

NEUROCRINE BIOSCIENCES INC

Form 10-K

February 10, 2011

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**UNITED STATES**  
**SECURITIES AND EXCHANGE COMMISSION**

Washington, D.C. 20549

**Form 10-K**

(Mark One)

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

For the fiscal year ended December 31, 2010

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)

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

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

**12780 El Camino Real, San Diego, CA**  
(Address of principal executive offices)

**92130**  
(Zip Code)

**Registrant's telephone number, including area code:**  
**(858) 617-7600**

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

<b>Title of Each Class</b>	<b>Name of Each Exchange on Which Registered</b>
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

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

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

Indicate by check mark 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  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.

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  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

The aggregate market value of the common equity held by non-affiliates of the registrant as of June 30, 2010 totaled approximately \$265,426,118 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, 2010. The identification of 10% or

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greater stockholders as of June 30, 2010 is based on Schedule 13G and amended Schedule 13G reports publicly filed before June 30, 2010. This calculation does not reflect a determination that such parties are affiliates for any other purposes.

As of February 1, 2011, there were 54,887,088 shares of the registrant's Common Stock outstanding.

### DOCUMENTS INCORPORATED BY REFERENCE

<b>Document Description</b>	<b>10-K Part</b>
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, 2010 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 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, 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.

**Table of Contents****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
<b>Products in clinical development:</b>			
Elagolix	Endometriosis	Phase II	Abbott/Neurocrine
Vesicular Monoamine Transporter 2 Inhibitor (VMAT2)	Movement Disorders	Phase II	Neurocrine
CRF <sub>2</sub> Peptide Agonist urocortin 2	Cardiovascular	Phase II	Neurocrine
CRF <sub>1</sub> Antagonist (561679)	Stress-related Disorders	Phase II	GlaxoSmithKline/Neurocrine
CRF <sub>1</sub> Antagonist (586529)	Mood Disorders	Phase I	GlaxoSmithKline/Neurocrine
Elagolix	Uterine Fibroids	Phase I	Abbott/Neurocrine
	Men's and Women's Health		
<b>Research programs:</b>			
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
<b>Product subject to regulatory review:</b>			
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<sub>1</sub> and CRF<sub>2</sub> refer to two CRF receptor subtypes.

**Products 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

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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 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 (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 elagolix 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.



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The first additional Phase IIb trial (Lilac PETAL study 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 endometriosis in this trial. The three-month placebo controlled portion of the 702 study showed that elagolix 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 study or 703 study) consisted of four arms, elagolix 150mg once daily, elagolix 250mg once daily, Prostag<sup>®</sup> 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 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 have scheduled an end of Phase II meeting with the FDA in March 2011, 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 agreement with the FDA on the Phase III trial design, we expect elagolix to enter Phase III clinical trials in 2011.

### ***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.

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We have identified a highly selective VMAT2 inhibitor that is effective in pre-clinical 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, our VMAT2 inhibitor completed a Phase I single ascending dose clinical trial in healthy male volunteers in Canada under an approved Clinical Trial Application with Health Canada. This trial showed our VMAT2 inhibitor 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 our VMAT2 inhibitor 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 in healthy male volunteers. This trial also showed our VMAT2 inhibitor 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 dose exploration study in patients with tardive dyskinesia in late 2010. In the event of successful completion of this Phase IIa study, we plan to approach the FDA regarding the filing of an IND in the United States with the purpose of initiating larger Phase IIb studies in patients with tardive dyskinesia.

Tardive dyskinesia is characterized by involuntary movements of the muscles of the face, trunk or limbs which arise after months or years of dopamine antagonist treatment, e.g. typical and atypical antipsychotics for schizophrenia, bipolar, and refractory depression, and metoclopramide for gastroparesis. While the prevalence rates of tardive dyskinesia can vary greatly in accordance with the population being studied, it is estimated that 150,000-250,000 individuals suffering from schizophrenia are affected by tardive dyskinesia in the United States alone.

In addition to tardive dyskinesia, we believe that this clinical candidate may be effective in the management of other hyperkinetic movement disorders characterized by involuntary bodily movements such as Tourette's syndrome, tardive dystonia, and Huntington's disease. Additionally, the modulation of dopamine pathways may also be useful for patients suffering from schizophrenia, one population at risk for tardive dyskinesia.

