,368	144,424	70,818	118,182	276,654
Long-term debt					
Accumulated deficit	(724,698)	(762,269)	(754,301)	(703,263)	(614,650)
Total stockholders equity	60,081	19,345	3,954	36,774	118,697

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

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

Overview

We discover, develop and intend to commercialize drugs for the treatment of neurological and endocrine-related diseases and disorders. Our product candidates address some of the largest pharmaceutical markets in the world, including endometriosis, stress-related disorders, pain, diabetes, insomnia, and other neurological and endocrine-related diseases and disorders. To date, we have not generated any revenues from the sale of products. We have funded our operations primarily through private and public offerings of our common stock and payments received under research and development collaboration agreements. We are developing certain products with corporate collaborators and intend to rely on existing and future collaborators to meet funding requirements. We expect to generate future operating cash flow losses as product candidates are advanced through the various stages of clinical development. As of December 31, 2011, we had an accumulated deficit of $724.7 million and expect to incur operating cash flow losses for the foreseeable future, which may be greater than losses in prior years. We currently have eleven programs in various stages of research and development, including six programs in clinical development. While we independently develop several of our product candidates, we have entered into collaborations for six of our programs. Our lead clinical development program, elagolix, is a drug candidate for the treatment of endometriosis and uterine fibroids that is partnered with Abbott.

Critical Accounting Policies

Our discussion and analysis of our financial condition and results of operations is based upon financial statements that we have prepared in accordance with accounting principles generally accepted in the United States. The preparation of these financial statements requires management to make estimates and judgments that affect the reported amounts of assets, liabilities and expenses, and related disclosures. On an on-going basis, we evaluate these estimates, including those related to revenues under collaborative research agreements, clinical trial accruals (research and development expense), share-based compensation, lease related activities, and fixed assets. Estimates are based on historical experience, information received from third parties and on various other assumptions that are believed to be reasonable under the circumstances, the results of which form the basis for making judgments about the carrying values of assets and liabilities that are not readily apparent from other sources. Actual results may differ from these estimates under different assumptions or conditions. Historically, revisions to our estimates have not resulted in a material change to the financial statements. The items in our financial statements requiring significant estimates and judgments are as follows:

Revenue Recognition

Revenues under collaborative research and development agreements are recognized as costs are incurred over the period specified in the related agreement or as the services are performed. These agreements are on a best-efforts basis, and do not require scientific achievement as a performance obligation, and provide for payment to be made when costs are incurred or the services are performed. All fees are nonrefundable to the collaborators. Prior to the revised multiple element guidance adopted by us on January 1, 2011, upfront, nonrefundable payments for license fees and advance payments for sponsored research revenues received in

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excess of amounts earned were classified as deferred revenue and recognized as income over the contract or development period. Estimating the duration of the development period includes continual assessment of development stages and regulatory requirements. If we enter into a new collaboration agreement or materially modify an existing collaboration agreement, we will be required to apply the revised multiple element guidance. Milestone payments are recognized as revenue upon achievement of pre-defined scientific events, which requires substantive effort, and for which achievement of the milestone was not readily assured at the inception of the agreement. In 2010, we entered into collaboration agreements for our gonadotropin-releasing hormone (GnRH) antagonist program and our GPR119 agonist program.

Abbott International Luxembourg S.à r.l. (Abbott). In June 2010, we announced an exclusive worldwide collaboration with Abbott to develop and commercialize elagolix and all next-generation GnRH antagonists (collectively, GnRH Compounds) for women s and men s health. Under the terms of our agreement with Abbott, we and Abbott will work jointly to advance GnRH Compounds towards commercialization. Abbott made an upfront payment of $75 million and agreed to make additional development and regulatory event based payments of up to $480 million and up to an additional $50 million in commercial event based payments. We have assessed event based payments under the revised authoritative guidance for research and development milestones and determined that the event based payments prior to commencement of a Phase III clinical study, as defined in the agreement, meet the definition of a milestone as they are 1) events that can only be achieved in part on our past performance, 2) there is substantive uncertainty at the date the arrangement is entered into that the event will be achieved and 3) they result in additional payments being due to us. Development and regulatory event based payments subsequent to the commencement of a Phase III clinical study, however, currently do not meet this criteria as their achievement is based on the performance of Abbott. As of December 31, 2011, there are no further milestones, that meet the definition of a milestone, in accordance with authoritative guidance.

