NEUROCRINE BIOSCIENCES INC
Form 10-K
February 11, 2016
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UNITED STATES

SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

Form 10-K

(Mark One)

þ **ANNUAL REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934**
For the fiscal year ended December 31, 2015

OR

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

Commission file number: 0-22705

NEUROCRINE BIOSCIENCES, INC.

(Exact name of registrant as specified in its charter)

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

Registrant s telephone number, including area code:

(858) 617-7600

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

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

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

Indicate by check mark if the registrant is a well-known seasoned issuer, as defined in Rule 405 of the Securities Act. Yes þ 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 þ

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

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

Indicate by check mark if disclosure of delinquent filers pursuant to Item 405 of Regulation S-K (§ 229.405 of this chapter) is not contained herein, and will not be contained, to the best of registrant s knowledge, in definitive proxy or information statements incorporated by reference in Part III of this Form 10-K or any amendment to this Form 10-K. þ

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

Large accelerated filer þ	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 þ

The aggregate market value of the common equity held by non-affiliates of the registrant as of June 30, 2015 totaled approximately $3,026,332,411 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, 2015. The identification of 10% or greater stockholders as of June 30, 2015 is based on Schedule 13G and amended Schedule 13G reports publicly filed before June 30, 2015. This

calculation does not reflect a determination that such parties are affiliates for any other purposes.

As of February 1, 2016, there were 86,452,994 shares of the registrant s Common Stock outstanding.

DOCUMENTS INCORPORATED BY REFERENCE

Document Description	**10-K Part**
Portions of the registrant s notice of annual meeting of stockholders and proxy statement to be filed pursuant to Regulation 14A within 120 days after registrant s fiscal year end of December 31, 2015 are incorporated by reference into Part III of this report	III

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PART I

FORWARD-LOOKING STATEMENTS

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

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

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

ITEM 1. ***BUSINESS***

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

We discover and develop innovative and life-changing pharmaceuticals, in diseases with high unmet medical needs, through our novel R&D platform, focused on neurological and endocrine based diseases and disorders. Our two lead late-stage clinical programs are elagolix, a gonadotropin-releasing hormone (GnRH) antagonist for women s health that is partnered with AbbVie Inc. (AbbVie), and NBI-98854 (valbenazine) a vesicular monoamine transporter 2 (VMAT2) inhibitor for the treatment of movement disorders. We intend to maintain certain commercial rights to our VMAT2 inhibitor and evolve into a fully-integrated pharmaceutical company.

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Our Product Pipeline

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

Program	Target Indication(s)	Status	Rights
Product candidates in clinical development:			
elagolix	Endometriosis	Phase III	AbbVie
valbenazine (NBI-98854)	Tardive Dyskinesia	Phase III	Neurocrine/Mitsubishi Tanabe
elagolix	Uterine Fibroids	Phase III	AbbVie
valbenazine (NBI-98854)	Tourette Syndrome	Phase II	Neurocrine/Mitsubishi Tanabe
NBI-640756	Essential Tremor	Phase I	Neurocrine
Research programs:			
Endocrine (e.g. CRF1 Antagonists)	Classic Congenital Adrenal Hyperplasia	Research	Neurocrine
Neurological/Neuropsychiatric (e.g. VMAT2 Inhibitors)	Movement Disorders, Bipolar Disorder and Schizophrenia	Research	Neurocrine
CNS Disorders (Targeted by G Protein-Coupled Receptors and Ion Channels)	Epilepsy, Essential Tremor, Pain, Other Indications	Research	Neurocrine

Phase III indicates that we or our collaborators are conducting large-scale, multicenter comparative clinical trials on patients afflicted with a target disease in order to provide substantial evidence for efficacy and safety of the product candidate.

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 of the product candidate.

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 candidate in human volunteers.

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

Product Candidates In Clinical Development

elagolix Gonadotropin-Releasing Hormone (GnRH) Antagonist

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

injected via a depot formulation rather than the preferred oral route of administration. In addition, GnRH agonists can take up to several weeks to exert their desired effect once the initial stimulation has occurred, a factor not seen with the use of GnRH antagonists. Upon administration, GnRH agonists have shown a tendency to exacerbate the condition via a hormonal flare. More importantly the 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.

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Orally active, nonpeptide GnRH antagonists potentially offer several advantages over injectable GnRH peptide drugs, including rapid onset of hormone suppression without 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. Additionally, 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.

In June 2010, we entered into an exclusive worldwide collaboration with AbbVie to develop and commercialize elagolix and all next-generation non-peptide GnRH antagonists (collectively, GnRH Compounds) for women s and men s health indications. Under the terms of the agreement, AbbVie is responsible for all development, marketing and commercialization costs and has primary responsibility for all regulatory interactions with the U.S. Food and Drug Administration (FDA) related to elagolix and other GnRH Compounds covered by the collaboration. AbbVie is currently in Phase III evaluation of elagolix in two indications, endometriosis and uterine fibroids.

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, including approximately 7.5 million women in the United States alone. We believe that the availability of an oral treatment, lacking the side effect profile of the currently available peptide GnRH agonists, may be a desirable alternative to current pharmaceutical therapies and ultimately encourage a significantly higher treatment rate.

During 2008, we completed the first Phase IIb study of elagolix (PETAL or 603 study) in which 252 patients, with a laparoscopic diagnosis of endometriosis, were treated over the initial six-month period. This multi-center, randomized, double-blind, double-dummy study consisted of three treatment groups, elagolix 150mg once daily, 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 scan, with a mean time of return to ovulation of 24 days for elagolix subjects.

Toward the conclusion of the 603 study, the 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 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 or 703 study) consisted of four arms, elagolix 150mg once daily, elagolix 250mg once daily, Prostap® SR 3.75mg (leuprorelin) and placebo. We enrolled 174 subjects with a laparoscopic diagnosis of endometriosis in this trial. The three-month placebo-controlled portion of the 703 study confirmed that elagolix and leuprorelin are associated with reductions in dysmenorrhea and non-menstrual pelvic pain daily scores when compared to placebo. However, the FDA-proposed non-menstrual pelvic pain daily scale numeric changes and dynamic range were both small. Although the adverse events reported in the 703 study as occurring more often with elagolix than with placebo were nausea and headache ($\leq$12%), consistent with previous clinical studies of elagolix, these events were generally mild or moderate, transient and not generally associated with study discontinuation. There were no treatment related serious adverse events.

In August 2009, we held a Type C meeting with the FDA to discuss the non-menstrual pelvic pain scale as proposed by the FDA and used in the 702 and 703 studies. Based on this meeting, we modified the wording of the non-menstrual pelvic pain and dysmenorrhea daily scales and launched a new clinical trial, the Daisy PETAL Study (901 study). This parallel, double-blind, placebo-controlled clinical trial was designed to provide an assessment of the modified scales 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 scales, both improved significantly in the elagolix treated arms (p-value<0.001 and p-value<0.01, respectively). Daily dysmenorrhea pain scores were 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 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.

The endometriosis Phase III program is assessing two separate doses of elagolix (150mg once daily and 200mg twice daily) over a 24-week treatment period. The initial randomized, parallel, double-blind, placebo-controlled pivotal trial (Violet PETAL) enrolled 872 women in approximately 160 clinical sites throughout the United States, Canada and Puerto Rico. The co-primary endpoints were a comparison of the daily non-menstrual pelvic pain and daily dysmenorrhea scores during the third month of treatment to the respective daily baseline scores utilizing a responder analysis. Maintenance of response at month six was also assessed utilizing the same daily scales.

In January 2015, AbbVie announced the top-line results of the initial six months of placebo controlled dosing of the Violet PETAL study. After six months of continuous treatment, both doses of elagolix (150mg once daily and 200mg twice daily) met the study s co-primary endpoints (p<0.001) of reducing scores of non-menstrual pelvic pain and dysmenorrhea associated with endometriosis, at month three, as well as at month six.

The observed safety profile of elagolix in the Violet PETAL study was consistent with observations from prior studies. Among the most common adverse events were hot flash, headache, nausea and fatigue. While most adverse events were similar across treatment groups, some, such as hot flash and bone mineral density loss, were dose-dependent. Overall discontinuation rates were similar across treatment groups and discontinuations specifically due to adverse events were 5.9%, 6.4%, and 9.7% for placebo, 150 mg once daily and 200 mg twice daily, respectively.

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Additional efficacy and safety endpoints for the patients enrolled in the Violet PETAL study were measured through one year of continuous dosing as well as for a period of time after the final dose. The one-year dosing portion of this study concluded in mid-2015. In July 2015, AbbVie announced that the efficacy and safety data at one year was consistent with the data witnessed at six months.

In February 2016, AbbVie announced the top-line results from the second of the two Phase III elagolix endometriosis clinical trials, the Solstice Study, a multinational study designed to evaluate the efficacy and safety of elagolix in 815 premenopausal women with endometriosis. The top-line results from this trial were consistent with those of the Violet PETAL Study; after six months of treatment, both doses of elagolix (150 mg once daily and 200 mg twice daily) met the Solstice study s co-primary endpoints of reducing scores of non-menstrual pelvic pain and menstrual pain (or dysmenorrhea) associated with endometriosis at month three, as well as month six. The observed safety profile of elagolix in the Solstice study was consistent with observations from prior studies. Among the most common adverse events were hot flush, headache, and nausea. While most adverse events were similar across treatment groups some, such as hot flush and bone mineral density loss, were dose-dependent. Overall discontinuation rates were similar across treatment groups (25.3%, 21.2%, and 19.7% for placebo, 150 mg once daily and 200 mg twice daily, respectively); discontinuations specifically due to treatment emergent adverse events were 6.1%, 4.4%, and 10.0% for placebo, 150 mg once daily and 200 mg twice daily, respectively. Patients in the Solstice study were eligible to continue on in either post-treatment follow-up or a blinded extension study for an additional six-month safety and efficacy evaluation of elagolix.

AbbVie is targeting a 2017 New Drug Application filing with the FDA for elagolix in endometriosis.

Uterine Fibroids. Uterine fibroids are benign hormonally responsive tumors that form in the wall of the uterus. They are the most common solid tumor in women with a prevalence rate of at least 25% (American College of Obstetricians and Gynecologists). While many women do not have symptoms, depending on the size, location and number, uterine fibroids can cause symptoms such as: longer, more frequent, or heavy menstrual bleeding, menstrual pain, vaginal bleeding at time other than menstruation, pain in the abdomen or lower back, pain during sex, difficulty urinating, frequent urination, constipation or rectal pain. Due to the severity of symptoms, treatment sometimes requires surgery, including the removal of the uterus. In fact, uterine fibroids is a leading indication for hysterectomy in the United States, with approximately 250,000 hysterectomies performed each year related to uterine fibroids (Whiteman *et al AJOG* 2008, *198,* e1). We believe that a safe and effective oral therapy would be a preferred treatment regimen rather than surgical intervention.

During 2011, AbbVie initiated a randomized, double-blind, placebo-controlled, Phase IIa study of approximately 300 women to assess the safety and efficacy of elagolix in the treatment of uterine fibroids. The primary endpoint in this study was an assessment of blood loss after three months of treatment with elagolix. The dose ranging study evaluated various doses of elagolix compared to placebo. Additional efficacy endpoints were also evaluated including change in uterine volume, fibroid volume, and change in menstrual patterns. Based on the results of this study, AbbVie launched a Phase IIb uterine fibroids study for elagolix in 2013.

The single Phase IIb clinical trial enrolled approximately 570 women with heavy uterine bleeding due to uterine fibroids at approximately 100 sites in the United States, Canada, Puerto Rico, Chile and the United Kingdom. The trial was a 24-week, randomized, double-blind, multicenter, placebo-controlled, two cohort design study that evaluated the safety and efficacy of two different elagolix treatment regimens (300mg twice daily and 600mg once daily) alone and in combination with two different strengths of hormonal add-back therapy (estradiol/norethindrone acetate). The primary endpoint of the study was an assessment of uterine blood loss after six months of treatment. Secondary efficacy endpoints included change in uterine volume, fibroid volume, and menstrual patterns. Safety assessments of bone mineral density, comparing baseline to month six, were performed via DXA scan. Patients were also followed off drug for up to six months.

Results show elagolix reduced heavy menstrual bleeding in all treatment arms. The study s primary endpoint, a composite design where subjects had to achieve a menstrual blood loss (MBL) volume of less than

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80 mL as well as a 50 percent or greater reduction in MBL volume from baseline at the final study month, was met ($p<0.001$) as assessed utilizing a quantitative measure of reduction in uterine blood flow, the alkaline hematin method.

Among the most common adverse events were hot flash, headache, nausea, and vomiting. Some adverse events such as hot flash were more frequent in the elagolix only treatment arms versus the placebo and elagolix with add back therapy treatment arms. Reduction in bone mineral density associated with elagolix alone was attenuated when elagolix was co-administered with hormonal add-back therapy.

AbbVie initiated Phase III studies of elagolix in patients with uterine fibroids in early 2016. The Phase III program will include two replicate, pivotal, six-month efficacy and safety studies followed by a six-month safety and efficacy extension study. The primary endpoint in Phase III studies will be the same as that employed in the Phase IIb study: percent of subjects with reduction in uterine blood flow as measured by the alkaline hematin method.

NBI-98854/valbenazine - 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 packaging and transporting monoamines (dopamine, norepinephrine, serotonin, and histamine) in neurons. Specifically, dopamine enables neurotransmission among nerve cells that are involved in voluntary and involuntary motor control. Disease states such as tardive dyskinesia (TD), Tourette syndrome, Huntington s chorea, schizophrenia, and tardive dystonia are characterized in part by a hyperdopaminergic state in the brain, and modulation of neuronal dopamine levels may provide symptomatic benefits for patients with these conditions.

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

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

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

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

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

Upon successful completion of this open-label Phase IIa study, we filed an Investigational New Drug (IND) Application with the FDA to permit the initiation of larger Phase II studies in patients with TD in the United States.

In September 2011, we began a second Phase II study in TD patients. This 32 patient placebo-controlled, double-blind, randomized, cross-over study, used a within-subject comparison for safety and efficacy evaluation. Patients were randomized to either 12.5mg or 50mg doses of NBI-98854 for a two-week dosing period, and each patient also had a two-week placebo dosing period. The primary efficacy endpoint of the study was a comparison of placebo versus active AIMS scores at the end of the two dosing periods.

After database lock and unblinding of study data, an inconsistent pattern of AIMS scores emerged at one of the eight sites that was not evident during the blinded data review. Based on these findings, the AIMS data from this single site was removed and a post-hoc analysis was completed which demonstrated a clinically meaningful and statistically significant improvement in TD symptoms for the subjects receiving the 50mg once daily dose. These subjects had a significant reduction in TD symptoms at the end of two weeks of active treatment versus the end of two weeks of placebo (difference in LS mean of 4.2 for the 50mg period versus the placebo period, p-value=0.002). As expected, the 12.5mg dosing group was not statistically better during the active treatment period than during the placebo period (difference in LS mean of 0.4 for the 12.5mg period versus placebo period, p-value=0.68).

When including the data from the site in question, this study did not meet the pre-specified primary endpoint of reducing the AIMS scores during active treatment periods. The efficacy results from the entire study population showed a non-significant reduction in TD at the end of two weeks of active treatment versus the end of two weeks of placebo (difference in LS mean of 1.1 for the 50mg period versus the placebo period (n=15), p-value=0.42) (difference in LS mean of 0.7 for the 12.5mg period versus placebo period (n=17), p-value=0.59).

We also performed a second post-hoc analysis, engaging a single, independent, blinded AIMS assessor to review the videotaped AIMS assessments at all of the eight sites that participated in the trial. This AIMS assessor scored, in a blinded fashion, the videotaped baseline, day fifteen and day twenty-nine AIMS assessments. This independent secondary post-hoc analysis demonstrated a clinically meaningful and statistically significant improvement in TD symptoms for the subjects receiving the 50mg once daily dose. These subjects had a

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significant reduction in TD symptoms at the end of two weeks of active treatment versus the end of two weeks of placebo (difference in LS mean of 3.0 for the 50mg period versus the placebo period, p-value=0.008). As expected, the 12.5mg dosing group was not statistically better during the active treatment period than during the placebo period (difference in LS mean of 0.7 for the 12.5mg period versus placebo period, p-value=0.54).

NBI-98854 was generally well tolerated during the fourteen days of treatment. The frequency of treatment-emergent adverse events was 17% during the placebo period and 24% and 32% in the 12.5mg and 50mg treatment periods, respectively. There were no serious adverse events during the treatment period. The most common adverse event was headache and one subject in the 50mg group discontinued due to akathisia.

The larger Phase IIb TD program began in 2012. The initial Phase IIb study (Kinect 1 Study) was a randomized, parallel, double-blind, placebo-controlled, clinical trial utilizing the capsule formulation of NBI-98854 in moderate to severe TD patients with underlying schizophrenia or schizoaffective disorder. This 109 subject study assessed two doses of once daily NBI-98854 over a six-week placebo-controlled dosing period. Approximately half of the randomized subjects received placebo and half received one of two doses of NBI-98854. The two NBI-98854 dosing groups consisted of a 50mg group for six weeks and a group that began at 100mg for the initial two weeks and then converted to 50mg for the final four weeks of placebo-controlled dosing period. Subsequent to the placebo-controlled dosing, all subjects were eligible to enter a six-week open label safety extension, during which 50mg of NBI-98854 was administered once daily with additional AIMS assessments. The primary endpoint of the study was a comparison of placebo versus active scores utilizing the AIMS at the end of week six as assessed by the on-site AIMS assessors.

The 50mg dose of NBI-98854 did not reach statistical significance for the primary endpoint at week six. As discussed below, in a post-hoc analysis, utilizing a blinded central video AIMS assessment, both the 100mg dose (at Week 2) and the 50 mg dose (at Week 6) showed a statistically significant and clinically meaningful reduction in TD symptoms.

NBI-98854 was generally well tolerated during the twelve weeks of the Kinect 1 Study. During the six-week placebo-controlled treatment period the frequency of treatment-emergent adverse events was 37% for placebo and 26% for NBI-98854. There were no drug-related serious adverse events. The most common treatment emergent adverse event was mild and transient somnolence during the placebo-controlled portion of the study.