### ***CRF<sub>2</sub> 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 (2011), 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<sub>2</sub> 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.

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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 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 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 currently underway. A subset of 10 subjects are also undergoing right heart catheterization for more detailed evaluation of their cardiac status and response to treatment. We anticipate having the results of this study in mid-2011.

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<sub>1</sub> 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<sub>1</sub> and CRF<sub>2</sub>, 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<sub>1</sub> 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.

GSK has also successfully completed a Phase I single dose escalating clinical trial with 586529, an additional CRF<sub>1</sub> receptor antagonist compound.

## **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 over \$90 billion in worldwide drug sales according to Datamonitor (2007).

### ***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 Type II diabetes in the United States alone with a worldwide prevalence in excess of 200 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 pre-clinical development. Boehringer Ingelheim will then be responsible for the global development and commercialization of potential GPR119 agonist products.

### ***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 Subject to Regulatory Review**

#### ***Indiplon***

Indiplon is a non-benzodiazepine GABA<sub>A</sub> 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 \$31.2 million, \$33.7 million and \$55.5 million for the years ended December 31, 2010, 2009 and 2008, 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. For example, during 2003, we licensed our urocortin 2 product candidate from the Research Development Foundation.

### **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, regulatory and commercial milestone payments of up to approximately \$530 million. 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

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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. For the year ended December 31, 2010, we recorded revenues of \$16.9 million in amortization of up-front license fees and \$10.1 million in sponsored development related to the Abbott agreement. In addition, at December 31, 2010 we had \$58.1 million of deferred revenue related to the Abbott agreement, which is being amortized over 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 will work jointly to identify and advance GPR119 agonist candidates into pre-clinical 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, we are currently receiving research funding to support discovery efforts, and we are eligible to receive up to approximately \$225 million in development, regulatory and commercial milestone 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 pre-clinical 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. For the year ended December 31, 2010, we recorded revenues of \$2.7 million in amortization of up-front license fees and \$0.8 million in sponsored research related to the Boehringer Ingelheim agreement. At December 31, 2010, we had \$7.3 million of deferred license fees that will be amortized over the remaining term of the collaborative research period 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 milestone 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.

*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 milestone payments upon specified future events related to the development and commercialization of indiplon in Japan. Should all milestones 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, 2010, we had recorded revenues of \$9.2 million in license fees from DSP over the life of the agreement.

## **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

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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.

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 98854 is currently in clinical trials and is subject to a pending patent application.

Urocortin 2 is an endogenous peptide ligand of the CRF<sub>2</sub> 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<sub>A</sub> 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.



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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.

### **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

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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 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, diabetes, insomnia, and other neurological and endocrine-related diseases and disorders.

Lupron Depot<sup>®</sup>, marketed by Abbott Laboratories, and Synarel<sup>®</sup> and Depo-Provera<sup>®</sup>, 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 gonadotropin-releasing hormone (GnRH) antagonists we develop for these indications.

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<sup>®</sup> marketed by Valeant Pharmaceuticals International, Inc., 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<sup>®</sup> marketed by Eli Lilly, Xanax<sup>®</sup>, marketed by Pfizer, Lexapro<sup>®</sup>, marketed by Forest Laboratories, Zoloft<sup>®</sup>, marketed by Pfizer, Paxil<sup>®</sup>, marketed by GSK and Pristiq<sup>®</sup>, 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<sup>®</sup>, Sonata<sup>®</sup>, Lunesta<sup>®</sup>, and Rozerem<sup>®</sup>, which are currently marketed by Sanofi-Aventis, King Pharmaceuticals, Inc., Sunovion Pharmaceuticals, Inc. and Takeda Pharmaceutical Company, respectively. During 2006, Sanofi-Aventis launched a controlled-release formulation of Ambien<sup>®</sup> called Ambien CR<sup>®</sup> and during 2007 generic Ambien<sup>®</sup> 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, 2010, we had approximately 66 full-time employees, of which 14 hold Ph.D., M.D. or equivalent degrees, and 11 others hold an M.S., M.B.A., or equivalent degrees. Of these full-time employees, 48 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](http://www.neurocrine.com), as soon as reasonably practicable after such reports are available on the Securities and Exchange Commission website at [www.sec.gov](http://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 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 U.S. Food and Drug Administration (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 GnRH program, if the modified wording of the non-menstrual pain and dysmenorrhea daily scales used in our elagolix Daisy PETAL Study (901 study) is not accepted by the FDA as the appropriate endpoint for elagolix Phase III clinical trials, additional Phase II trials will be necessary and the development of elagolix will be delayed or otherwise adversely affected. Similarly, while academic collaborative clinical trials are ongoing to evaluate the effects of our lead Corticotropin Releasing Factor (CRF<sub>1</sub>) receptor 561679 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 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.