Under the terms of the agreement, Abbott is responsible for all development, marketing and commercialization costs. We will receive funding for certain internal collaboration expenses which includes reimbursement from Abbott for internal and external expenses related to the GnRH Compounds, which reimbursement includes up to approximately $24 million in personnel funding through the end of 2012. We will be entitled to a percentage of worldwide sales of GnRH Compounds for the longer of ten years or the life of the related patent rights. Under the terms of our agreement with Abbott, the collaboration effort between the parties to advance the GnRH compounds toward commercialization is governed by a joint development committee with representatives from both Neurocrine and Abbott; provided, however, that final decision making authority rests with Abbott. Abbott may terminate the collaboration at its discretion upon 180 days written notice to us. In such event, we would be entitled to specified payments for ongoing clinical development and related activities and all GnRH Compound product rights would revert to us. Our participation in the joint development committee has been determined to be a substantive deliverable under the contract, and therefore, the upfront payment has been deferred and is being recognized over the estimated term of the joint development committee, which is expected to be through the end of 2012. For the years ended December 31, 2011 and 2010, we recorded revenues of $29.0 million and $16.9 million in amortization of up-front license fees, respectively, and $9.1 million and $10.1 million in sponsored development revenue, respectively, under the Abbott collaboration agreement. Additionally, during 2011 we recorded $30.0 million in milestone revenue, $10.0 million of which was related to advancing elagolix into Phase II clinical trials for uterine fibroids and $20.0 million of which was related to the outcome of an elagolix pre-Phase III meeting with the FDA for endometriosis. At December 31, 2011, we had $29.0 million of deferred revenue related to the Abbott agreement, which is being amortized over the estimated remaining collaborative development period.

Boehringer Ingelheim International GmbH (Boehringer Ingelheim). In June 2010, we announced a worldwide collaboration with Boehringer Ingelheim to research, develop and commercialize small molecule GPR119 agonists for the treatment of Type II diabetes and other indications. Under the terms of the agreement, we and Boehringer Ingelheim will work jointly to identify and advance GPR119 agonist candidates into preclinical development. Boehringer Ingelheim will then be responsible for the global development and commercialization of potential GPR119 agonist products. We received a $10 million upfront payment, and we are currently receiving research funding to support discovery efforts. We are eligible to receive up to

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approximately $3 million in additional preclinical milestone payments and $223 million in clinical development and commercial event based payments. We have assessed milestones under the revised authoritative guidance for research and development milestones and determined that the preclinical milestone payments, as defined in the agreement, meet the definition of a milestone as they are 1) events that can only be achieved in part on our past performance or upon the occurrence of a specific outcome resulting from our performance, 2) there is substantive uncertainty at the date the arrangement is entered into that the event will be achieved and 3) they result in additional payments being due to us. Clinical development and commercial milestone payments, however, currently do not meet this criteria as their achievement is solely based on the performance of Boehringer Ingelheim. No milestone payments have been recognized to date. We will be entitled to a percentage of any future worldwide sales of GPR119 agonists resulting from the collaboration. Under the terms of the agreement, the collaboration effort between the parties to identify and advance GPR119 agonist candidates into preclinical development is governed by a steering committee with representatives from both Neurocrine and Boehringer Ingelheim; provided, however, that the final decision making authority rests with Boehringer Ingelheim. Boehringer Ingelheim may terminate the agreement at its discretion upon prior written notice to us. In such event, we may be entitled to specified payments and product rights would revert to us. Our participation in the steering committee has been determined to be a substantive deliverable under the contract, and therefore, the upfront payment has been deferred and is being recognized over the estimated term of the steering committee, which is expected to be through June 2012. For the years ended December 31, 2011 and 2010, we recorded revenues of $5.0 million and $2.7 million in amortization of up-front license fees and $1.3 million and $0.8 million in sponsored research related to the Boehringer Ingelheim agreement, respectively. At December 31, 2011, we had $2.3 million of deferred license fees that will be amortized over the estimated remaining collaborative research period of the agreement.