Participants in the Kinect 1 Study were assessed utilizing the Barnes Akathisia Ratings Scale (BARS) for akathisia and the Simpson-Angus Scale (SAS) for parkinsonism. Both of these scales documented minimal symptoms at baseline and were measured as stable to improved during the twelve weeks of treatment. Subjects were also assessed using various safety scales including the Positive and Negative Syndrome Scale (PANSS) for Schizophrenia, the Calgary Depression Scale for Schizophrenia and the Columbia-Suicide Severity Rating Scale (C-SSRS); all of these scores were measured as stable to improved from baseline. Clinical hematology, chemistry and ECG monitoring indicated no emergent safety signals. There were no apparent drug-drug interactions identified in subjects who were utilizing a range of psychotropic and other concomitant medications.

In November 2013, we convened a Scientific Advisory Board (SAB) to review the results of the Kinect 1 Study. The SAB was formed to specifically focus on the dose levels and the AIMS assessment tool. Based on the results of the Kinect 1 Study and the advice from the SAB, the protocol for the second Phase IIb study (Kinect 2 Study) was amended to change the primary endpoint from on-site AIMS assessments to a blinded central video assessment conducted by two movement disorder specialists who would review the AIMS videos in a scrambled fashion and concur on a final AIMS score for each video.

The Kinect 2 Study was a randomized, parallel, double-blind, placebo-controlled, clinical trial utilizing the capsule formulation of NBI-98854 in moderate to severe TD patients with underlying mood disorders, schizophrenia and schizoaffective disorders, and gastrointestinal disorders. This study randomized 102 patients into a six-week placebo-controlled dosing period where half of the subjects received placebo and half received

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NBI-98854. The study began with all subjects on once daily 25mg of NBI-98854, or placebo. The treating physician was then permitted to escalate the dose at two-week intervals, at the end of week two and at the end of week four, to a maximum dose of once daily 75mg. The dose escalation was determined by the treating physician based on week two and week four on-site AIMS assessments coupled with safety and tolerability assessments at these same time points. By week six, approximately 70% of the ITT subjects, randomized to NBI-98854, were titrated to the 75 mg dose, approximately 20% were titrated to the 50mg dose and the remaining subjects received 25 mg of NBI-98854. The primary endpoint of the study was a comparison of placebo versus active scores utilizing the AIMS at the end of week six as assessed by scrambled blinded central video assessment conducted by two movement disorder specialists. The mean baseline AIMS score for the placebo group was 7.9 compared to 8.0 for the NBI-98854 group.

At week six, AIMS scores, as assessed by blinded central video raters, were reduced by 2.6 points in the NBI-98854 intention-to-treat (ITT) group (n=45) compared to a reduction of 0.2 points in the placebo arm (n=44) ($p<0.001$). Additionally, the responder rate (>= 50% improvement from baseline) was 49% in the NBI-98854 ITT group compared to 18% in placebo ($p=0.002$). In the per-protocol (PP) group (n=78) AIMS scores were reduced by 3.3 points for those subjects taking NBI-98854 ($p<0.001$), with a corresponding responder rate of 59% ($p<0.001$). The improvement in week six AIMS was also corroborated by on-site treating physicians utilizing the Clinical Global Impression Tardive Dyskinesia (CGI-TD) scale scores. Treating clinicians determined that approximately 67% of the subjects taking NBI-98854 were much improved or very much improved at week six compared to only 16% of the placebo subjects ($p<0.001$) in this pre-specified key secondary efficacy endpoint.

In the Kinect 2 Study NBI-98854 was generally safe and well tolerated. During the six-week treatment period the frequency of treatment-emergent adverse events was 33% for placebo and 43% for NBI-98854. There were no drug related serious adverse events. The most common treatment emergent adverse events were fatigue in five subjects (9.8%) randomized to NBI-98854 versus two subjects (4.1%) in the placebo group, and headache reported by four subjects (7.8%) on NBI-98854 versus two subjects (4.1%) on placebo. Discontinuation rates were similar in both the NBI-98854 and placebo treatment groups with five per study arm (none of which were study drug related).

Participants in the Kinect 2 Study were assessed utilizing the BARS for akathisia and the SAS for parkinsonism. Both of these scales documented minimal symptoms at baseline and there was no worsening during the six weeks of treatment. Clinical hematology, chemistry and ECG monitoring indicated no emergent safety signals. There were no drug-drug interactions identified in subjects who were utilizing a range of psychotropic and other concomitant medications.

Subsequent to completion of the Kinect 2 Study, in a post-hoc analysis, the Kinect 1 Study videos were evaluated by performing the same comparison of placebo versus active scores employed in the Kinect 2 Study. We engaged two movement disorder specialists, both of whom were not involved with the Kinect 1 Study, to assess the Kinect 1 Study baseline and week six videos utilizing AIMS in a randomized blinded central video assessment. These raters scored the mean baseline AIMS of 8.0 for the Kinect 1 Study. After six weeks of treatment, these raters scored the placebo group in the Kinect 1 Study with a mean reduction from baseline of 0.1 points while the valbenazine group was scored with a mean reduction from baseline of 1.3 points. Utilizing this analysis, valbenazine in the Kinect 1 Study showed a statistically significant change from baseline.

The data from the Kinect 1 and Kinect 2 studies, along with the other Phase I and Phase II clinical studies, preclinical work, and drug manufacturing data formed the basis for an end of Phase II meeting that was held with the FDA in June of 2014. During this meeting, the FDA reviewed the current data package and overall clinical development plan for valbenazine including the proposed Phase III development to support the registration of valbenazine in the United States as a treatment for TD. Based on the results of this meeting and the related minutes, we conducted a single placebo-controlled Phase III study of valbenazine, the Kinect 3 Study.

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The Kinect 3 Study was initiated during the fourth quarter of 2014. The Kinect 3 Study is a randomized, parallel-group, double-blind, placebo-controlled clinical trial utilizing the capsule formulation of valbenazine in moderate to severe TD subjects with an underlying diagnosis of mood disorder, schizophrenia or schizoaffective disorder. The primary endpoint in the Kinect 3 Study was the mean change from baseline in the AIMS as assessed by blinded central raters. The Kinect 3 Study randomized approximately 230 subjects to either placebo, once daily 40mg of valbenazine or once daily 80mg of valbenazine for 6 weeks of placebo-controlled dosing followed by an extension of active dosing through week 48.

The AIMS ratings at week 6 for the 80mg once-daily NBI-98854 ITT population was reduced 3.1 points (Least-Squares Mean) more than placebo ($p<0.0001$). In addition to the primary efficacy endpoint, the AIMS rating for the 40mg once-daily dose and the CGI-TD for both doses were also evaluated. The table below summarizes the results of the AIMS ratings and CGI-TD at week 6 for both the ITT population and a preliminary pre-specified per-protocol (PP) population, which excludes subjects whose plasma concentrations of NBI-98854 were below the lower limit of quantitation and it was determined that these subjects had not ingested the study drug.

	Week 6			
	40mg qd	**p-value***	**80mg qd**	**p-value***
AIMS Difference from Placebo				
Least-Squares Mean (ITT population)	-1.8	0.0021	-3.1	<0.0001
Least-Squares Mean (PP population)	-2.1	0.0009	-3.6	<0.0001
CGI-TD Difference from Placebo				
Least-Squares Mean (ITT population)	-0.3	0.0742	-0.3	0.0560
Least-Squares Mean (PP population)	-0.4	0.0097	-0.4	0.0122

* *Assessment of the significance of p-values based on pre-specified, fixed-sequence testing procedure*

During the six-week placebo-controlled treatment period NBI-98854 was generally well tolerated. The frequency of adverse events was similar among all treatment groups and treatment emergent adverse effects were consistent with those of prior studies. Clinical hematology, chemistry and ECG monitoring indicated no emergent safety signals. There were no drug-drug interactions identified in subjects who were utilizing a wide range of psychotropic and other concomitant medications.

The Kinect 3 Study is currently completing the 48-week safety extension portion of the study. In addition to the Kinect 3 Study, we are also conducting a separate one-year open-label safety study of 40mg once daily and 80mg once daily valbenazine (the Kinect 4 Study) which we believe will be used to support the filing of a New Drug Application (NDA) in TD that is expected in 2016.

In October 2014, the FDA granted us breakthrough therapy designation for valbenazine, for the treatment of TD. Breakthrough therapy designation is granted for a drug that is intended to treat a serious or life-threatening disease or condition and preliminary clinical evidence indicates that the drug may demonstrate substantial improvement on clinically significant endpoints over available therapies. This designation also allows intensive discussions with the FDA which are intended to expedite the development and review process of eligible drugs.

Tourette syndrome. Tourette syndrome is a neurological disorder that consists of rapid, non-rhythmic stereotyped motor and vocal tics. Motor tics are typically characterized by facial grimacing, head jerks, extremity movements and other dystonic movements. Vocal tics typically include grunting, throat clearing, and repeating words and phrases. The average age of onset for Tourette syndrome is approximately six years, with symptoms reaching their peak severity at approximately age ten. Tourette syndrome is more commonly diagnosed in males than females and may also be associated with attention deficit hyperactivity disorder and obsessive compulsive disorder. We believe there are approximately 400,000 people with Tourette syndrome in the United States.

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We have completed juvenile rodent preclinical studies of valbenazine and based on the results of these preclinical studies, we initiated the T-Force Study in children and adolescents with Tourette syndrome in early 2015. The T-Force Study was an open-label, multiple ascending dose, pharmacokinetic and pharmacodynamic study to evaluate the safety, tolerability and exposure-response of valbenazine in children and adolescents with Tourette syndrome. A total of 28 patients were evaluated over 14 days of once daily dosing followed by 7 days off-drug at approximately 10 study centers in the United States. The study was divided into two dosing groups consisting of children (ages 6-11) and adolescents (ages 12-18), and each age group was further divided into three dosing cohorts. Subsequent dose escalations for children and adolescents were based, in part, on the pharmacokinetic and safety data from the previous cohort in each age group. The Yale Global Tic Severity Scale was also assessed and after two weeks of treatment showed a mean reduction of 31% from baseline scores, with over half of the subjects considered clinical responders. Based on the results of the T-Force study, we initiated the Phase II program in Tourette syndrome.

The T-Force GREEN study is a multicenter, randomized, double-blind, placebo-controlled, multi-dose, parallel group, Phase II study to evaluate the safety, tolerability and efficacy of valbenazine in up to 90 pediatric patients with moderate to severe Tourette syndrome. Two once-daily fixed doses of NBI-98854 will be evaluated vs. placebo in a 1:1:1 randomization. The three-arm study will evaluate up to 45 children and 45 adolescents over six weeks of dosing followed by two weeks off-drug at approximately 40 study centers in the United States. The primary endpoint of this study is the change from baseline of the Yale Global Tic Severity Scale between placebo and active treatment groups at the end of week six. Tourette symptoms will also be evaluated via the Rush Video-Based Tic Rating Scale, Premonitory Urge for Tics Scale as well as Clinical Global Impression scales, among others.

We have also initiated a Phase II clinical trial of valbenazine in adults with Tourette syndrome. The T-Forward study is a randomized, double-blind, placebo-controlled, multi-dose, parallel group, study that is expected to enroll up to 90 adults with moderate to severe Tourette syndrome. Two once-daily fixed doses of NBI-98854 will be evaluated versus placebo in a 1:1:1 randomization. The three-arm study will evaluate up to 90 patients over eight weeks of dosing followed by two weeks off-drug at approximately 40 study centers in the United States to assess the safety, tolerability and efficacy of valbenazine in Tourette patients. The primary endpoint of this study is a change from baseline of placebo versus active scores utilizing the Yale Global Tic Severity Scale at the end of week 8. Tourette symptoms will also be evaluated via the Premonitory Urge for Tics Scale as well as Clinical Global Impression of Change scales, among others.

Data readouts from both of these Phase II Tourette studies are expected around year-end 2016.

NBI-640756, Essential Tremor

Essential Tremor. Essential tremor is one of the most common neurological disorders in adults, impacting an estimated 10 million individuals in the United States (International Essential Tremor Foundation). The disorder is characterized by involuntary, rhythmic, oscillatory movements that most often affect the upper limbs. As the disease progresses, tremor severity often increases and spreads to other parts of the body. Essential tremor has a significant impact on the activities of daily living often resulting in functional disability as the disease progresses and is associated with a high comorbidity rate of social phobia, depression and anxiety. Current pharmacological therapies utilized in the treatment of essential tremor include propranolol and primidone. Deep brain stimulation, an invasive procedure involving the implantation of electrodes within certain areas of the brain, is sometimes utilized for severe essential tremor.

NBI-640756 was discovered in our laboratories. We have initiated a single site, randomized, double-blind, placebo-controlled sequential dose-escalation, Phase I safety and pharmacokinetics study exploring a once-daily dose of NBI-640756 in up to 32 healthy volunteers. The study will be conducted in multiple sequential cohorts of eight subjects per cohort with top-line data expected the first-half of 2016. If this initial Phase I study is successful, we intend on initiating a multiple ascending dose study of NBI-640756 later in 2016.

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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 HPA disorders to stress-related disorders and neurological/neuropsychiatric diseases. Central nervous system and endocrinology drug therapies are among the largest therapeutic categories, accounting for over $150 billion in worldwide drug sales according to GlobalData (2014).

Endocrine: Corticotropin-Releasing Factor (CRF) Receptor$_1$ Antagonist (Classic Congenital Adrenal Hyperplasia)

CRF is a hypothalamic hormone released directly into the hypophyseal portal vasculature which acts on specific CRF_1 receptors on corticotropes in the anterior pituitary to stimulate the release of adrenocorticotropin hormone (ACTH). The primary role of ACTH is the stimulation of the synthesis and release of adrenal steroids including cortisol. Cortisol from the adrenals have a negative feedback role at the level of the hypothalamus that decreases CRF release as well as at the level of the pituitary to inhibit the release of ACTH. This tight control loop is known as the hypothalamic-pituitary-adrenal (HPA) axis. Blockade of CRF receptors at the pituitary has been shown to decrease the release of ACTH and subsequently attenuate the production and release of adrenal steroids.

Classic congenital adrenal hyperplasia (classic CAH) is a group of autosomal recessive genetic disorders that affects approximately 20,000-30,000 people in the United States and results in an enzyme deficiency altering the production of adrenal steroids. Because of this deficiency, the adrenal glands have little to no cortisol biosynthesis resulting in a potentially life-threatening condition. If left untreated, classic CAH can result in salt wasting, dehydration and eventually death. Even with cortisol replacement, persistent elevation of ACTH from the pituitary gland results in excessive androgen levels leading to virilization of females including precocious puberty, menstrual irregularity, short stature, hirsutism, acne and fertility problems.

Corticosteroids are the current standard of care for classic CAH and are used chronically to both correct the endogenous cortisol deficiency and reduce the excessive ACTH levels and androgen excess. However, the dose and duration of steroid use required to suppress ACTH is well above the normal physiological level of cortisol; resulting in metabolic syndrome, bone loss, growth impairment, and Cushing s syndrome as common and serious side effects.

Blockade of CRF receptors at the pituitary has been shown to decrease the release of ACTH, which in turn decreases the production of adrenal steroids including androgens, and potentially the symptoms associated with classic CAH. Lower ACTH levels would also reduce the amount of exogenous corticosteroid necessary for classic CAH patients to thrive avoiding the side-effects currently associated with excessive steroid therapy.

In 2014, we conducted an initial pilot clinical trial of NBI-77860 in adult females with refractory classic CAH. The trial was a blinded, single-site, pharmacokinetic/pharmacodynamic study assessing two single, ascending doses of NBI-77860 against placebo. The eight study participants visited the investigative site for three separate overnight visits consisting of bedtime dosing with placebo or one of two active doses of NBI-77860. Each of the visits was separated by a three-week washout period. Key pharmacodynamic biomarker measurements included ACTH, 17-hydroxyprogesterone (17-OHP), androgens, and cortisol levels collected in the morning after dosing. Data from this initial single dose exploratory study demonstrated a robust decrease in both ACTH and 17-OHP.

Based on the results of this initial pilot clinical study we initiated certain preclinical studies in juvenile rodents to permit NBI-77860 to be clinically evaluated in younger patients. The results of these preclinical studies showed certain toxicological findings that were not observed in previous animal studies. We have determined that these findings are specific to NBI-77860 and have halted all clinical development of NBI-77860.

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We have a strategic position in the CRF field through our intellectual property portfolio and relationship with experts in the endocrine and neuropsychiatric fields. We have patents covering both the receptor subtypes termed CRF_1 and CRF_2, and we have pending patent applications on small molecule organic compounds modulating the CRF receptors.

We are currently investigating two other CRF antagonist compounds in preclinical evaluations and anticipate filing an IND for at least one of these compounds as well as initiating a Phase I study during 2016.

Neurological/Neuropsychiatric: VMAT2 Inhibitors

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

CNS Disorders (Targeted by G Protein-Coupled Receptors and Ion Channels)

G Protein-Coupled Receptors (GPCRs) are the largest known gene superfamily of the human genome. Greater than thirty percent of all marketed prescription drugs act on GPCRs; which makes this class of proteins historically the most successful therapeutic target family. However, only a small fraction of the GPCR gene superfamily has been exploited. Ion channels appear to be represented by approximately 400 genes in the human genome and are currently the targets for approximately seven percent of the current marketed drugs. Next generation therapies derived from targeting GPCRs and ion channels 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, now also applied to ion channels, provides an unbiased profile of pharmacological protein/ligand interactions coupled with in vivo efficacy using discrete animal models allowing for rapid discovery of initial leads and advancement into preclinical and clinical development. Importantly, this design cycle is not limited to GPCRs or ion channel targets, but can be utilized for other recently identified proteins that play a role in human disease where current treatments or therapies are either inadequate or nonexistent.