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*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 International Luxembourg S.à r.l., 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 recently executed 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.

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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.

***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.

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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 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)

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covering the potential sale of shares of our common stock for up to \$75 million in gross proceeds. 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, including net losses of \$8.0 million and \$51.0 million for the years ended December 31, 2010 and 2009, respectively. As a result of ongoing operating losses, we had an accumulated deficit of \$762.3 million as of December 31, 2010. While we expect to be profitable for the year ending December 31, 2011, we do not expect to be operating cash flow positive in 2011 nor do we expect to remain profitable for the foreseeable future after 2011.

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 over a period of three years, 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; 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.



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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.***

On December 12, 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 (REMS) 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 \$2.00 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. 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<sub>1</sub> 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

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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 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;

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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

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;



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the safety and efficacy of the products;

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

the cost-effectiveness of the products.

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

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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, 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;

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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.

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 (USPTO) 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



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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 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 70,000 square feet of office space located at 12790 El Camino Real (Front Building) and approximately 140,000 square feet of laboratory and office space located at 12780 El Camino Real (Rear Building) in San Diego, California. We sold our facility and associated real property for \$109 million in a sale-leaseback transaction in December 2007 and entered into a twelve year lease with the purchaser, DMH Campus Investors, LLC (DMH). In December 2008, we entered into a first amendment to the lease (First Lease Amendment) that provided for the renovation of the Front Building in a manner that facilitates multiple tenant usage and establishes a mechanism for us to terminate our use of the Front Building. We are obligated to reimburse the landlord for the total cost of renovating the Front Building so that it becomes suitable for multiple tenant usage. The amendment also terminated our prior right to repurchase the facility and associated real property.

Effective September 25, 2009, we entered into a second amendment to the lease (Second Lease Amendment). The Second Lease Amendment obligated us to vacate the Front Building and make an immediate payment of \$4.0 million to DMH as an initial release fee, which was paid October 2, 2009. We continue to occupy the entire Rear Building. Upon payment of the initial release fee, we were released from our obligations with respect to the Front Building, except with respect to 1) certain indemnity obligations for events prior to the payment of the initial release fee, 2) certain operating expenses for the Front Building in accordance with the terms of the Lease through July 2011, and 3) 50% of tenant improvement costs between \$65 and \$100 per square foot in connection with initial leases between DMH and other third parties for space in the Front Building which amounts were paid in 2009. Pursuant to the Second Lease Amendment, we are also obligated to pay DMH an amount equivalent to the rent on the Front Building through July 2011 and then approximately \$44,000 per month beginning in August 2011 through December 2019 as a rent differential payment for the Front Building, which such rent differential amounts may be prepaid by us in our sole discretion. Should we be in monetary default under our lease agreement with DMH beyond the normal cure periods and prior to repaying the entire rent differential balance, the rent differential payment will double.

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**

**Table of Contents****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
<b>Year Ended December 31, 2010</b>		
1st Quarter	\$ 2.85	\$ 2.12
2nd Quarter	6.23	2.30
3rd Quarter	6.64	4.98
4th Quarter	9.30	5.80
<b>Year Ended December 31, 2009</b>		
1st Quarter	\$ 4.25	\$ 3.02
2nd Quarter	3.97	2.87
3rd Quarter	3.67	2.93
4th Quarter	3.10	1.94

As of January 31, 2011, there were approximately 101 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 2010 that have not been previously disclosed in a Current Report on Form 8-K.

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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, 2005 (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 12/31/05 IN STOCK OR INDEX INCLUDING REINVESTMENT OF DIVIDENDS AT FISCAL YEARS ENDING DECEMBER 31.**



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**ITEM 6.**