Research and Development Expense

Research and development (R&D) expenses consists primarily of salaries, payroll taxes, employee benefits, and share-based compensation charges, for those individuals involved in ongoing research and development efforts; as well as scientific contractor fees, preclinical and clinical trial costs, research and development facilities costs, laboratory supply costs, and depreciation of scientific equipment. All such costs are charged to R&D expense as incurred. These expenses result from our independent R&D efforts as well as efforts associated with collaborations and in-licensing arrangements. In addition, we fund R&D and clinical trials at other companies and research institutions under agreements, which are generally cancelable. We review and accrue clinical trials expense based on work performed, which relies on estimates of total costs incurred based on patient enrollment, completion of studies and other events. We follow this method since reasonably dependable estimates of the costs applicable to various stages of a research agreement or clinical trial can be made. Accrued clinical costs are subject to revisions as trials progress to completion. Revisions are charged to expense in the period in which the facts that give rise to the revision become known. Historically, revisions have not resulted in material changes to R&D expenses, however a modification in the protocol of a clinical trial or cancellation of a trial could result in a charge to our results of operations.

Share-Based Compensation

We grant stock options to purchase our common stock to our employees and directors under our 2011 Equity Incentive Plan (the 2011 Plan) and grant stock options to certain employees pursuant to Employment Commencement Nonstatutory Stock Option Agreements. We also grant certain employees stock bonuses and restricted stock units under the 2011 Plan. Additionally, we have outstanding options that were granted under previous option plans from which we no longer make grants. Share-based compensation expense recognized in accordance with authoritative guidance for the years ended December 31, 2011, 2010, and 2009 was $2.9 million, $3.1 million, and $5.5 million, respectively.

Stock option awards and restricted stock units generally vest over a three to four year period and expense is ratably recognized over those same time periods. However, due to certain retirement provisions in our

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2003 Incentive Stock Plan, share-based compensation expense may be recognized over a shorter period of time, and in some cases the entire share-based compensation expense may be recognized upon grant of the share-based compensation award. Employees who are age 55 or older and have five or more years of service with us are entitled to accelerated vesting of certain unvested share-based compensation awards upon retirement. This retirement provision leads to variability in the quarterly expense amounts recognized in accordance with authoritative guidance, and therefore individual share-based compensation awards may impact earnings disproportionately in any individual fiscal quarter.

For purposes of calculating share-based compensation, we estimate the fair value of share-based compensation awards using a Black-Scholes option-pricing model. The determination of the fair value of share-based compensation awards utilizing the Black-Scholes model is affected by our stock price and a number of assumptions, including but not limited to expected stock price volatility over the term of the awards and the expected term of stock options. Our stock options have characteristics significantly different from those of traded options, and changes in the assumptions can materially affect the fair value estimates.

If factors change and we employ different assumptions, share-based compensation expense may differ significantly from what we have recorded in the past. If there is a difference between the assumptions used in determining share-based compensation expense and the actual factors which become known over time, specifically with respect to anticipated forfeitures, we may change the input factors used in determining share-based compensation expense for future grants. These changes, if any, may materially impact our results of operations in the period such changes are made. If actual forfeitures vary from our estimates, we will recognize the difference in compensation expense in the period the actual forfeitures occur or at the time of vesting.