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 extend our product pipeline, we can mitigate some of the clinical development risks associated with drug development. We currently have multiple programs in various stages of research and development. Our two lead late-stage clinical programs are elagolix, a GnRH antagonist in Phase III development for endometriosis and uterine fibroids that is partnered with AbbVie, and a VMAT2 inhibitor for the treatment of movement disorders that is currently in Phase III development for TD and in Phase II development for Tourette syndrome. 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.

Maintaining Certain Commercial Rights to Our Product Portfolio to Evolve into a Fully-Integrated Pharmaceutical Company. We intend to retain commercial rights to certain products, including valbenazine, that

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we can effectively and efficiently develop, secure regulatory approval and economically commercialize. These include products with a concentrated prescriber base and well-defined patient population that can be accessed with an efficient patient and prescriber outreach program.

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.

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-injectable means of treatment of endometriosis. We believe 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 $81.5 million, $46.4 million and $39.2 million for the years ended December 31, 2015, 2014 and 2013, respectively.

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

Our Corporate Collaborations and Strategic Alliances

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

AbbVie Inc. (AbbVie). In June 2010, we announced an exclusive worldwide collaboration with AbbVie to develop and commercialize elagolix and all next-generation GnRH antagonists (collectively, GnRH Compounds) for women s and men s health. AbbVie made an upfront payment of $75 million and has agreed to make additional development and regulatory event based payments of up to $480 million and up to an additional $50 million in commercial event based payments. Under the terms of the agreement, AbbVie is responsible for all development, marketing and commercialization costs. We received funding for certain internal collaboration expenses which included reimbursement from AbbVie for internal and external expenses related to the GnRH Compounds and 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 AbbVie, the collaborative development effort between the parties to advance GnRH compounds towards commercialization was governed by a joint development committee with representatives from both us and AbbVie. The collaborative development portion of the agreement concluded, as scheduled, on December 31, 2012. AbbVie may terminate the collaboration at its discretion upon 180 days written notice to us. In such event, we would be entitled to specified payments for ongoing clinical development and related activities and all GnRH Compound product rights would revert to us. Since the inception of the agreement, we have recorded revenues of $75.0 million related to the amortization of up-front license fees, $30.0 million in milestone revenue, and $37.0 million of sponsored development revenue.

Mitsubishi Tanabe Pharma Corporation (Mitsubishi Tanabe). In March 2015, we entered into a collaboration and license agreement with Mitsubishi Tanabe for the development and commercialization of valbenazine for movement disorders in Japan and other select Asian markets. Mitsubishi Tanabe made an up-front license fee payment of $30 million and has agreed to make additional development and commercialization event-based payments totaling up to $85 million, payments for the manufacture of pharmaceutical products, and

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royalties on product sales in select territories in Asia. Under the terms of the agreement, Mitsubishi Tanabe is responsible for all third-party development, marketing and commercialization costs in Japan and other select Asian markets with the exception of a single Huntington s chorea clinical trial to be performed by us, at an estimated cost of approximately $12 million, should Mitsubishi Tanabe request the clinical trial. We will be entitled to a percentage of sales of NBI-98854 in Japan and other select Asian markets for the longer of ten years or the life of the related patent rights. Mitsubishi Tanabe may terminate the agreement at its discretion upon 180 days written notice to the Company. In such event, all NBI-98854 product rights for Japan and other select Asian markets would revert to the Company.

The Mount Sinai School of Medicine of the City University of New York (Mt. Sinai). In August 1999, we entered into an agreement with Mt. Sinai pursuant to which we acquired a nonexclusive license to certain patents and patent applications related to GnRH, to develop and commercialize licensed products worldwide. Pursuant to the terms of the agreement, we have the right to grant sublicenses to third parties only with the prior written consent of Mt. Sinai. Upon entering into the agreement, we paid a $50,000 upfront fee and are required to pay an additional $10,000 annual license fee on each anniversary of the agreement. In addition, we are obligated to pay Mt. Sinai a royalty equal to 1% of net sales of licensed products. The agreement will remain in effect until the later of 15 years after the date of the first commercial sale of the first licensed product or the expiration of the last to expire of the licensed patents, unless terminated earlier at our election or for material breach by either party. Mt. Sinai also has the right to terminate the agreement if we become insolvent or bankrupt or have suspended our business operations. Pursuant to the terms of the agreement, in the event that Mt. Sinai grants a third party a license to the GnRH patents and patent applications on economic terms and conditions less favorable to Mt. Sinai than those in our agreement, we have the right to substitute the terms and conditions of the other third party license for those currently set forth in our agreement. In December 2015, Mt. Sinai initiated litigation against us related to an alleged breach of our agreement (see Item 3 Legal Proceedings in this Form 10-K)

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 the rights to issued United States patents, pending United States patent applications, and issued and pending foreign filings. We face the risk that one or more of the above patent applications may be denied. We also face the risk that issued patents that we own or license may be challenged or circumvented or may otherwise not provide protection for any commercially viable products we develop.

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 and uterine fibroids, 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).

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Valbenazine, our highly selective VMAT2 inhibitor, currently in clinical trials for the treatment of TD and Tourette syndrome, is covered by U.S. Patent No. 8,039,627 which expires in 2029 and U.S. Patent No. 8,357,697 which expires in 2027 (not including a potential patent term extension of up to five years). NBI-98854 is also covered by European Patent No. 2,081,929 which expires in 2027.

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

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

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

Marketing and Sales

We currently have limited experience in marketing or selling pharmaceutical products. To market any of our 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, distribution, marketing and sale 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. 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. In the United States, various federal and state statutes and regulation also govern or influence testing, manufacturing, safety, labeling, storage, and record-keeping of human therapeutic products and their marketing. Recent federal legislation imposes additional obligations on pharmaceutical manufacturers regarding product tracking and tracing.

In addition, federal and state healthcare laws restrict business practices in the pharmaceutical industry. These laws include, without limitation, federal and state fraud and abuse laws, false claims laws, data privacy and security laws, as well as transparency laws regarding payments or other items of value provided to healthcare providers.

The federal Anti-Kickback Statute makes it illegal for any person or entity, including a prescription drug manufacturer (or a party acting on its behalf) to knowingly and willfully, directly or indirectly, solicit, receive, offer, or pay any remuneration that is intended to induce the referral of business, including the purchase, order, lease of any good, facility, item or service for which payment may be made under a federal healthcare program, such as Medicare or Medicaid. The term remuneration has been broadly interpreted to include anything of value.

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Federal false claims and false statement laws, including the federal civil False Claims Act, prohibits, among other things, any person or entity from knowingly presenting, or causing to be presented, for payment to, or approval by, federal programs, including Medicare and Medicaid, claims for items or services, including drugs, that are false or fraudulent or not provided as claimed.

The federal Health Insurance Portability and Accountability Act of 1996 (HIPAA) created additional federal criminal statutes that prohibit among other actions, knowingly and willfully executing, or attempting to execute, a scheme to defraud any healthcare benefit program, including private third-party payors, knowingly and willfully stealing from a healthcare benefit program, willfully obstructing a criminal investigation of a healthcare offense, and knowingly and willfully falsifying, concealing or covering up a material fact or making any materially false, fictitious or fraudulent statement in connection with the delivery of or payment for healthcare benefits, items or services.

Also, many states have similar fraud and abuse statutes or regulations that may be broader in scope and may apply regardless of payor, in addition to items and services reimbursed under Medicaid and other state programs. Additionally, to the extent that our product is sold in a foreign country, we may be subject to similar foreign laws.

HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act and their implementing regulations, requires certain types of individuals and entities to abide by standards relating to the privacy and security of individually identifiable health information, including the adoption of administrative, physical and technical safeguards to protect such information. In addition, certain state laws govern the privacy and security of health information in certain circumstances, some of which are more stringent than HIPAA and many of which differ from each other in significant ways and may not have the same effect, thus complicating compliance efforts.

The federal Physician Payments Sunshine Act, which requires certain manufacturers of drugs, devices, biologics and medical supplies for which payment is available under Medicare, Medicaid or the Children s Health Insurance Program, with specific exceptions, to report annually to the Centers for Medicare & Medicaid Services (CMS) information related to payments or other transfers of value made to physicians and teaching hospitals, and applicable manufacturers and applicable group purchasing organizations to report annually to CMS ownership and investment interests held by the physicians and their immediate family members.

Failure to comply with these laws, where applicable, can result in significant penalties, including the imposition of significant civil, criminal and administrative penalties, damages, monetary fines, disgorgement, individual imprisonment, possible exclusion from participation in Medicare, Medicaid and other federal healthcare programs, contractual damages, reputational harm, diminished profits and future earnings, and curtailment of our operations, any of which could adversely affect our ability to operate our business and our results of operations.

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.

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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, re-evaluate, 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 license application for approval to commence commercial sales. In most cases, the submission of an NDA is subject to a substantial application user fee. Under the Prescription Drug User Fee Act (PDUFA) guidelines that are currently in effect, the FDA has a goal of ten months from the date of filing of a standard NDA for a new molecular entity to review and act on the submission. This review typically takes twelve months from the date the NDA is submitted to FDA because the FDA has approximately two months to make a filing decision.

In addition, under the Pediatric Research Equity Act of 2003 (PREA) as amended and reauthorized, certain NDAs or supplements to an NDA must contain data that are adequate to assess the safety and effectiveness of the drug for the claimed indications in all relevant pediatric subpopulations, and to support dosing and administration for each pediatric subpopulation for which the product is safe and effective. The FDA may, on its own initiative or at the request of the applicant, grant deferrals for submission of some or all pediatric data until after approval of the product for use in adults or full or partial waivers from the pediatric data requirements.

The FDA also may require submission of a risk evaluation and mitigation strategy (REMS) plan to ensure that the benefits of the drug outweigh its risks. The REMS plan could include medication guides, physician communication plans, assessment plans, and/or elements to assure safe use, such as restricted distribution methods, patient registries, or other risk minimization tools.

The FDA conducts a preliminary review of all NDAs within the first 60 days after submission, before accepting them for filing, to determine whether they are sufficiently complete to permit substantive review. The FDA may request additional information rather than accept an NDA for filing. In this event, the application must be resubmitted with the additional information. The resubmitted application is also subject to review before the FDA accepts it for filing. Once the submission is accepted for filing, the FDA begins an in-depth substantive review. The FDA reviews an NDA to determine, among other things, whether the drug is safe and effective and whether the facility in which it is manufactured, processed, packaged or held meets standards designed to assure the product s continued safety, quality and purity.

The FDA may refer an application for a novel drug to an advisory committee. An advisory committee is a panel of independent experts, including clinicians and other scientific experts, that reviews, evaluates and provides a recommendation as to whether the application should be approved and under what conditions. The FDA is not bound by the recommendations of an advisory committee, but it considers such recommendations carefully when making decisions.

Before approving an NDA, the FDA typically will inspect the facility or facilities where the product is manufactured. The FDA will not approve an application unless it determines that the manufacturing processes and facilities are in compliance with current Good Manufacturing Practice requirements and adequate to assure consistent production of the product within required specifications. Additionally, before approving an NDA, the FDA may inspect one or more clinical trial sites to assure compliance with Good Clinical Practice requirements.

After evaluating the NDA and all related information, including the advisory committee recommendation, if any, and inspection reports regarding the manufacturing facilities and clinical trial sites, the FDA may issue an approval letter, or, in some cases, a complete response letter. A complete response letter generally contains a statement of specific conditions that must be met in order to secure final approval of the NDA and may require additional clinical or preclinical testing in order for FDA to reconsider the application. Even with submission of

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this additional information, the FDA ultimately may decide that the application does not satisfy the regulatory criteria for approval. If and when those conditions have been met to the FDA s satisfaction, the FDA will typically issue an approval letter. An approval letter authorizes commercial marketing of the drug with specific prescribing information for specific indications.

Even if the FDA approves a product, it may limit the approved indications for use of the product, require that contraindications, warnings or precautions be included in the product labeling, require that post-approval studies, including Phase 4 clinical trials, be conducted to further assess a drug s safety after approval, require testing and surveillance programs to monitor the product after commercialization, or impose other conditions, including distribution and use restrictions or other risk management mechanisms under a REMS, which can materially affect the potential market and profitability of the product. The FDA may prevent or limit further marketing of a product based on the results of post-marketing studies or surveillance programs. After approval, some types of changes to the approved product, such as adding new indications, manufacturing changes, and additional labeling claims, are subject to further testing requirements and FDA review and 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.

Special FDA Expedited Review and Approval Programs

The FDA has various programs, including fast track designation, accelerated approval, priority review, and breakthrough therapy designation, which are intended to expedite or simplify the process for the development and FDA review of drugs that are intended for the treatment of serious or life threatening diseases or conditions and demonstrate the potential to address unmet medical needs. The purpose of these programs is to provide important new drugs to patients earlier than under standard FDA review procedures.

To be eligible for a fast track designation, the FDA must determine, based on the request of a sponsor, that a product is intended to treat a serious or life-threatening disease or condition and demonstrates the potential to address an unmet medical need. The FDA will determine that a product will fill an unmet medical need if it will provide a therapy where none exists or provide a therapy that may be potentially superior to existing therapy based on efficacy or safety factors. The FDA may review sections of the NDA for a fast track product on a rolling basis before the complete application is submitted, if the sponsor provides a schedule for the submission of the sections of the NDA, the FDA agrees to accept sections of the NDA and determines that the schedule is acceptable, and the sponsor pays any required user fees upon submission of the first section of the NDA.

The FDA may give a priority review designation to drugs that offer major advances in treatment, or provide a treatment where no adequate therapy exists. A priority review means that the goal for the FDA to review an application is six months, rather than the standard review of ten months under current PDUFA guidelines. These six and ten month review periods are measured from the filing date rather than the receipt date for NDAs for new molecular entities, which typically adds approximately two months to the timeline for review and decision from the date of submission. Most products that are eligible for fast track designation are also likely to be considered appropriate to receive a priority review.

In addition, products studied for their safety and effectiveness in treating serious or life-threatening illnesses and that provide meaningful therapeutic benefit over existing treatments may be eligible for accelerated approval and may be approved on the basis of adequate and well-controlled clinical trials establishing that the drug product has an effect on a surrogate endpoint that is reasonably likely to predict clinical benefit, or on a clinical endpoint that can be measured earlier than irreversible morbidity or mortality, that is reasonably likely to predict

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an effect on irreversible morbidity or mortality or other clinical benefit, taking into account the severity, rarity or prevalence of the condition and the availability or lack of alternative treatments. As a condition of approval, the FDA may require a sponsor of a drug receiving accelerated approval to perform post-marketing studies to verify and describe the predicted effect on irreversible morbidity or mortality or other clinical endpoint, and the drug may be subject to accelerated withdrawal procedures.

A breakthrough therapy is defined as a drug that is intended, alone or in combination with one or more other drugs, to treat a serious or life-threatening disease or condition, and preliminary clinical evidence indicates that the drug may demonstrate substantial improvement over existing therapies on one or more clinically significant endpoints, such as substantial treatment effects observed early in clinical development. Drugs designated as breakthrough therapies are also eligible for accelerated approval. The FDA must take certain actions, such as holding timely meetings and providing advice, intended to expedite the development and review of an application for approval of a breakthrough therapy.

Even if a product qualifies for one or more of these programs, the FDA may later decide that the product no longer meets the conditions for qualification or decide that the time period for FDA review or approval will not be shortened.

Post-Approval Requirements

Drugs manufactured or distributed pursuant to FDA approvals are subject to pervasive and continuing regulation by the FDA, including, among other things, requirements relating to recordkeeping, periodic reporting, product sampling and distribution, advertising and promotion and reporting of adverse experiences with the product. After approval, most changes to the approved product, such as adding new indications or other labeling claims are subject to prior FDA review and approval. There also are continuing, annual user fee requirements for any marketed products and the establishments at which such products are manufactured, as well as new application fees for supplemental applications with clinical data.

The FDA may impose a number of post-approval requirements as a condition of approval of an NDA. For example, the FDA may require post-marketing testing, including Phase 4 clinical trials, and surveillance to further assess and monitor the product s safety and effectiveness after commercialization.

In addition, drug manufacturers and other entities involved in the manufacture and distribution of approved drugs are required to register their establishments with the FDA and state agencies, and are subject to periodic unannounced inspections by the FDA and these state agencies for compliance with current Good Manufacturing Practices (cGMP) requirements. Changes to the manufacturing process are strictly regulated and often require prior FDA approval before being implemented. FDA regulations also require investigation and correction of any deviations from cGMP requirements and impose reporting and documentation requirements upon the sponsor and any third-party manufacturers that the sponsor may decide to use. Accordingly, manufacturers must continue to expend time, money, and effort in the area of production and quality control to maintain cGMP compliance.

Once an approval is granted, the FDA may withdraw the approval if compliance with regulatory requirements and standards is not maintained or if problems occur after the product reaches the market. Later discovery of previously unknown problems with a product, including adverse events of unanticipated severity or frequency, or with manufacturing processes, or failure to comply with regulatory requirements, may result in mandatory revisions to the approved labeling to add new safety information; imposition of post-market studies or clinical trials to assess new safety risks; or imposition of distribution or other restrictions under a REMS program. Other potential consequences include, among other things:

- restrictions on the marketing or manufacturing of the product, complete withdrawal of the product from the market or product recalls;
- fines, warning letters or holds on post-approval clinical trials;

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refusal of the FDA to approve pending NDAs or supplements to approved NDAs, or suspension or revocation of product approvals;

product seizure or detention, or refusal to permit the import or export of products; or

injunctions or the imposition of civil or criminal penalties.

The FDA strictly regulates marketing, labeling, advertising and promotion of products that are placed on the market. Drugs may be promoted only for the approved indications and in accordance with the provisions of the approved label. The FDA and other agencies actively enforce the laws and regulations prohibiting the promotion of off-label uses, and a company that is found to have improperly promoted off-label uses may be subject to significant liability.

Reimbursement

Significant uncertainty exists as to the coverage and reimbursement status of any product candidates for which we obtain regulatory approval. In the United States and markets in other countries, sales of any products for which we receive regulatory approval will depend, in part, on the extent to which third-party payors provide coverage and establish adequate reimbursement levels for such drug products.

In the United States, third-party payors include federal and state healthcare programs, government authorities, private managed care providers, private health insurers and other organizations. Third-party payors are increasingly challenging the price, examining the medical necessity and reviewing the cost-effectiveness of medical drug products and medical services, in addition to questioning their safety and efficacy. Such payors may limit coverage to specific drug products on an approved list, also known as a formulary, which might not include all of the FDA-approved drugs for a particular indication. We may need to conduct expensive pharmaco-economic studies in order to demonstrate the medical necessity and cost-effectiveness of our products, in addition to the costs required to obtain the FDA approvals. Nonetheless, our product candidates may not be considered medically necessary or cost-effective.

Moreover, the process for determining whether a third-party payor will provide coverage for a drug product may be separate from the process for setting the price of a drug product or for establishing the reimbursement rate that such a payor will pay for the drug product. A payor s decision to provide coverage for a drug product does not imply that an adequate reimbursement rate will be approved. Further, one payor s determination to provide coverage for a drug product does not assure that other payors will also provide coverage for the drug product. Adequate third-party reimbursement may not be available to enable us to maintain price levels sufficient to realize an appropriate return on our investment in product development.

The marketability of any product candidates for which we or our collaborators receive regulatory approval for commercial sale may suffer if the government and third-party payors fail to provide adequate coverage and reimbursement. In addition, emphasis on managed care in the United States has increased and we expect will continue to increase the pressure on pharmaceutical pricing. Coverage policies and third-party reimbursement rates may change at any time. Even if favorable coverage and reimbursement status is attained for one or more products for which we receive regulatory approval, less favorable coverage policies and reimbursement rates may be implemented in the future.

Healthcare Reform

The United States and some foreign jurisdictions are considering or have enacted a number of legislative and regulatory proposals to change the healthcare system in ways that could affect our ability to sell our products profitably. Among policy makers and payors in the United States and elsewhere, there is significant interest in promoting changes in healthcare systems with the stated goals of containing healthcare costs, improving quality or expanding access. In the United States, the pharmaceutical industry has been a particular focus of these efforts and has been significantly affected by major legislative initiatives.

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By way of example, in March 2010, the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act of 2010, collectively the ACA, was signed into law, which intended to broaden access to health insurance, reduce or constrain the growth of healthcare spending, enhance remedies against fraud and abuse, add transparency requirements for the healthcare and health insurance industries, impose taxes and fees on the health industry and impose additional health policy reforms. Among the provisions of the ACA of importance to our potential drug candidates are:

- an annual, nondeductible fee on any entity that manufactures or imports specified branded prescription drugs and biologic agents, apportioned among these entities according to their market share in certain government healthcare programs;
- an increase in the statutory minimum rebates a manufacturer must pay under the Medicaid Drug Rebate Program to 23.1% and 13.0% of the average manufacturer price for branded and generic drugs, respectively;
- a new methodology by which rebates owed by manufacturers under the Medicaid Drug Rebate Program are calculated for drugs that are inhaled, infused, instilled, implanted or injected;
- extension of a manufacturer s Medicaid rebate liability to covered drugs dispensed to individuals who are enrolled in Medicaid managed care organizations;
- expansion of eligibility criteria for Medicaid programs by, among other things, allowing states to offer Medicaid coverage to certain individuals with income at or below 133% of the federal poverty level, thereby potentially increasing a manufacturer s Medicaid rebate liability;
- a new Medicare Part D coverage gap discount program, in which manufacturers must agree to offer 50% point-of-sale discounts off negotiated prices of applicable brand drugs to eligible beneficiaries during their coverage gap period, as a condition for a manufacturer s outpatient drugs to be covered under Medicare Part D;
- expansion of the entities eligible for discounts under the Public Health Service pharmaceutical pricing program; and
- a new Patient-Centered Outcomes Research Institute to oversee, identify priorities in, and conduct comparative clinical effectiveness research, along with funding for such research.

We expect that the ACA, as well as other healthcare reform measures that may be adopted in the future, may result in more rigorous coverage criteria and lower reimbursement, and in additional downward pressure on the price that we receive for any approved product. Any reduction in reimbursement from Medicare or other government-funded programs may result in a similar reduction in payments from private payor.

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, tardive dyskinesia, uterine fibroids, Tourette syndrome, classic congenital adrenal hyperplasia, stress-related disorders, pain, and other neurological and endocrine-related diseases and disorders.

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Lupron Depot®, marketed by AbbVie, and Synarel® and depo-subQ provera104®, marketed by Pfizer, are products that have been approved for the treatment of endometriosis, infertility, and central precocious puberty. These drugs, and any generic alternatives, may compete with any small molecule non-peptide GnRH antagonists we, in conjunction with our collaborative partner AbbVie, develop for these indications. Approximately 130,000 hysterectomies are performed annually in the United States as a direct result of endometriosis, as well as a significant number of laparoscopic procedures to ablate endometrial explants. Our oral small molecule pharmaceutical agent, elagolix, would also compete directly with these current invasive standards of care.

We, in conjunction with our collaborative partner AbbVie, are developing elagolix for the treatment of heavy menstrual bleeding associated with uterine fibroids. There are no current pharmaceutical therapies approved in the United States for the chronic treatment of uterine fibroids. Lupron Depot® is approved for short-term use to improve the outcome of uterine fibroid surgery. However, approximately 250,000 hysterectomies are performed annually in the United States as a direct result of uterine fibroids, as well as myomectomies (surgery) to remove the fibroids. Our oral small molecule pharmaceutical agent, elagolix, would compete directly with these current invasive standards of care. Additionally, Esmya® (ulipristal) by Allergan Pharmaceuticals, Inc. is being evaluated in Phase III clinical trials for potential use in the treatment of heavy menstrual bleeding associated with uterine fibroids.

Our VMAT2 inhibitor, valbenazine, is currently in clinical trials for the treatment of movement disorders, specifically TD and Tourette syndrome. At present there are no approved drug therapies for TD; however, off-label 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 TD. Generic neuroleptic medications (pimozide and haloperidol) as well as Abilify® (apriprizole) are approved by the FDA to control the tics associated with Tourette syndrome. Additionally, Teva Pharmaceuticals, Inc. is conducting clinical trials for its VMAT2 inhibitor SD-809 for the treatment of TD and Tourette syndrome and has filed an NDA for the chorea associated with Huntington s disease for the same compound. Other potential indications for our VMAT2 inhibitor are Huntington s disease, schizophrenia and tardive dystonia. Currently, Xenazine®, marketed by Lundbeck, as well as its generic alternatives, are approved for the chorea associated with Huntington s disease.

NBI-640756 is currently in clinical trials for the treatment of essential tremor. Current pharmacological therapies utilized in the treatment of essential tremor include propranolol and primidone. Deep brain stimulation, an invasive procedure involving the implantation of electrodes within certain areas of the brain, is sometimes utilized for severe essential tremor. Additionally, Sage Therapeutics is conducting clinical trials for its GABA modulator SAGE-547 for essential tremor.

We are studying CRF antagonists for treating classic CAH, for which there are limited therapies. High doses of corticosteroids are the current standard of care to both correct the endogenous cortisol deficiency as well as reduce the excessive ACTH levels. However, the level of dose as well as the duration of steroid use required to suppress ACTH is well above the normal physiological level of cortisol; resulting in metabolic syndrome, bone loss, growth impairment, and Cushing s syndrome as common and serious side effects.

If one or more of these competitive 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;

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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, 2015, we had approximately 120 full-time employees, of which 32 hold Ph.D., M.D. or equivalent degrees, and 23 others hold an M.S., M.B.A., or equivalent degrees. Of these full-time employees, 94 were engaged in, or directly support, research and development activities, and 26 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.

Insurance

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

Available Information

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

Additionally, copies of our Annual Report will be made available, free of charge, upon written request.

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

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

Risks Related to Our Company

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

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

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

the U.S. Food and Drug Administration (FDA) or similar foreign regulatory authority may not approve an Investigational New Drug (IND) Application or foreign equivalent filings required to initiate human clinical studies for our drug candidates or the FDA may require additional preclinical or clinical studies as a condition of the initiation of Phase I clinical studies, progression from Phase I to Phase II, or Phase II to Phase III, or for New Drug Application (NDA) approval;

the product candidate may not prove to be effective or as effective as other competing product candidates;

we may discover that a product candidate may cause harmful side effects or results of required toxicology studies may not be acceptable to the FDA;

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

the FDA or similar foreign regulatory authorities may require use of new or experimental endpoints that may prove insensitive to treatment effects;

we or the FDA or similar foreign regulatory authorities may suspend the trials;

the results may not be statistically significant;

patient recruitment may be slower than expected;

patients may drop out of the trials; and

regulatory requirements may change.

These risks and uncertainties impact all of our clinical programs. Specifically, with respect to our gonadotropin-releasing hormone (GnRH) program with AbbVie Inc. (AbbVie), any of the clinical, regulatory or operational events described above could delay timelines for the completion of the Phase III endometriosis program or the Phase III uterine fibroids program, require suspension of these programs and/or obviate filings for regulatory approvals. Similarly, our VMAT2 inhibitor program will be impacted if any of the events above lead to delayed timelines for the enrollment in, or completion of, the Phase III tardive dyskinesia or the Tourette syndrome Phase II clinical trials of valbenazine.

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 our current collaborators, and may need to enter into future collaborations to develop and commercialize certain of our product candidates.

Our strategy for fully developing and commercializing elagolix is dependent upon maintaining our current collaboration agreement with AbbVie. This collaboration agreement provides for significant future payments should certain development, regulatory and commercial milestones be achieved, and royalties on future sales of elagolix. Under this agreement, AbbVie is responsible for, among other things, conducting clinical trials and obtaining required regulatory approvals for elagolix; as well as manufacturing and commercialization of elagolix in the event it receives regulatory approval.

Because of our reliance on AbbVie, the development and commercialization of elagolix could be substantially delayed, and our ability to receive future funding could be substantially impaired, if AbbVie:

- failed to gain the requisite regulatory approval of elagolix;
- did not successfully launch and commercialize elagolix;
- did not conduct its collaborative activities in a timely manner;
- did not devote sufficient time and resources to our partnered program;
- terminated its agreement with us;
- developed, either alone or with others, products that may compete with elagolix;
- disputed our respective allocations of rights to any products or technology developed during our collaboration; or
- merged with a third party that wants to terminate our agreement.

In March 2015, we entered into a collaboration and license agreement with Mitsubishi Tanabe to develop and commercialize NBI-98854 in Japan and other select Asian markets. We will rely on Mitsubishi Tanabe to achieve certain development, regulatory and commercial milestones which, if achieved, could generate significant future revenue for us. Our collaboration with Mitsubishi Tanabe is subject to risks and uncertainties similar to those described above. In addition, we may need to enter into other collaborations to assist in the development and commercialization of other product candidates we are developing now or may develop in the future, and any such future collaborations would be subject to similar risks and uncertainties.

These issues and possible disagreements with AbbVie, Mitsubishi Tanabe or any future corporate collaborators could lead to delays in the collaborative research, development or commercialization 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 currently in research or clinical development. Only a small number of research and development programs ultimately result in commercially successful drugs. Potential products that appear to be promising at early stages of development may not reach the market for a number of reasons. These reasons include the possibilities that the potential products may:

be found ineffective or cause harmful side effects during preclinical studies or clinical trials;

fail to receive necessary regulatory approvals on a timely basis or at all;

be precluded from commercialization by proprietary rights of third parties;

be difficult to manufacture on a large scale; or

be uneconomical to commercialize or fail to achieve market acceptance.

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

We do not and will not have access to all information regarding the product candidates we licensed to AbbVie.

We do not and will not have access to all information regarding the products being developed and potentially commercialized by AbbVie, including potentially material information about clinical trial design and execution, safety reports from clinical trials, spontaneous safety reports if a product candidate is later approved and marketed, regulatory affairs, process development, manufacturing, marketing and other areas known by AbbVie. In addition, we have confidentiality obligations under our agreement with AbbVie. Thus, our ability to keep our shareholders informed about the status of product candidates under our collaboration with AbbVie will be limited by the degree to which AbbVie keeps us informed and allows us to disclose such information to the public. If AbbVie fails to keep us informed about the clinical development and regulatory approval of our collaboration and product candidates licensed to it, we may make operational and investment decisions that we would not have made had we been fully informed, which may materially and adversely affect our business and operations.

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

Since our inception, we have incurred significant net losses and negative cash flow from operations. As a result of historical operating losses, we had an accumulated deficit of $915.2 million as of December 31, 2015. We do not expect to be profitable, or generate positive cash flows from operations, for the year ending December 31, 2016.

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 in the coming years 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 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 for these securities 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 $20.00 per share to approximately $58.00 per share. The market price of our common stock may fluctuate in response to many factors, including:

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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, including economic and market conditions affecting the biotechnology industry;

developments in patent or other proprietary rights;

developments related to the FDA;

future sales of our common stock by us or our stockholders;

comments by securities analysts;

fluctuations in our operating results;

developments related to on-going litigation;

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, or violate the terms of these licenses, we could lose our rights to those technologies and drug candidates or be forced to pay

damages.

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 license some of the core technologies used in our research and development activities and collaborations from third parties, including the GnRH receptor which we license from The Mount Sinai School of Medicine of the City University of New York (Mount Sinai). If we were to default on our obligations under any of our licenses, we could lose some or all of our rights to develop, market and sell products covered by these licenses. If we were to violate any of the terms of our licenses, we could become subject to damages. For example, on December 1, 2015, Mount Sinai filed a complaint against us, seeking unspecified monetary damages, future sublicensing fees and attorney s fees, alleging that we violated the terms of our license with Mount Sinai by entering into an exclusive worldwide collaboration with AbbVie. While we believe that we have meritorious defenses to the claims made in the complaint and intend to vigorously defend ourselves against such claims, we are not able to predict the ultimate outcome of this action. 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.

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We have limited marketing experience, no sales force, no third-party reimbursement 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 and secure adequate third-party reimbursement 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, sales and reimbursement 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, or not in compliance with Good Clinical Practices, 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, including current Good Manufacturing Practice regulations. Our third-party manufacturers might not comply with FDA regulations relating to manufacturing our products for clinical trials and commercial purposes or other regulatory requirements now or in the future. Our reliance on contract manufacturers also exposes us to the following risks:

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

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

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

- 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 current 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.

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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 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 and complexity 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;
- developments related to on-going litigation;
- 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, for so long as we continue to satisfy the requirements to be deemed a well-known seasoned issuer, allows us to issue an unlimited number of shares of our common stock from time to time. In addition, we have previously financed capital purchases and may continue to pursue opportunities to obtain additional debt financing in the future. Additional equity or debt financing might not be available on

reasonable terms, if at all. Any additional equity financings will be dilutive to our stockholders and any additional debt financings may involve operating covenants that restrict our business.

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 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

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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 or limit coverage and/or reimbursement for our products that could limit our product revenues and delay sustained profitability.

Our ability to commercialize any products successfully also will depend in part on the extent to which coverage and adequate reimbursement for these products and related treatments will be available. 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.

Assuming we obtain coverage for a given product by a third-party payor, the resulting reimbursement payment rates may not be adequate or may require co-payments that patients find unacceptably high. Patients who are prescribed medications for the treatment of their conditions, and their prescribing physicians, generally rely on third-party payors to reimburse all or part of the costs associated with their prescription drugs. Patients are unlikely to use our products unless coverage is provided and reimbursement is adequate to cover all or a significant portion of the cost of our products. Coverage decisions may depend upon clinical and economic standards that disfavor new drug products when more established or lower cost therapeutic alternatives are already available or subsequently become available regardless of whether they are approved by the FDA for that particular use.

Government authorities and other third-party payors are developing increasingly sophisticated methods of controlling healthcare costs, such as by limiting coverage and the amount of reimbursement for particular medications. Further, no uniform policy requirement for coverage and reimbursement for drug products exists among third-party payors in the United States. Therefore, coverage and reimbursement for drug products can differ significantly from payor to payor. As a result, the coverage determination process is often a time-consuming and costly process that will require us to provide scientific and clinical support for the use of our products to each payor separately, with no assurance that coverage and adequate reimbursement will be applied consistently or obtained in the first instance.

There may also be significant delays in obtaining coverage and reimbursement for newly approved drugs, and coverage may be more limited than the purposes for which the drug is approved by the FDA or comparable foreign regulatory authorities. Moreover, eligibility for coverage and reimbursement does not imply that a drug will be paid for in all cases or at a rate that covers our costs, including research, development, manufacture, sale and distribution. If coverage and reimbursement are not available or reimbursement is available only to limited levels, we may not successfully commercialize any product candidate for which we obtain marketing approval.

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Our inability to promptly obtain coverage and profitable reimbursement rates from both government-funded and private payors for any approved products that we develop could have a material adverse effect on our operating results, our ability to raise capital needed to commercialize products and our overall financial condition.

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

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

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

- the timing of receipt of marketing approvals;
- the safety and efficacy of the products;
- the availability of coverage and adequate reimbursement for 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.

Even if we receive regulatory approval for any of our product candidates, we will be subject to ongoing obligations and continued regulatory review, which may result in significant additional expense. Additionally, our product candidates, if approved, could be subject to labeling and other restrictions and market withdrawal and we may be subject to penalties if we fail to comply with regulatory requirements or experience unanticipated problems with our products.

Any regulatory approvals that we receive for our product candidates may also be subject to limitations on the approved indicated uses for which the product may be marketed or to the conditions of approval, or contain requirements for potentially costly post-marketing testing, including Phase IV clinical trials, and surveillance to monitor the safety and efficacy of the product candidate. In addition, if the FDA or a comparable foreign regulatory authority approves any of our product candidates, the manufacturing processes, labeling, packaging, distribution, adverse event reporting, storage, advertising, promotion and recordkeeping for the product will be subject to extensive and ongoing regulatory requirements. These requirements include submissions of safety and other post-marketing information and reports, registration, as well as continued compliance with current Good Manufacturing Practices for any clinical trials that we conduct post-approval. Later discovery of previously unknown problems with a product, including adverse events of unanticipated severity or frequency, or with our third-party manufacturers or manufacturing processes, or failure to comply with regulatory requirements, may result in, among other things:

- restrictions on the marketing or manufacturing of the product, withdrawal of the product from the market, or voluntary or mandatory product recalls;
- fines, warning letters or holds on clinical trials;

refusal by the FDA to approve pending applications or supplements to approved applications filed by us, or suspension or revocation of product license approvals;

product seizure or detention, or refusal to permit the import or export of products; and

product injunctions or the imposition of civil or criminal penalties.