Real Estate

In December 2007, we closed the sale of our facility and associated real property for a purchase price of $109 million. Concurrent with the sale we retired the entire $47.7 million in mortgage debt previously outstanding with respect to the facility and associated real property, and received cash of $61.0 million net of transaction costs and debt retirement.

Upon the closing of the sale of the facility and associated real property, we entered into a lease agreement (Lease) with DMH Campus Investors, LLC (DMH) whereby we leased back for an initial term of 12 years our corporate headquarters comprised of two buildings located at 12790 El Camino Real (Front Building) and 12780 El Camino Real (Rear Building) in San Diego, California. We entered into a series of lease amendments (Amendments), beginning in late 2008, through which we vacated the Front Building, but continue to occupy the Rear Building. At December 31, 2011 and 2010, the liability related to vacating the Front Building was $0 and $7.5 million, respectively.

The ultimate result of this real estate sale was a net gain of $39.1 million which was deferred in accordance with authoritative guidance in 2008. For the year ended 2011, 2010 and 2009, we recognized $3.0 million, $2.9 million and $2.8 million, respectively, of the deferred gain and will recognize the remaining $27.0 million of the deferred gain over the initial Lease term which will expire at the end of 2019.

Under the terms of the Lease and the Amendments, we pay base annual rent (subject to an annual fixed percentage increase), plus a 3.5% annual management fee, property taxes and other normal and necessary expenses associated with the Lease such as utilities, repairs and maintenance. In lieu of a cash security deposit under the Lease, Wells Fargo Bank, N.A. issued on our behalf a letter of credit in the amount of $4.2 million. The letter of credit is secured by a deposit of $4.2 million with the same bank. We have the right to extend the Lease for two consecutive ten-year terms.

In December 2010, we entered into a sublease agreement (Sublease) for approximately 16,000 square feet of the Rear Building. The Sublease is expected to result in approximately $0.6 million of rental income per year

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over the three year term of the Sublease and is recorded as an offset to rent expense. The Sublease provides the subtenant with an option to extend the term for two one-year renewal periods. The income generated under the Sublease is lower than our financial obligation under our Lease for the Rear Building as determined on a per square foot basis. Consequently, at December 31, 2010, we were required to record a cease use liability for the net present value estimated difference between the expected income to be generated under the Sublease and future subleases and the Lease obligation over the remaining term of the Lease for the space that is occupied by the subtenant. This transaction resulted in $2.5 million of gross cease use expense, and a reversal of associated deferred rent of $173,000.

In September 2011, we entered into a second sublease agreement (Second Sublease) for approximately 3,300 square feet of space in the Rear Building. The Second Sublease is expected to result in approximately $0.1 million in rental income per year over the three year term and is recorded as an offset to rent expense. The Second Sublease provides the subtenant with an option to extend the term for a one-year renewal period. Similar to the Sublease, this Second Sublease resulted in $0.3 million of gross cease use expense, and a reversal of associated deferred rent of $47,000.

At December 31, 2011 and 2010, we had recorded in our consolidated balance sheet a cease use liability related to both the Sublease and the Second Sublease of $2.6 million and $2.5 million, respectively.

Asset Impairment

In accordance with authoritative accounting guidance, if indicators of impairment exist, we assess the recoverability of the affected long-lived assets by determining whether the carrying value of such assets can be recovered through undiscounted future operating cash flows. If impairment is indicated, we measure the amount of such impairment by comparing the carrying value of the asset to the estimated fair value of the related asset, which is generally determined based on the present value of the expected future cash flows.