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The FDA s policies may change and additional government regulations may be enacted that could prevent, limit or delay regulatory approval of our product candidates. If we are slow or unable to adapt to changes in existing requirements or the adoption of new requirements or policies, or if we are not able to maintain regulatory compliance, we may lose any marketing approval that we may have obtained, which would adversely affect our business, prospects and ability to achieve or sustain profitability.

If we receive regulatory approval from the FDA for any of our product candidates, we could face liability if a regulatory authority determines that we are promoting any such product for off-label uses.

A company may not promote off-label uses for its drug products. An off-label use is the use of a product for an indication that is not described in the product s FDA-approved label in the United States or for uses in other jurisdictions that differ from those approved by the applicable regulatory agencies. Physicians, on the other hand, may prescribe products for off-label uses. Although the FDA and other regulatory agencies do not regulate a physician s choice of drug treatment made in the physician s independent medical judgment, they do restrict promotional communications from companies or their sales force with respect to off-label uses of products for which marketing clearance has not been issued. A company that is found to have promoted off-label use of its product may be subject to significant liability, including civil and criminal sanctions. If we begin marketing any of our product candidates, we intend to comply with the requirements and restrictions of the FDA and other regulatory agencies with respect to our promotion of our products, but we cannot be sure that the FDA or other regulatory agencies will agree that we have not violated their restrictions. As a result, we may be subject to criminal and civil liability. In addition, our management s attention could be diverted to handle any such alleged violations. A significant number of companies have been the target of inquiries and investigations by various U.S. federal and state regulatory, investigative, prosecutorial and administrative entities in connection with the promotion of products for unapproved uses and other sales practices, including the Department of Justice and various U.S. Attorneys Offices, the Office of Inspector General of the Department of Health and Human Services, the FDA, the Federal Trade Commission and various state Attorneys General offices. These investigations have alleged violations of various U.S. federal and state laws and regulations, including claims asserting antitrust violations, violations of the federal False Claims Act, the Prescription Drug Marketing Act, anti-kickback laws, and other alleged violations in connection with the promotion of products for unapproved uses, pricing and Medicare and/or Medicaid reimbursement. If the FDA or any other governmental agency initiates an enforcement action against us or if we are the subject of a *qui tam* suit and it is determined that we violated prohibitions relating to the promotion of products for unapproved uses, we could be subject to substantial civil or criminal fines or damage awards and other sanctions such as consent decrees and corporate integrity agreements pursuant to which our activities would be subject to ongoing scrutiny and monitoring to ensure compliance with applicable laws and regulations. Any such fines, awards or other sanctions would have an adverse effect on our revenue, business, financial prospects, and reputation.

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, the Dodd-Frank Wall Street Reform and Consumer Protection Act, 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. 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.

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Risks Related to Our Industry

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

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

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

Health care reform measures and other recent legislative initiatives 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 payors 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. Additionally, other recent federal legislation imposes new obligations on manufacturers of pharmaceutical products, among others, related to product tracking and tracing. Among the requirements of this new legislation, manufacturers are required to provide certain information regarding the drug product to individuals and entities to which product ownership is transferred, label drug product with a product identifier, and keep certain records regarding distribution of the drug product. Further, under this new legislation, manufacturers will have drug product investigation, quarantine, disposition, notification and purchaser license verification responsibilities related to counterfeit, diverted, stolen, and intentionally adulterated products, as well as products that are the subject of fraudulent transactions or which are otherwise unfit for distribution such that they would be reasonably likely to result in serious health consequences or death.

Additionally, in March 2010, the ACA was signed into law, which was intended to broaden access to health insurance, reduce or constrain the growth of healthcare spending, enhance remedies against fraud and abuse, add transparency requirements for the healthcare and health insurance industries, impose taxes and fees on the health industry and impose additional health policy reforms. Among the provisions of the ACA of importance to our potential drug candidates are:

- an annual, nondeductible fee on any entity that manufactures or imports specified branded prescription drugs and biologic agents, apportioned among these entities according to their market share in certain government healthcare programs;

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an increase in the statutory minimum rebates a manufacturer must pay under the Medicaid Drug Rebate Program to 23.1% and 13.0% of the average manufacturer price for branded and generic drugs, respectively;

a new methodology by which rebates owed by manufacturers under the Medicaid Drug Rebate Program are calculated for drugs that are inhaled, infused, instilled, implanted or injected;

extension of a manufacturer s Medicaid rebate liability to covered drugs dispensed to individuals who are enrolled in Medicaid managed care organizations;

expansion of eligibility criteria for Medicaid programs by, among other things, allowing states to offer Medicaid coverage to certain individuals with income at or below 133% of the federal poverty level, thereby potentially increasing a manufacturer s Medicaid rebate liability;

a new Medicare Part D coverage gap discount program, in which manufacturers must agree to offer 50% point-of-sale discounts off negotiated prices of applicable brand drugs to eligible beneficiaries during their coverage gap period, as a condition for a manufacturer s outpatient drugs to be covered under Medicare Part D;

expansion of the entities eligible for discounts under the Public Health Service pharmaceutical pricing program; and

a new Patient-Centered Outcomes Research Institute to oversee, identify priorities in, and conduct comparative clinical effectiveness research, along with funding for such research.

We expect that the ACA, as well as other healthcare reform measures that may be adopted in the future, may result in more rigorous coverage criteria and lower reimbursement, and in additional downward pressure on the price that we receive for any approved product. Any reduction in reimbursement from Medicare or other government-funded programs may result in a similar reduction in payments from private payors. The implementation of cost containment measures or other healthcare reforms may prevent us from being able to generate revenue, attain profitability or commercialize our drugs.

We are currently unable to predict what additional legislation or regulation, if any, relating to the health care industry may be enacted in the future or what effect recently enacted Federal 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.

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We are performing research on or developing products for the treatment of several disorders including endometriosis, tardive dyskinesia, uterine fibroids, Tourette syndrome, essential tremor, classic congenital adrenal hyperplasia, pain, and other neurological and endocrine-related diseases and disorders, and there are a number of competitors to products in our research pipeline. If one or more of our competitors products or programs are successful, the market for our products may be reduced or eliminated.

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

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

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Interference proceedings declared by the United States Patent and Trademark Office may be necessary to determine the priority of inventions with respect to our patent applications or those of our licensors. Litigation or interference proceedings may fail and, even if successful, may result in substantial costs and be a distraction to management. We cannot assure you that we will be able to prevent misappropriation of our proprietary rights, particularly in countries where the laws may not protect such rights as fully as in the United States.

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

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

Our employees, independent contractors, principal investigators, consultants, commercial partners and vendors may engage in misconduct or other improper activities, including non-compliance with regulatory standards and requirements.

We are exposed to the risk of employee fraud or other misconduct. Misconduct by employees and independent contractors, such as principal investigators, consultants, commercial partners and vendors, could include failures to comply with FDA regulations, to provide accurate information to the FDA, to comply with manufacturing standards we have established, to comply with federal and state healthcare fraud and abuse laws, to report financial information or data accurately or to disclose unauthorized activities to us. In particular, sales, marketing and other business arrangements in the healthcare industry are subject to extensive laws intended to prevent fraud, kickbacks, self-dealing and other abusive practices. Employee and independent contractor misconduct could also involve the improper use of individually identifiable information, including, without limitation, information obtained in the course of clinical trials, which could result in regulatory sanctions and serious harm to our reputation.

Breakthrough therapy designation for valbenazine for the treatment of tardive dyskinesia may not lead to a faster development or regulatory review or approval process.

A breakthrough therapy is defined as a product that is intended, alone or in combination with one or more other products, to treat a serious condition, and preliminary clinical evidence indicates that the product may demonstrate substantial improvement over existing therapies on one or more clinically significant endpoints, such as substantial treatment effects observed early in clinical development. Products designated as breakthrough therapies by the FDA may also be eligible for priority review if supported by clinical data at the time the NDA is submitted to FDA.

Designation as a breakthrough therapy is within the discretion of the FDA. The receipt of such designation for a product candidate may not result in a faster development or regulatory review or approval process compared to products considered for approval under conventional FDA procedures and does not assure ultimate approval by the FDA. In addition, the FDA may later decide that the product candidate no longer meets the conditions for qualification or decide that the time period for FDA review or approval will not be shortened.

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Any relationships with healthcare professionals, principal investigators, consultants, customers (actual and potential) and third-party payors in connection with our current and future business activities are and will continue to be subject, directly or indirectly, to federal and state healthcare laws. If we are unable to comply, or have not fully complied, with such laws, we could face penalties, contractual damages, reputational harm, diminished profits and future earnings and curtailment or restructuring of our operations.

Our business operations and activities may be directly, or indirectly, subject to various federal and state healthcare laws, including without limitation, fraud and abuse laws, false claims laws, data privacy and security laws, as well as transparency laws regarding payments or other items of value provided to healthcare providers. These laws may restrict or prohibit a wide range of business activities, including, but not limited to, research, manufacturing, distribution, pricing, discounting, marketing and promotion, sales commission, customer incentive programs and other business arrangements. These laws may impact, among other things, our current activities with principal investigators and research subjects, as well as proposed and future sales, marketing and education programs.

Such laws include:

the federal Anti-Kickback Statute which prohibits, among other things, persons and entities from knowingly and willfully soliciting, offering, receiving or providing remuneration, directly or indirectly, in cash or in kind, to induce or reward, or in return for, either the referral of an individual for, or the purchase, order or recommendation of, any good or service, for which payment may be made under a federal healthcare program such as Medicare and Medicaid;

the federal false claims and civil monetary penalties laws, including the civil False Claims Act, which impose criminal and civil penalties against individuals or entities for, among other things, knowingly presenting, or causing to be presented, to the federal government, claims for payment that are false or fraudulent or making a false statement to avoid, decrease or conceal an obligation to pay money to the federal government;

the federal Health Insurance Portability and Accountability Act of 1996 (HIPAA) which imposes criminal and civil liability for, among other things, executing a scheme to defraud any healthcare benefit program or making false statements relating to healthcare matters;

HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act and its implementing regulations, which also imposes obligations, including mandatory contractual terms, on certain types of individuals and entities, with respect to safeguarding the privacy, security and transmission of individually identifiable health information;

the federal Physician Payments Sunshine Act, which requires certain manufacturers of drugs, devices, biologics and medical supplies for which payment is available under Medicare, Medicaid or the Children s Health Insurance Program, with specific exceptions, to report annually to CMS information related to payments or other transfers of value made to physicians and teaching hospitals, and applicable manufacturers and applicable group purchasing organizations to report annually to CMS ownership and investment interests held by the physicians and their immediate family members; and

analogous state and foreign laws and regulations, such as state anti-kickback and false claims laws, which may apply to sales or marketing arrangements and claims involving healthcare items or services reimbursed by non-governmental third party payors, including private insurers; state laws that require pharmaceutical companies to comply with the pharmaceutical industry s voluntary compliance guidelines and the relevant compliance guidance promulgated by the federal government; state laws that require drug manufacturers to report information related to payments and other transfers of value to physicians and other healthcare providers or marketing expenditures; and state and foreign laws governing the privacy and security of health information in some circumstances, many of which differ from each other in significant ways and often are not preempted by HIPAA, thus complicating compliance efforts.

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Efforts to ensure that our business arrangements will comply with applicable healthcare laws may involve substantial costs. It is possible that governmental and enforcement authorities will conclude that our business practices may not comply with current or future statutes, regulations or case law interpreting applicable fraud and abuse or other healthcare laws. If our operations or activities are found to be in violation of any of the laws described above or any other governmental regulations that apply to us, we may be subject to, without limitation, civil, criminal and administrative penalties, damages, monetary fines, disgorgement, possible exclusion from participation in Medicare, Medicaid and other federal healthcare programs, contractual damages, reputational harm, diminished profits and future earnings and curtailment or restructuring of our operations, any of which could adversely affect our ability to operate.

In addition, any sales of our product candidates once commercialized outside the United States will also likely subject us to foreign equivalents of the healthcare laws mentioned above, among other foreign laws.

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.

Security breaches and other disruptions could compromise our information and expose us to liability, which would cause our business and reputation to suffer.

In the ordinary course of our business, we collect and store confidential and sensitive information on our networks and in our data centers. This information includes, among other things, our intellectual property and proprietary information, the confidential information of our collaborators and licensees, and the personally identifiable information of our employees. It is important to our operations and business strategy that this information remains secure and is perceived to be secure. Despite security measures, however, our information technology and network infrastructure may be vulnerable to attacks by hackers or breached due to employee error, malfeasance, or other disruptions. Any such attack or breach could compromise our networks and data centers and the information stored there could be accessed, publicly disclosed, lost, or stolen. Any such access, disclosure, or other loss of information could result in legal claims or proceedings, liability under laws that protect the privacy of personal information, delays and impediments to our discovery and development efforts, and damage to our reputation.

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

None.

ITEM 2. ***PROPERTIES***

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

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

ITEM 3. ***LEGAL PROCEEDINGS***

On December 1, 2015, Icahn School of Medicine at Mount Sinai (Mount Sinai) filed a complaint against us in the United States District Court for the Southern District of New York: *Icahn School of Medicine at Mount Sinai v. Neurocrine Biosciences, Inc.*, Case No. 1:15-cv-09414. In the complaint, Mount Sinai alleges that we, by entering into an exclusive worldwide collaboration with AbbVie Inc. to develop and commercialize next-generation gonadotropin-releasing hormone antagonists, breached our license agreement with Mount Sinai dated August 27, 1999. Mount Sinai is seeking unspecified monetary damages, future sublicensing fees and attorney s fees. We believe that we have meritorious defenses to the claims made in the complaint and intend to vigorously defend ourselves against such claims, but we are not able to predict the ultimate outcome of this action.

ITEM 4. ***MINE SAFETY DISCLOSURES***

None.

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PART II

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

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

	High	Low
Year Ended December 31, 2014		
1st Quarter	$ 20.29	$ 9.19
2nd Quarter	16.47	12.17
3rd Quarter	17.00	12.63
4th Quarter	24.86	15.20
Year Ended December 31, 2015		
1st Quarter	$ 45.36	$ 19.68
2nd Quarter	49.49	32.67
3rd Quarter	56.97	33.61
4th Quarter	58.46	37.76

As of February 1, 2016, there were approximately 56 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 2015.

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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, 2010 (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.

* *The material in this section is not soliciting material , is not deemed filed with the SEC and is not to be incorporated by reference into any of our SEC filings whether made before or after the date hereof and irrespective of any general incorporation language in any such SEC filing except to the extent we specifically incorporate this section by reference.*

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

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

	2015	2014	2013	2012	2011
	(In thousands, except for net (loss) income per share data)				
STATEMENT OF COMPREHENSIVE (LOSS) INCOME DATA					
Revenues:					
Sponsored research and development	$	$	$	$ 18,897	$ 10,462
Milestones and license fees	19,769		2,919	34,243	66,951
Total revenues	19,769		2,919	53,140	77,413
Operating expenses:					
Research and development	81,491	46,425	39,248	37,163	30,951
General and administrative	32,480	17,986	13,349	13,437	12,458
Cease-use expense				1,092	82
Total operating expenses	113,971	64,411	52,597	51,692	43,491
(Loss) income from operations	(94,202)	(64,411)	(49,678)	1,448	33,922
Other income:					
Gain on sale/disposal of assets	3,334	3,222	3,170	3,074	3,195
Other income, net	1,939	647	418	503	454
Total other income, net	5,273	3,869	3,588	3,577	3,649
Net (loss) income	$ (88,929)	$ (60,542)	$ (46,090)	$ 5,025	$ 37,571
Net (loss) income per common share:					
Basic	$ (1.05)	$ (0.81)	$ (0.69)	$ 0.08	$ 0.68
Diluted	$ (1.05)	$ (0.81)	$ (0.69)	$ 0.08	$ 0.67
Shares used in calculation of net (loss) income per common share:					
Basic	84,496	74,577	66,989	65,619	55,176
Diluted	84,496	74,577	66,989	66,946	56,347
BALANCE SHEET DATA					
Cash, cash equivalents and investments	$ 461,679	$ 231,301	$ 145,739	$ 173,493	$ 129,103
Working capital	358,359	182,539	136,763	173,618	85,366
Total assets	474,785	243,033	154,676	195,979	138,368
Long-term debt					
Accumulated deficit	(915,234)	(826,305)	(765,763)	(719,673)	(724,698)
Total stockholders equity	424,454	208,699	120,410	154,372	60,081

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

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

Overview

We discover and develop innovative and life-changing pharmaceuticals, in diseases with high unmet medical needs, through our novel research and development (R&D) platform, focused on neurological and endocrine based diseases and disorders. Utilizing a portfolio approach to drug discovery, we have multiple small molecule drug candidates at various stages of pharmaceutical development. We develop proprietary pharmaceuticals for our pipeline, as well as collaborate with other pharmaceutical companies on our discoveries.

To date, we have not generated any revenues from the sale of products. We have funded our operations primarily through private and public offerings of our common stock and payments received under research and development collaboration agreements. While we independently develop many of our product candidates, we have entered into collaborations for several of our programs, and intend to rely on existing and future collaborators to meet funding requirements. We expect to generate future operating cash flow losses as product candidates are advanced through the various stages of clinical development. As of December 31, 2015, we had an accumulated deficit of $915.2 million and expect to incur operating cash flow losses for the foreseeable future, which may be greater than losses in prior years.

Our two lead late-stage clinical programs are elagolix, a gonadotropin-releasing hormone (GnRH) antagonist in Phase III development for endometriosis and uterine fibroids that is partnered with AbbVie Inc. (AbbVie), and a vesicular monoamine transporter 2 (VMAT2) inhibitor for the treatment of movement disorders, currently in Phase III development for tardive dyskinesia and Phase II development for Tourette syndrome. We intend to maintain certain commercial rights to our VMAT2 inhibitor program to evolve into a fully-integrated pharmaceutical company.

Critical Accounting Policies

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

Revenue Recognition

We recognize revenue for the performance of services when each of the following four criteria is met: (i) persuasive evidence of an arrangement exists; (ii) services are rendered or products are delivered; (iii) the sales price is fixed or determinable; and (iv) collectability is reasonably assured.

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Since 2011, we have followed the Accounting Standards Codification (ASC) for Revenue Recognition - Multiple-Element Arrangements, if applicable, to determine the recognition of revenue under license and collaboration agreements. The terms of these agreements generally contain multiple elements, or deliverables, which may include (i) licenses to our intellectual property, (ii) materials and technology, (iii) pharmaceutical supply, (iv) participation on joint development or joint steering committees, and (v) development services. The payments we receive under these arrangements typically include one or more of the following: up-front license fees; funding of research and/or development efforts; amounts due upon the achievement of specified milestones; manufacturing and royalties on future product sales.

The ASC provides guidance relating to the separation of deliverables included in an arrangement into different units of accounting and the allocation of consideration to the units of accounting. The evaluation of multiple-element arrangements requires management to make judgments about (i) the identification of deliverables, (ii) whether such deliverables are separable from the other aspects of the contractual relationship, (iii) the estimated selling price of each deliverable, and (iv) the expected period of performance for each deliverable.

To determine the units of accounting under a multiple-element arrangement, we evaluate certain separation criteria, including whether the deliverables have stand-alone value, based on the relevant facts and circumstances for each arrangement. The selling prices of deliverables under an arrangement may be derived using vendor specific objective evidence (VSOE), third-party evidence, or a best estimate of selling price (BESP), if VSOE or third-party evidence is not available. For most pharmaceutical licensing and collaboration agreements, BESP is utilized. The objective of BESP is to determine the price at which we would transact a sale if the element within the agreement was sold on a standalone basis. Establishing BESP involves our judgment and considers multiple factors, including market conditions and company-specific factors, including those factors contemplated in negotiating the agreements, as well as internally developed models that include assumptions related to market opportunity, discounted cash flows, estimated development costs, probability of success and the time needed to commercialize a product candidate pursuant to the agreement. In validating the BESP, we consider whether changes in key assumptions used to determine the BESP will have a significant effect on the allocation of the arrangement consideration between the multiple deliverables. The allocated consideration for each unit of accounting is recognized over the related obligation period in accordance with the applicable revenue recognition criteria.

If there are deliverables in an arrangement that are not separable from other aspects of the contractual relationship, they are treated as a combined unit of accounting, with the allocated revenue for the combined unit recognized in a manner consistent with the revenue recognition applicable to the final deliverable in the combined unit. Payments received prior to satisfying the relevant revenue recognition criteria are recorded as deferred revenue in the accompanying balance sheets and recognized as revenue when the related revenue recognition criteria are met.

We typically receive up-front payments when licensing our intellectual property, which often occurs in conjunction with a research and development agreement. We recognize revenue attributed to the license upon delivery, provided that the license has stand-alone value.

Revenues from development milestones are accounted for in accordance with the Revenue Recognition Milestone Method Topic of the Financial Accounting Standards Board (FASB) ASC (Milestone Method). Milestones are recognized when earned, as evidenced by written acknowledgment from the collaborator or other persuasive evidence that the milestone has been achieved, provided that the milestone event is substantive. A milestone event is considered to be substantive if its achievability was not reasonably assured at the inception of the agreement and our efforts led to the achievement of the milestone or the milestone was due upon the occurrence of a specific outcome resulting from our performance. We assesses whether a milestone is substantive at the inception of each agreement. For payments payable on achievement of milestones that do not meet all of the conditions to be considered substantive, we recognize the portion of the payment allocable to delivered items as revenue when the specific milestone is achieved, and the contingency is removed.

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Prior to the revised multiple element guidance described above, adopted by us on January 1, 2011, upfront, nonrefundable payments for license fees, grants, and advance payments for sponsored research revenues received in excess of amounts earned were classified as deferred revenue and recognized as income over the contract or development period.

Mitsubishi Tanabe Pharma Corporation (Mitsubishi Tanabe). On March 31, 2015, we entered into a collaboration and license agreement with Mitsubishi Tanabe for the development and commercialization of NBI-98854 (valbenazine) for movement disorders in Japan and other select Asian markets. Payments to us under this agreement include an up-front license fee of $30 million, up to $85 million in development and commercialization event-based payments, payments for the manufacture of pharmaceutical products, and royalties on product sales in select territories in Asia. Under the terms of the agreement, Mitsubishi Tanabe is responsible for all third-party development, marketing and commercialization costs in Japan and other select Asian markets with the exception of a single Huntington s chorea clinical trial to be performed by us, at an estimated cost of approximately $12 million, should Mitsubishi Tanabe request the clinical trial. We will be entitled to a percentage of sales of NBI-98854 in Japan and other select Asian markets for the longer of ten years or the life of the related patent rights.

Under our agreement with Mitsubishi Tanabe, the collaboration effort between the parties to advance NBI-98854 towards commercialization in Japan and other select Asian markets is governed by a joint steering committee and joint development committee with representatives from both us and Mitsubishi Tanabe. There are no performance, cancellation, termination or refund provisions in the agreement that would have a material financial consequence to us. We do not directly control when event-based payments will be achieved or when royalty payments will begin. Mitsubishi Tanabe may terminate the agreement at its discretion upon 180 days written notice to us. In such event, all NBI-98854 product rights for Japan and other select Asian markets would revert to us.

We have identified the following deliverables associated with the Mitsubishi Tanabe agreement: NBI-98854 technology license and existing know-how, development activities to be performed as part of the collaboration, and the manufacture of pharmaceutical products. The respective standalone value from each of these deliverables has been determined by applying the BESP method and the revenue was allocated based on the relative selling price method with revenue recognition timing to be determined either by delivery or the provision of services.

As discussed above, the BESP method required the use of significant estimates. We used an income approach to estimate the selling price for the technology license and an expense approach for estimating development activities and the manufacture of pharmaceutical products. The development activities and the manufacture of pharmaceutical products are expected to be delivered throughout the duration of the agreement. The technology license and existing know-how was delivered on the effective date of the agreement.

For the year ended December 31, 2015, we recognized revenue under this agreement of $19.8 million associated with the delivery of a technology license and existing know-how. In accordance with our continuing performance obligations, $10.2 million of the $30 million up-front payment is being deferred and recognized in future periods. Under the terms of the agreement, there is no general obligation to return the up-front payment for any non-contingent deliverable.

We also evaluated the event-based payments under the Milestone Method and concluded only one immaterial event-based payment represents a substantive milestone. Event-based payments will be recognized when earned.

We are eligible to receive tiered royalty payments based on product sales in Japan and other select Asian markets. Royalties will be recognized as earned in accordance with the terms of the agreement, when product sales are reported by Mitsubishi Tanabe, the amount can be reasonably estimated, and collectability is reasonably assured.

AbbVie Inc. (AbbVie). In June 2010, we announced an exclusive worldwide collaboration with AbbVie to develop and commercialize elagolix and all next-generation GnRH antagonists (collectively, GnRH Compounds) for women s and men s health. AbbVie made an upfront payment of $75 million and agreed to make additional

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development and regulatory event-based payments of up to $480 million and up to an additional $50 million in commercial event-based payments. We assessed event-based payments under the revised authoritative guidance for research and development milestones and determined that event-based payments prior to commencement of a Phase III clinical study, as defined in the agreement, meet the definition of a milestone in accordance with authoritative guidance as (i) they are events that can only be achieved in part on our past performance, (ii) there is substantive uncertainty at the date the arrangement was entered into that the event will be achieved and (iii) they result in additional payments being due to us. Development and regulatory event-based payments subsequent to the commencement of a Phase III clinical study, however, currently do not meet these criteria as their achievement is based on the performance of AbbVie. As of December 31, 2015, $500 million remains outstanding in future event-based payments under the agreement. However, none of the remaining event-based payments meet the definition of a milestone in accordance with authoritative accounting guidance.

Under the terms of the agreement, AbbVie is responsible for all third-party development, marketing and commercialization costs. We received funding for certain internal collaboration expenses, which included reimbursement from AbbVie for internal and external expenses related to the GnRH Compounds, 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 AbbVie, the collaboration effort between the parties to advance GnRH Compounds towards commercialization was governed by a joint development committee with representatives from both us and AbbVie. Our participation in the joint development committee was determined to be a substantive deliverable under the contract, and therefore, the upfront payment was deferred and recognized over the term of the joint development committee, which was completed, as scheduled, in December 2012. AbbVie 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.

Research and Development Expense

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

Share-Based Compensation

We grant stock options to purchase our common stock to our employees and directors under our 2011 Equity Incentive Plan (the 2011 Plan) and grant stock options to certain employees pursuant to Employment Commencement Nonstatutory Stock Option Agreements (inducement grants). We also grant certain employees stock bonuses and restricted stock units under the 2011 Plan. Additionally, we have outstanding options that were granted under previous option plans from which we no longer make grants. Share-based compensation expense related to these equity instruments for the years ended December 31, 2015, 2014 and 2013 was $28.4 million, $10.4 million and $6.8 million, respectively.

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Stock option awards and restricted stock units (RSUs) generally vest over a three to four year period and expense is ratably recognized over those same time periods. For RSUs with performance-based vesting requirements (PRSUs), no expense is recorded until the performance condition is probable of being achieved; upon which expense is then recognized ratably over the expected performance period. Because the performance based criteria for vesting for the PRSUs was not immediately probable, no associated expense was recorded for the year ended December 31, 2014. During 2015, we recognized approximately $8.8 million in expense related to PRSUs as it became probable that the pre-defined performance conditions would be met mainly due to the Phase III results of the Kinect 3 clinical study. Unrecognized estimated compensation expense related to these PRSUs will continue to be recognized ratably over the remaining estimated expected performance period.

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

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

Results of Operations for Years Ended December 31, 2015, 2014 and 2013

Revenue

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

	Year Ended December 31,		
	2015	2014	2013
	(In millions)		
Revenues under collaboration agreements:			
Mitsubishi Tanabe Pharma, Inc.	$ 19.8	$	$
Dainippon Sumitomo Pharma Co. Ltd. (DSP)			2.9
Total revenues	$ 19.8	$	$ 2.9

As discussed above, during 2015, we entered into a collaboration and license agreement with Mitsubishi Tanabe for the development and commercialization of our VMAT2 inhibitor NBI-98854 for movement disorders in Japan and other select Asian markets. Payments from Mitsubishi Tanabe under this agreement included an up-front license fee of $30 million. During 2015, we recorded revenues of $19.8 million related to the up-front license fee.

During the year ended December 31, 2013, we recognized $2.9 million in revenue under our collaboration agreement with Dainippon Sumitomo Pharma Co. Ltd. from the amortization of up-front licensing fees. The up-front licensing fee under this collaboration agreement was fully amortized as of December 31, 2013.

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Operating Expenses

Research and Development

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

The following table presents our total R&D expenses by category during the periods presented:

	Years Ended December 31,		
	2015	2014	2013
		(In millions)	
External development expense:			
VMAT2	$ 29.3	$ 9.0	$ 12.3
CRF	3.3	2.8	
Other	1.2	2.6	1.5
Total external development expense	33.8	14.4	13.8
R&D personnel expense	32.8	20.2	15.4
R&D facility and depreciation expense	6.0	5.8	5.4
Other R&D expense	8.9	6.0	4.6
Total research and development expense	$ 81.5	$ 46.4	$ 39.2

R&D expense increased from $46.4 million in 2014 to $81.5 million in 2015. The $35.1 million increase in R&D expense was due in part to a $19.4 million increase in external development expenses primarily related to our VMAT2 Phase III clinical program, which was initiated during the second half of 2014. Approximately $12.6 million of the increase in R&D expense was due to higher R&D personnel related expense. Share-based compensation expense increased by approximately $7.9 million from 2014 to 2015; approximately $4.2 million of which was related to PRSUs recognized during 2015. An increase in R&D headcount and other personnel related costs accounted for the balance of the increase in personnel expense. Other R&D expense also increased by $2.9 million from 2014 to 2015 primarily due to external consulting expenses as we expanded our efforts on the NDA for valbenazine in tardive dyskinesia.

R&D expense increased from $39.2 million in 2013 to $46.4 million in 2014. This increase was primarily due to higher personnel related expenses coupled with higher early discovery and preclinical costs. The $4.8 million increase in personnel related expenses was attributable to increased R&D headcount and performance-based compensation. Additionally, $1.9 million of the increase in R&D personnel expense was due to higher share-based compensation expense. Other R&D expense increased by $1.4 million primarily due to higher laboratory related costs and external scientific consulting and testing expenses. Preclinical and manufacturing efforts related to early stage programs resulted in a $1.1 million increase in other external development expenses from 2013 to 2014. The CRF program for congenital adrenal hyperplasia was initiated in 2014, and resulted in $2.8 million of expense for the year. These increases in R&D external development expense were offset by lower VMAT2 external development expenses which decreased by $3.3 million due to this program substantially completing its Phase IIb development during 2013 and the initiation of Phase III studies later in 2014.

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The funding necessary to bring a drug candidate to market is subject to numerous uncertainties, which may adversely affect our liquidity and capital resources. Once a drug candidate is identified, the further development of that drug candidate can be halted or abandoned at any time due to a number of factors. These factors include, but are not limited to, funding constraints, safety or a change in market demand.

The nature and efforts required to develop our drug candidates into commercially viable products include research to identify a clinical candidate, preclinical development, clinical testing, FDA approval and commercialization. For each drug candidate that successfully completes all stages of R&D, and is commercialized, total R&D spending in the pharmaceutical industry may exceed $2 billion. Additionally, the stages of R&D can take in excess of ten years to complete for each drug candidate.

For each of our drug candidate programs, we periodically assess the scientific progress and merits of the programs to determine if continued R&D is economically viable. Certain of our programs have been terminated due to the lack of scientific progress and lack of prospects for ultimate commercialization. Because of the uncertainties associated with R&D of these programs, we may not be successful in achieving commercialization. As such, the ultimate timeline and costs to commercialize a product cannot be accurately estimated. Additionally, due to the uncertainty inherent in drug development, R&D costs are subject to considerable variation.

We expect research and development expenses to increase in 2016 as compared to 2015. We have recently initiated VMAT2 Phase II development in Tourette syndrome as well as announced a new clinical program investigating NBI-640756 in essential tremor. Additionally, we expect to file a new IND application in 2016 for another drug candidate. The development efforts around these programs, increased headcount to support these programs, coupled with higher share-based compensation expense due to increased Black-Scholes estimates and the expensing of certain RSUs and PRSUs, will result in an increase in R&D expense in 2016.

General and Administrative

General and administrative expenses were $32.5 million in 2015 compared to $18.0 million in 2014 and $13.3 million in 2013. The majority of this $14.5 million increase in expenses from 2014 to 2015 was due to higher personnel related expenses. Share-based compensation expense increased by approximately $10.1 million from 2014 to 2015; approximately $4.6 million of which was related to PRSUs expense recognized in 2015. An increase in headcount and other personnel related costs accounted for approximately $2.1 million of additional increase in personnel expense. Higher market research, licensing and other professional fees accounted for approximately $1.9 million of the increase in general and administrative expenses from 2014 to 2015.

The $4.7 million increase in expenses from 2013 to 2014 resulted primarily from a $3.5 million increase in personnel related costs, of which $1.7 million was related to higher share-based compensation costs. Higher market research and professional fees accounted for $0.6 million of the increase in general and administrative expenses from 2013 to 2014.

We expect our general and administrative expenses in 2016 to increase significantly from 2015 expense levels due to increasing pre-commercialization activities related to our VMAT2 inhibitor for tardive dyskinesia.

Net Loss

Our net loss for 2015 was $88.9 million, or $1.05 net loss per common share, our net loss for 2014 was $60.5 million, or $0.81 net loss per common share, and our net loss for 2013 was $46.1 million, or $0.69 net loss per common share.

The increase in our net loss from 2014 to 2015 was a result of the above mentioned higher overall expenses offset partially by an increase in revenue of approximately $19.8 million from the Mitsubishi Tanabe agreement.

The increase in our net loss from 2013 to 2014 was a result of the above mentioned higher overall expenses coupled with a $2.9 million decrease in revenue.

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We expect to have a net loss in 2016, primarily due to significantly higher general and administrative expenses as we prepare for commercialization of valbenazine in tardive dyskinesia. R&D expenses will also increase due to our expanded clinical pipeline and early stage R&D efforts. Revenue is also expected to decrease modestly in 2016.

Liquidity and Capital Resources

At December 31, 2015, our cash, cash equivalents, and investments totaled $461.7 million compared with $231.3 million at December 31, 2014.

Net cash used in operating activities during 2015 was $38.0 million compared to $47.1 million in 2014. The $9.1 million change in cash flows from operating activities is primarily due to an increase in operating expenses of approximately $49.6 million; of which approximately $18.0 million consisted of non-cash share-based compensation expense. This increase in operating expenses was offset by a $30 million up-front payment from Mitsubishi Tanabe received in the second quarter of 2015, and an increase in current accounts payable and accrued liabilities of approximately $9.8 million.

Net cash used in operating activities during 2014 was $47.1 million compared to $29.6 million in 2013. The $17.5 million change is primarily due to the increase in net loss coupled with a decrease in receivables of approximately $14.1 million from 2012 receivables that were collected during the first quarter of 2013.

Net cash used in investing activities was $195.8 million in 2015 compared to net cash used in investing activities of $105.4 million in 2014 and net cash provided by investing activities of $5.3 million in 2013. The fluctuation in net cash used in investing activities resulted primarily from the timing differences in investment purchases, sales and maturities, and the fluctuation of our portfolio mix between cash equivalents and short-term investment holdings. The average term to maturity in our investment portfolio is less than one year.