Results of Operations for Years Ended December 31, 2011, 2010 and 2009

Revenue

The following table summarizes our primary sources of revenue during the periods presented:

	Year Ended December 31,		
	2011	2010	2009
	(In millions)		
Revenues under collaboration agreements:			
Abbott International Luxembourg S.à r.l. (Abbott)	$ 68.1	$ 27.0	$
GlaxoSmithKline (GSK)	0.1	0.1	0.1
Dainippon Sumitomo Pharma Co. Ltd. (DSP)	2.9	2.9	2.9
Boehringer Ingelheim International GmbH (Boehringer Ingelheim)	6.3	3.5	
Total revenues	$ 77.4	$ 33.5	$ 3.0

The increase in revenues from the year ended December 31, 2010 to the year ended December 31, 2011 was primarily due to two milestones recognized under the Abbott collaboration agreement. During 2011, we recorded an aggregate of $30.0 million in milestone revenue, $10.0 million of which was related to advancing elagolix into Phase II clinical trials for uterine fibroids and $20.0 million of which was related to the outcome of an elagolix pre-Phase III meeting with the FDA for endometriosis. Additionally, 2011 represented the first full year under the Abbott and Boehringer Ingelheim collaboration agreements and revenue recognized from the amortization of up-front license fees increased from $19.6 million in 2010 to $34.0 million in 2011.

The increase in revenues from the year ended December 31, 2009 to the year ended December 31, 2010 was primarily due to executing collaboration agreements with Abbott and Boehringer Ingelheim, for our GnRH

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(including elagolix) and GPR119 programs, respectively. During 2010, we recognized revenue of $19.6 million from amortization of up-front license fees and $10.9 million resulting from sponsored research and development reimbursement under these two collaboration agreements.

During each of the three years ended December 31, 2011, 2010 and 2009, we recognized $2.9 million in revenue under our collaboration agreement with DSP from amortization of up-front licensing fees.

We expect revenue to decrease significantly during 2012, primarily due to lower milestone revenue under the Abbott collaboration agreement. In 2011, we recognized an aggregate of $30 million in milestone revenue. We do not expect to recognize any milestone revenue in 2012.

Operating Expenses

Research and Development

Our research and development expenditures include costs related to preclinical and clinical trials, scientific personnel, equipment, consultants, sponsored research, share-based compensation and allocated facility costs. We do not track fully burdened research and development costs separately for each of our drug candidates. We review our research and development expenses by focusing on four categories: external development, personnel, facility and depreciation, and other. External development expenses consist of costs associated with our external preclinical and clinical trials, including pharmaceutical development and manufacturing. Personnel expenses include salaries and wages, share-based compensation, payroll taxes and benefits for those individuals involved in ongoing research and development efforts. Other research and development expenses mainly represent lab supply expenses, scientific consulting expenses and other expenses. We currently have eleven programs in various stages of research and development, including six programs in clinical development.

The following table presents our total research and development expenses by category during the periods presented:

	Years Ended December 31,		
	2011	2010	2009
		(In millions)	
External development expense:			
Elagolix	$ 4.0	$ 7.9	$ 8.9
VMAT2	4.4	1.8	0.6
Other	0.1		0.3
Total external development expense	8.5	9.7	9.8
R&D personnel expense	11.6	11.3	11.8
R&D facility and depreciation expense	6.2	7.0	8.8
Other R&D expense	4.7	3.2	3.3
Total research and development expense	$ 31.0	$ 31.2	$ 33.7

R&D expense decreased from $31.2 million in 2010 to $31.0 million in 2011. The increase in VMAT2 external development expense, due to Phase II clinical trial activity, was offset by a decrease in elagolix external development expenses as responsibility for that program has been shifted to Abbott. Other R&D expense increased from 2010 to 2011, primarily attributable to outside consultants who advise us on research and clinical projects. The $2.5 million decrease in research and development expense from 2009 to 2010 was primarily due to our restructuring program in 2009 coupled with lower depreciation expense which decreased by $1.5 million due to asset sales and assets reaching the end of their depreciable lives.

The funding necessary to bring a drug candidate to market is subject to numerous uncertainties, which may adversely affect our liquidity and capital resources. Once a drug c