Net cash provided by financing activities during 2015 was $277.0 million compared to $138.7 million and $5.3 million in 2014 and 2013, respectively. Cash provided by financing activities included approximately $270.7 and $133.2 million from our public offering of common stock in February 2015 and 2014, respectively. During 2014, 2013 and 2012 stock option exercises yielded $6.3 million, $5.6 million and $5.3 million, respectively, in cash proceeds. We had no outstanding debt at December 31, 2015.

Equity Financing. In February 2015, we completed a public offering of common stock in which we sold 8.0 million shares of our common stock at an offering price of $36.00 per share. The shares were sold pursuant to a shelf registration statement with the Securities and Exchange Commission (SEC). The net proceeds generated from this transaction, after underwriting discounts and commissions and offering costs, were approximately $270.7 million.

In February 2014, we completed a public offering of common stock in which we sold 8.0 million shares our common stock at an offering price of $17.75 per share. The shares were sold pursuant to a shelf registration statement with the SEC. The net proceeds generated from this transaction, after underwriting discounts and commissions and offering costs, were approximately $133.2 million.

Shelf Registration Statement. In February 2014, we filed an automatic shelf registration statement which immediately became effective by rule of the SEC. For so long as we continue to satisfy the requirements to be deemed a well-known seasoned issuer, this shelf registration statement allows us to issue an unlimited number of shares of our common stock from time to time. As of December 31, 2015, we had sold 16.0 million shares under this shelf registration statement.

Factors That May Affect Future Financial Condition and Liquidity

We anticipate increases in expenditures as we continue to expand our R&D activities. Because of our limited financial resources, our strategies to develop some of our programs include collaborative agreements with major pharmaceutical companies and sales of our common stock in both public and private offerings. Our collaborative agreements typically include a partial recovery of our research costs through license fees, contract

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research funding and milestone revenues. Our collaborators are also financially and managerially responsible for clinical development and commercialization. In these cases, the estimated completion date would largely be under the control of the collaborator. We cannot forecast, with any degree of certainty, which other proprietary products or indications, if any, will be subject to future collaborative arrangements, in whole or in part, and how such arrangements would affect our capital requirements.

Our inlicensed, research and clinical development agreements are generally cancelable with written notice within 180 days or less. In addition to the minimum payments due under inlicense and research agreements, we may be required to pay up to approximately $17 million in milestone payments, plus sales royalties, in the event that all scientific research under these agreements is successful.

From time to time, we may be subject to legal proceedings and claims in the ordinary course of business. On December 1, 2015, Icahn School of Medicine at Mount Sinai (Mount Sinai) filed a complaint against us in the United States District Court for the Southern District of New York: *Icahn School of Medicine at Mount Sinai v. Neurocrine Biosciences, Inc.*, Case No. 1:15-cv-09414. In the complaint, Mount Sinai alleges that we, by entering into an exclusive worldwide collaboration with AbbVie to develop and commercialize GnRH antagonists breached our license agreement with Mount Sinai dated August 27, 1999. Mount Sinai is seeking unspecified monetary damages, future sublicensing fees and attorney s fees. We believe that we have meritorious defenses to the claims made in the complaint and intend to vigorously defend ourselves against such claims, but are not able to predict the ultimate outcome of this action.

We lease our office and research laboratories under an operating lease with an initial term that expires at the end of 2019. Additionally, our facility lease agreement calls for us to maintain $50 million in cash and investments at all times, or to increase our security deposit by $5 million.

As of December 31, 2015, the total estimated future annual minimum lease payments under our non-cancelable operating lease obligations are as follows *(in thousands):*

	Payment Amount
Year ending:	
2016	$ 7,606
2017	7,834
2018	8,070
2019	8,311
2020 and thereafter	
Total future minimum lease payments	$ 31,821

The funding necessary to execute our business strategies is subject to numerous uncertainties, which may adversely affect our liquidity and capital resources. Completion of clinical trials may take several years or more, but the length of time generally varies substantially according to the type, complexity, novelty and intended use of a product candidate. It is also important to note that if a clinical candidate is identified, the further development of that candidate can be halted or abandoned at any time due to a number of factors. These factors include, but are not limited to, funding constraints, safety or a change in market demand.

The nature and efforts required to develop our product candidates into commercially viable products include research to identify a clinical candidate, preclinical development, clinical testing, FDA approval and commercialization. For each drug candidate that successfully completes all stages of R&D, and is commercialized, total R&D spending in the pharmaceutical industry may exceed $2 billion. Additionally, the stages of research and development can take in excess of ten years to complete for each drug candidate.

We test our potential product candidates in numerous preclinical studies to identify disease indications for which our product candidates may show efficacy. We may conduct multiple clinical trials to cover a variety of indications for each product candidate. As we obtain results from trials, we may elect to discontinue clinical trials

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for certain product candidates or for certain indications in order to focus our resources on more promising product candidates or indications. The duration and the cost of clinical trials may vary significantly over the life of a project as a result of differences arising during the clinical trial protocol, including, among others, the following:

- we or the FDA or similar foreign regulatory authorities may suspend the trials;
- we may discover that a product candidate may cause harmful side effects;
- patient recruitment may be slower than expected; and
- patients may drop out of the trials.

For each of our programs, we periodically assess the scientific progress and merits of the programs to determine if continued R&D is economically viable. Certain of our programs have been terminated due to the lack of scientific progress and lack of prospects for ultimate commercialization. Because of the uncertainties associated with R&D of these programs, we may not be successful in achieving commercialization. As such, the ultimate timeline and costs to commercialize a product cannot be accurately estimated.

Our product candidates have not yet achieved FDA regulatory approval, which is required before we can market them as therapeutic products in the United States. In order to proceed to subsequent clinical trial stages and to ultimately achieve regulatory approval, the FDA must conclude that our clinical data establish safety and efficacy. We must satisfy the requirements of similar regulatory authorities in foreign countries in order to market products in those countries. The results from preclinical testing and early clinical trials may not be predictive of results in later clinical trials. It is possible for a candidate to show promising results in clinical trials, but subsequently fail to establish sufficient safety and efficacy data necessary to obtain regulatory approvals.

As a result of the uncertainties discussed above, among others, the duration and completion costs of our R&D projects are difficult to estimate and are subject to considerable variation. Our inability to complete our R&D projects in a timely manner or our failure to enter into collaborative agreements, when appropriate, could significantly increase our capital requirements and could adversely impact our liquidity. These uncertainties could force us to seek additional, external sources of financing from time to time in order to continue with our business strategy. Our inability to raise additional capital, or to do so on terms reasonably acceptable to us, would jeopardize the future success of our business.

We also may be required to make further substantial expenditures if unforeseen difficulties arise in other areas of our business. In particular, our future capital requirements will depend on many factors, including:

- continued scientific progress in our R&D programs;
- the magnitude of our R&D programs;
- progress with preclinical testing and clinical trials;
- the time and costs involved in obtaining regulatory approvals;
- the costs involved in filing and pursuing patent applications and enforcing patent claims;

competing technological and market developments;

the establishment of additional collaborations and strategic alliances;

developments related to on-going litigation;

the cost of manufacturing facilities and of commercialization activities and arrangements; and

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

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, we cannot guarantee that our existing capital resources and anticipated revenues will be sufficient to conduct and complete all of our research and development programs as planned.

We will require additional funding to continue our research and product development programs, to conduct preclinical studies and clinical trials, for operating expenses, to pursue regulatory approvals for our product

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candidates, for the costs involved in filing and prosecuting patent applications and enforcing or defending patent claims, if any, for the cost of product in-licensing and for any possible acquisitions, and we may require additional funding to establish manufacturing and marketing capabilities in the future. We may seek to access the public or private equity markets whenever conditions are favorable. For example, we have an effective shelf registration statement on file with the SEC which allows us to issue an unlimited number of shares of our common stock from time to time. We may also seek additional funding through strategic alliances or other financing mechanisms. We cannot assure you that adequate funding will be available on terms acceptable to us, if at all. Any additional equity financings will be dilutive to our stockholders and any additional debt may involve operating covenants that may restrict our business. If adequate funds are not available through these means, we may be required to curtail significantly one or more of our research or development programs or obtain funds through arrangements with collaborators or others. This may require us to relinquish rights to certain of our technologies or product candidates. To the extent that we are unable to obtain third-party funding for such expenses, we expect that increased expenses will result in increased cash flow losses from operations. We cannot assure you that we will successfully develop our products under development or that our products, if successfully developed, will generate revenues sufficient to enable us to earn a profit.

Interest Rate Risk

We are exposed to interest rate risk on our short-term investments. The primary objective of our investment activities is to preserve principal while at the same time maximizing yields without significantly increasing risk. To achieve this objective, we invest in highly liquid and high quality government and other debt securities. To minimize our exposure due to adverse shifts in interest rates, we invest in short-term securities and ensure that the maximum average maturity of our investments does not exceed 12 months. If a 10% change in interest rates were to have occurred on December 31, 2015, this change would not have had a material effect on the fair value of our investment portfolio as of that date. Due to the short holding period of our investments, we have concluded that we do not have a material financial market risk exposure.

New Accounting Pronouncements

In May 2014, the Financial Accounting Standards Board (FASB) issued an Accounting Standards Update (ASU), Revenue from Contracts with Customers, which outlines a comprehensive revenue recognition model and supersedes most current revenue recognition guidance. The new standard requires a company to recognize revenue upon transfer of goods or services to a customer at an amount that reflects the expected consideration to be received in exchange for those goods or services. The ASU defines a five-step approach for recognizing revenue, which may require a company to use more judgment and make more estimates than under the current guidance. The ASU as currently issued will be effective for us starting in 2018. The new standard allows for two methods of adoption: (a) full retrospective adoption, meaning the standard is applied to all periods presented, or (b) modified retrospective adoption, meaning the cumulative effect of applying the new standard is recognized as an adjustment to the opening retained earnings balance. We are in the process of determining the adoption method we will implement as well as the effects the adoption will have on our consolidated financial statements.

In November 2015, the FASB issued an ASU, Income Taxes: Balance Sheet Classification of Deferred Taxes, which ASU eliminates the current requirement for organizations to present deferred tax assets and liabilities as current and noncurrent in a classified balance sheet. Instead, organizations will be required to classify all deferred tax assets and liabilities as noncurrent. This ASU applies to all organizations that present a classified balance sheet. The ASU is effective for financial statements issued for annual periods beginning after December 15, 2016, and interim periods within those annual periods. We adopted this standard as of December 31, 2015 with retroactive application.

ITEM 7A. ***QUANTITATIVE AND QUALITATIVE DISCLOSURES ABOUT MARKET RISK***

Information required by this item is contained in Item 7. Management s Discussion and Analysis of Financial Condition and Results of Operations Interest Rate Risk. Such information is incorporated herein by reference.

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ITEM 8. ***FINANCIAL STATEMENTS AND SUPPLEMENTARY DATA***

NEUROCRINE BIOSCIENCES, INC.

INDEX TO THE CONSOLIDATED FINANCIAL STATEMENTS

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Report of Independent Registered Public Accounting Firm

The Board of Directors and Stockholders of

Neurocrine Biosciences, Inc.

We have audited the accompanying consolidated balance sheets of Neurocrine Biosciences, Inc. as of December 31, 2015 and 2014, and the related consolidated statements of comprehensive loss, stockholders equity and cash flows for each of the three years in the period ended December 31, 2015. These financial statements are the responsibility of the Company s management. Our responsibility is to express an opinion on these financial statements based on our audits.

We conducted our audits in accordance with the standards of the Public Company Accounting Oversight Board (United States). Those standards require that we plan and perform the audit to obtain reasonable assurance about whether the financial statements are free of material misstatement. An audit includes examining, on a test basis, evidence supporting the amounts and disclosures in the financial statements. An audit also includes assessing the accounting principles used and significant estimates made by management, as well as evaluating the overall financial statement presentation. We believe that our audits provide a reasonable basis for our opinion.

In our opinion, the financial statements referred to above present fairly, in all material respects, the consolidated financial position of Neurocrine Biosciences, Inc. at December 31, 2015 and 2014, and the consolidated results of its operations and its cash flows for each of the three years in the period ended December 31, 2015, in conformity with U.S. generally accepted accounting principles.

We also have audited, in accordance with the standards of the Public Company Accounting Oversight Board (United States), Neurocrine Biosciences, Inc. s internal control over financial reporting as of December 31, 2015, based on criteria established in Internal Control-Integrated Framework issued by the Committee of Sponsoring Organizations of the Treadway Commission (2013 framework) and our report dated February 11, 2016 expressed an unqualified opinion thereon.

/s/ Ernst & Young LLP

San Diego, California

February 11, 2016

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NEUROCRINE BIOSCIENCES, INC.

Consolidated Balance Sheets

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

	December 31, 2015	2014
ASSETS		
Current assets:		
Cash and cash equivalents	$ 74,195	$ 31,014
Short-term investments, available-for-sale	304,996	162,795
Other current assets	4,883	4,394
Total current assets	384,074	198,203
Property and equipment, net	3,432	2,507
Long-term investments, available-for-sale	82,488	37,492
Restricted cash	4,791	4,831
Total assets	$ 474,785	$ 243,033
LIABILITIES AND STOCKHOLDERS EQUITY		
Current liabilities:		
Accounts payable	$ 2,561	$ 246
Accrued liabilities	19,034	11,508
Current portion of deferred rent	269	119
Current portion of cease-use liability	428	467
Current portion of deferred gain on sale of real estate	3,423	3,324
Total current liabilities	25,715	15,664
Deferred gain on sale of real estate	10,898	14,322
Deferred revenue	10,231	
Deferred rent	1,711	1,877
Cease-use liability	1,555	2,211
Other liabilities	221	260
Total liabilities	50,331	34,334
Commitments and contingencies		
Stockholders equity:		
Preferred stock, $0.001 par value; 5,000,000 shares authorized; no shares issued and outstanding		
Common stock, $0.001 par value; 110,000,000 shares authorized; issued and outstanding shares were 86,262,594 and 76,465,942 at December 31, 2015 and 2014, respectively	86	76
Additional paid-in capital	1,340,579	1,035,205
Accumulated other comprehensive loss	(977)	(277)
Accumulated deficit	(915,234)	(826,305)
Total stockholders equity	424,454	208,699
Total liabilities and stockholders equity	$ 474,785	$ 243,033

See accompanying notes.

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NEUROCRINE BIOSCIENCES, INC.

Consolidated Statements of Comprehensive Loss

(In thousands, except net loss per share data)

	Year Ended December 31,		
	2015	**2014**	**2013**
Revenues:			
Milestones and license fees	$ 19,769	$	$ 2,919
Total revenues	19,769		2,919
Operating expenses:			
Research and development	81,491	46,425	39,248
General and administrative	32,480	17,986	13,349
Total operating expenses	113,971	64,411	52,597
Loss from operations	(94,202)	(64,411)	(49,678)
Other income:			
Gain (loss) on sale/disposal of assets	9	(4)	37
Deferred gain on real estate	3,325	3,226	3,133
Investment income, net	1,928	629	402
Other income, net	11	18	16
Total other income	5,273	3,869	3,588
Net loss	$ (88,929)	$ (60,542)	$ (46,090)
Net loss per common share:			
Basic	$ (1.05)	$ (0.81)	$ (0.69)
Diluted	$ (1.05)	$ (0.81)	$ (0.69)
Shares used in the calculation of net loss per common share:			
Basic	84,496	74,577	66,989
Diluted	84,496	74,577	66,989
Other comprehensive loss:			
Net loss	$ (88,929)	$ (60,542)	$ (46,090)
Net unrealized (losses) gains on available-for-sale securities	(700)	(282)	7
Comprehensive loss	$ (89,629)	$ (60,824)	$ (46,083)

See accompanying notes.

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NEUROCRINE BIOSCIENCES, INC.

Consolidated Statements of Stockholders Equity

(In thousands)

	Common Stock		Additional Paid in Capital	Accumulated Other Comprehensive (Loss) Gain	Accumulated Deficit	Total Stockholders Equity
	Shares	Amount				
BALANCE AT DECEMBER 31, 2012	66,447	$ 66	$ 873,981	$ (2)	$ (719,673)	$ 154,372
Net income					(46.090)	(46,090)
Unrealized gains on investments				7		7
Share-based compensation			6,819			6,819
Issuance of common stock for option exercises	904	1	5,301			5,302
BALANCE AT DECEMBER 31, 2013	67,351	$ 67	$ 886,101	$ 5	$ (765,763)	$ 120,410
Net loss					(60,542)	(60,542)
Unrealized losses on investments				(282)		(282)
Share-based compensation			10,382			10,382
Issuance of common stock for restricted share units vested	93					
Issuance of common stock for option exercises	1,022	1	5,559			5,560
Issuance of common stock, net of offering costs	8,000	8	133,163			133,171
BALANCE AT DECEMBER 31, 2014	76,466	$ 76	$ 1,035,205	$ (277)	$ (826,305)	$ 208,699
Net loss					(88,929)	(88,929)
Unrealized losses on investments				(700)		(700)
Share-based compensation			28,392			28,392
Issuance of common stock for restricted share units vested	503	1				1
Issuance of common stock for option exercises	1,308	1	6,303			6,304
Issuance of common stock, net of offering costs	7,986	8	270,679			270,687
BALANCE AT DECEMBER 31, 2015	86,263	$ 86	$ 1,340,579	$ (977)	$ (915,234)	$ 424,454

See accompanying notes.

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NEUROCRINE BIOSCIENCES, INC.

Consolidated Statements of Cash Flows

(In thousands)

	Years Ended December 31,		
	2015	**2014**	**2013**
CASH FLOW FROM OPERATING ACTIVITIES			
Net loss	$ (88,929)	$ (60,542)	$ (46,090)
Adjustments to reconcile net loss to net cash used in operating activities:			
Depreciation and amortization	1,009	827	671
Gain on sale of assets, net	(3,334)	(3,222)	(3,170)
Cease-use expense	(85)		
Deferred revenues	10,231		(2,919)
Deferred rent	(16)	14	142
Amortization of premiums on investments	6,032	3,792	2,843
Non-cash share-based compensation expense	28,392	10,382	6,819
Change in operating assets and liabilities:			
Accounts receivable and other assets	(489)	(1,671)	13,528
Cease-use liability	(610)	(418)	(590)
Other liabilities	(39)		108
Accounts payable and accrued liabilities	9,841	3,698	(949)
Net cash used in operating activities	(37,997)	(47,140)	(29,607)
CASH FLOW FROM INVESTING ACTIVITIES			
Purchases of investments	(449,052)	(257,544)	(145,328)
Sales/maturities of investments	255,123	154,133	151,281
Deposits and restricted cash	40	(388)	(108)
Proceeds from sales of property and equipment	9	45	40
Purchases of property and equipment	(1,934)	(1,612)	(545)
Net cash (used in) provided by investing activities	(195,814)	(105,366)	5,340
CASH FLOW FROM FINANCING ACTIVITIES			
Issuance of common stock	276,992	138,731	5,302
Net cash provided by financing activities	276,992	138,731	5,302
Net change in cash and cash equivalents	43,181	(13,775)	(18,965)
Cash and cash equivalents at beginning of the year	31,014	44,789	63,754
Cash and cash equivalents at end of the year	$ 74,195	$ 31,014	$ 44,789
SUPPLEMENTAL DISCLOSURES			
Taxes paid	$	$	$

See accompanying notes.

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NEUROCRINE BIOSCIENCES, INC.

NOTES TO THE CONSOLIDATED FINANCIAL STATEMENTS

December 31, 2015

NOTE 1. ORGANIZATION AND SUMMARY OF SIGNIFICANT ACCOUNTING POLICIES

Business Activities. Neurocrine Biosciences, Inc. (the Company or Neurocrine) was incorporated in California in 1992 and reincorporated in Delaware in 1996. The Company discovers and develops innovative and life-changing pharmaceuticals, in diseases with high unmet medical needs, through its novel research and development (R&D) platform, focused on neurological and endocrine based diseases and disorders. The Company s two lead late-stage clinical programs are elagolix, a gonadotropin-releasing hormone (GnRH) antagonist for women s health that is partnered with AbbVie Inc. (AbbVie), and a vesicular monoamine transporter 2 (VMAT2) inhibitor for the treatment of movement disorders.

Neurocrine Continental, Inc., is a Delaware corporation and a wholly owned subsidiary of the Company and was inactive for all periods presented. The Company also has two wholly-owned Irish subsidiaries, Neurocrine Therapeutics, Ltd. and Neurocrine Europe, Ltd. which were formed in December 2014, both of which are inactive.

Principles of Consolidation. The consolidated financial statements include the accounts of Neurocrine as well as its wholly owned subsidiaries. The Company does not have any significant interests in any variable interest entities. All intercompany transactions and balances have been eliminated in consolidation.

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

Cash Equivalents. The Company considers all highly liquid investments that are readily convertible into cash and have an original maturity of three months or less at the time of purchase to be cash equivalents.

Short-Term and Long-Term Investments Available-for-Sale. Certain investments are classified as available-for-sale and, in accordance with authoritative guidance, are carried at fair value, with the unrealized gains and losses reported in other comprehensive loss. The amortized cost of debt securities in this category is adjusted for amortization of premiums and accretion of discounts to maturity. Such amortization and accretion is included in investment income. Realized gains and losses and declines in value judged to be other-than-temporary, if any, on available-for-sale securities are included in other income or expense. The cost of securities sold is based on the specific identification method. Interest and dividends on securities classified as available-for-sale are included in investment income.

Concentration of Credit Risk. Financial instruments that potentially subject the Company to concentrations of credit risk consist primarily of cash, cash equivalents and investments. The Company has established guidelines to limit its exposure to credit risk by placing investments with high credit quality financial institutions, diversifying its investment portfolio and placing investments with maturities that maintain safety and liquidity.

Collaboration Agreements. Collaborative R&D agreements accounted for all of the Company s revenue for all periods presented.

Property and Equipment. Property and equipment are stated at cost and depreciated over the estimated useful lives of the assets using the straight-line method. Equipment is depreciated over an average estimated useful life of three to seven years. Leasehold improvements are depreciated over the shorter of their estimated useful lives or the remaining lease term.

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Industry Segment and Geographic Information. The Company operates in a single industry segment the discovery and development of therapeutics for the treatment of neurological and endocrine based diseases and disorders. The Company had no foreign based operations during any of the years presented.

Impairment of Long-Lived Assets. The Company reviews long-lived assets for impairment whenever events or changes in circumstances indicate that the carrying value of an asset may not be recoverable. If indicators of impairment exist, the Company assesses the recoverability of the affected long-lived assets by determining whether the carrying value of such assets can be recovered through undiscounted future operating cash flows. If the carrying amount is not recoverable, the Company measures the amount of any impairment by comparing the carrying value of the asset to the present value of the expected future cash flows associated with the use of the asset.

Fair Value of Financial Instruments. Financial instruments, including cash and cash equivalents, accounts receivable, accounts payable, and accrued liabilities, are carried at cost, which management believes approximates fair value because of the short-term maturity of these instruments.

Research and Development Expenses. R&D expenses consists primarily of salaries, payroll taxes, employee benefits, and share-based compensation charges, for those individuals involved in ongoing R&D efforts; as well as scientific contractor fees, preclinical and clinical trial costs, R&D facilities costs, laboratory supply costs, and depreciation of scientific equipment. All such costs are charged to R&D expense as incurred. These expenses result from the Company s independent R&D efforts as well as efforts associated with collaborations and in-licensing arrangements. In addition, the Company funds R&D at other companies and research institutions under agreements, which are generally cancelable. The Company reviews and accrues clinical trial expenses based on work performed, which relies on estimates of total costs incurred based on patient enrollment, completion of patient studies and other events. The Company follows this method since reasonably dependable estimates of the costs applicable to various stages of a research agreement or clinical trial can be made. Accrued clinical costs are subject to revisions as trials progress. Revisions are charged to expense in the period in which the facts that give rise to the revision become known.

Share-Based Compensation. The Company estimates the fair value of stock options using the Black-Scholes option pricing model on the date of grant. Restricted stock units are valued based on the closing price of the Company s common stock on the date of grant. The fair value of equity instruments expected to vest are recognized and amortized on a straight-line basis over the requisite service period of the award, which is generally three to four years; however, certain provisions in the Company s equity compensation plans provide for shorter vesting periods under certain circumstances. Additionally, the Company has granted certain performance-based equity awards that vest upon the achievement of certain pre-defined Company-specific performance criteria. Expense related to these performance-based equity awards is generally recognized ratably over the performance period once the pre-defined performance based criteria for vesting becomes probable.

Investment Income, net. Investment income, net is comprised of interest and dividends earned on cash, cash equivalents and investments as well as gains and losses realized from activity in the Company s investment portfolio. The following table presents certain information related to the components of investment income (in thousands):

	Years Ended December 31,		
	2015	2014	2013
Interest income	$ 1,928	$ 629	$ 400
Realized gains, net			2
Total	$ 1,928	$ 629	$ 402

Net Loss Per Share. The Company computes basic net loss per share using the weighted average number of common shares outstanding during the period. Diluted net income per share is based upon the weighted average number of common shares and potentially dilutive securities (common share equivalents) outstanding during the

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period. Common share equivalents outstanding, determined using the treasury stock method, are comprised of shares that may be issued under the Company s stock option agreements. Common share equivalents are excluded from the diluted net loss per share calculation because of their anti-dilutive effect.

Due to the Company s net loss position in 2015, 2014 and 2013, approximately 4.1 million, 2.9 million and 2.1 million, respectively, of common share equivalents were excluded from the diluted common shares outstanding. For the years ended December 31, 2015, 2014 and 2013, there were employee stock options, calculated on a weighted average basis, to purchase 0.1 million, 1.0 million, and 0.3 million shares of our common stock with an exercise price greater than the average market price of the underlying common shares.

Impact of Recently Issued Accounting Standards. In May 2014, the Financial Accounting Standards Board (FASB) amended the existing accounting standards for revenue recognition, which outlines a comprehensive revenue recognition model and supersedes most current revenue recognition guidance. The new standard requires a company to recognize revenue upon transfer of goods or services to a customer at an amount that reflects the expected consideration to be received in exchange for those goods or services. The amended guidance defines a five-step approach for recognizing revenue, which may require a company to use more judgment and make more estimates than under the current guidance. The amended guidance as currently issued will be effective for the Company starting in 2018. The new standard allows for two methods of adoption: (a) full retrospective adoption, meaning the standard is applied to all periods presented, or (b) modified retrospective adoption, meaning the cumulative effect of applying the new standard is recognized as an adjustment to the opening retained earnings balance. The Company is in the process of determining the adoption method it will implement, as well as the effects the adoption will have on its consolidated financial statements.

In November 2015, the FASB issued an ASU, Income Taxes: Balance Sheet Classification of Deferred Taxes, which ASU eliminates the current requirement for organizations to present deferred tax assets and liabilities as current and noncurrent in a classified balance sheet. Instead, organizations will be required to classify all deferred tax assets and liabilities as noncurrent. This ASU applies to all organizations that present a classified balance sheet. The ASU is effective for financial statements issued for annual periods beginning after December 15, 2016, and interim periods within those annual periods. The Company has adopted this standard as of December 31, 2015 with retroactive application.

NOTE 2. REVENUE RECOGNITION AND SIGNIFICANT COLLABORATIVE RESEARCH AND DEVELOPMENT AGREEMENTS

Revenue Recognition Policy. The Company recognizes revenue for the performance of services when each of the following four criteria is met: (i) persuasive evidence of an arrangement exists; (ii) services are rendered or products are delivered; (iii) the sales price is fixed or determinable; and (iv) collectability is reasonably assured.

Since 2011, the Company has followed the Accounting Standards Codification (ASC) for Revenue Recognition - Multiple-Element Arrangements, if applicable, to determine the recognition of revenue under license and collaboration agreements. The terms of these agreements generally contain multiple elements, or deliverables, which may include (i) licenses to the Company s intellectual property, (ii) materials and technology, (iii) pharmaceutical supply, (iv) participation on joint development or joint steering committees, and (v) development services. The payments the Company receives under these arrangements typically include one or more of the following: up-front license fees; funding of research and/or development efforts; amounts due upon the achievement of specified milestones; manufacturing and royalties on future product sales.

The ASC provides guidance relating to the separation of deliverables included in an arrangement into different units of accounting and the allocation of consideration to the units of accounting. The evaluation of multiple-element arrangements requires management to make judgments about (i) the identification of deliverables, (ii) whether such deliverables are separable from the other aspects of the contractual relationship, (iii) the estimated selling price of each deliverable, and (iv) the expected period of performance for each deliverable.

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To determine the units of accounting under a multiple-element arrangement, management evaluates certain separation criteria, including whether the deliverables have stand-alone value, based on the relevant facts and circumstances for each arrangement. The selling prices of deliverables under an arrangement may be derived using vendor specific objective evidence (VSOE), third-party evidence, or a best estimate of selling price (BESP), if VSOE or third-party evidence is not available. For most pharmaceutical licensing and collaboration agreements, BESP is utilized. The objective of BESP is to determine the price at which the Company would transact a sale if the element within the agreement was sold on a standalone basis. Establishing BESP involves management s judgment and considers multiple factors, including market conditions and company-specific factors, including those factors contemplated in negotiating the agreements, as well as internally developed models that include assumptions related to market opportunity, discounted cash flows, estimated development costs, probability of success and the time needed to commercialize a product candidate pursuant to the agreement. In validating the BESP, management considers whether changes in key assumptions used to determine the BESP will have a significant effect on the allocation of the arrangement consideration between the multiple deliverables. The allocated consideration for each unit of accounting is recognized over the related obligation period in accordance with the applicable revenue recognition criteria.

If there are deliverables in an arrangement that are not separable from other aspects of the contractual relationship, they are treated as a combined unit of accounting, with the allocated revenue for the combined unit recognized in a manner consistent with the revenue recognition applicable to the final deliverable in the combined unit. Payments received prior to satisfying the relevant revenue recognition criteria are recorded as unearned revenue in the accompanying balance sheets and recognized as revenue when the related revenue recognition criteria are met.

The Company typically receives up-front payments when licensing its intellectual property, which often occurs in conjunction with a R&D agreement. The Company recognizes revenue attributed to the license upon delivery, provided that the license has stand-alone value.

For payments payable on achievement of milestones that do not meet all of the conditions to be considered substantive, the Company recognizes the portion of the payment allocable to delivered items as revenue when the specific milestone is achieved, and the contingency is removed.

Prior to the revised multiple element guidance described above, adopted by the Company on January 1, 2011, upfront, nonrefundable payments for license fees, grants, and advance payments for sponsored research revenues received in excess of amounts earned were classified as deferred revenue and recognized as income over the contract or development period. Revenues from development milestones are accounted for in accordance with the Revenue Recognition Milestone Method Topic of the FASB ASC (Milestone Method). Milestones are recognized when earned, as evidenced by written acknowledgment from the collaborator or other persuasive evidence that the milestone has been achieved, provided that the milestone event is substantive. A milestone event is considered to be substantive if its achievability was not reasonably assured at the inception of the agreement and the Company s efforts led to the achievement of the milestone or the milestone was due upon the occurrence of a specific outcome resulting from the Company s performance. The Company assesses whether a milestone is substantive at the inception of each agreement.

Mitsubishi Tanabe Pharma Corporation (Mitsubishi Tanabe). During 2015, the Company entered into a collaboration and license agreement with Mitsubishi Tanabe for the development and commercialization of valbenazine for movement disorders in Japan and other select Asian markets. Payments to the Company under this agreement include an up-front license fee of $30 million, up to $85 million in development and commercialization event-based payments, payments for the manufacture of pharmaceutical products, and royalties on product sales in select territories in Asia. Under the terms of the agreement, Mitsubishi Tanabe is responsible for all third-party development, marketing and commercialization costs in Japan and other select Asian markets with the exception of a single Huntington s chorea clinical trial to be performed by the Company, at an estimated cost of approximately $12 million, should Mitsubishi Tanabe request the clinical trial. The Company will be entitled to a percentage of sales of NBI-98854 in Japan and other select Asian markets for the longer of ten years or the life of the related patent rights.

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Under the terms of the Company s agreement with Mitsubishi Tanabe, the collaboration effort between the parties to advance NBI-98854 towards commercialization in Japan and other select Asian markets is governed by a joint steering committee and joint development committee with representatives from both the Company and Mitsubishi Tanabe. There are no performance, cancellation, termination or refund provisions in the agreement that would have a material financial consequence to the Company. The Company does not directly control when event-based payments will be achieved or when royalty payments will begin. Mitsubishi Tanabe may terminate the agreement at its discretion upon 180 days written notice to the Company. In such event, all valbenazine product rights for Japan and other select Asian markets would revert to the Company.

The Company has identified the following deliverables associated with the Mitsubishi Tanabe agreement: valbenazine technology license and existing know-how, development activities to be performed as part of the collaboration, and the manufacture of pharmaceutical products. The respective standalone value from each of these deliverables has been determined by applying the BESP method and the revenue was allocated based on the relative selling price method with revenue recognition timing to be determined either by delivery or the provision of services.

As discussed above, the BESP method required the use of significant estimates. The Company used an income approach to estimate the selling price for the technology license and an expense approach for estimating development activities and the manufacture of pharmaceutical products. The development activities and the manufacture of pharmaceutical products are expected to be delivered throughout the duration of the agreement. The technology license and existing know-how was delivered on the effective date of the agreement.

For the year ended December 31, 2015, the Company recognized revenue under this agreement of $19.8 million associated with the delivery of a technology license and existing know-how. In accordance with the Company s continuing performance obligations, $10.2 million of the $30 million up-front payment is being deferred and recognized in future periods. Under the terms of the agreement, there is no general obligation to return the up-front payment for any non-contingent deliverable.

The Company evaluated the event-based payments under the Milestone Method and concluded only one immaterial event-based payment represents a substantive milestone. Event-based payments will be recognized when earned.

The Company is eligible to receive from Mitsubishi Tanabe tiered royalty payments based on product sales in Japan and other select Asian markets. Royalties will be recognized as earned in accordance with the terms of the agreement, when product sales are reported by Mitsubishi Tanabe, the amount can be reasonably estimated, and collectability is reasonably assured.

AbbVie Inc. *(AbbVie)*. In June 2010, the Company announced an exclusive worldwide collaboration with AbbVie, to develop and commercialize elagolix and all next-generation GnRH antagonists (collectively, GnRH Compounds) for women s and men s health. AbbVie made an upfront payment of $75 million and has agreed to make additional development and regulatory event based payments of up to $480 million, of which $30 million has been received to date, and up to an additional $50 million in commercial event based payments. The Company has assessed event based payments under the revised authoritative guidance for research and development milestones and determined that event based payments prior to commencement of a Phase III clinical study, as defined in the agreement, meet the definition of a milestone in accordance with authoritative guidance as (1) they are events that can only be achieved in part on the Company s past performance, (2) there is substantive uncertainty at the date the arrangement was entered into that the event will be achieved and (3) they result in additional payments being due to the Company. Development and regulatory event based payments subsequent to the commencement of a Phase III clinical study, however, currently do not meet these criteria as their achievement is based on the performance of AbbVie. As of December 31, 2015, $500 million remains outstanding in future event based payments under the agreement as the performance is based solely on AbbVie. However, none of the remaining event based payments meet the definition of a milestone in accordance with authoritative accounting guidance.

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Under the terms of the agreement, AbbVie is responsible for all third-party development, marketing and commercialization costs. The Company 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. AbbVie may terminate the collaboration at its discretion upon 180 days written notice to the Company. In such event, the Company would be entitled to specified payments for ongoing clinical development and related activities and all GnRH Compound product rights would revert to the Company. There was no revenue recognized in 2015, 2014 or 2013 related to this collaboration.

NOTE 3. INVESTMENTS

Available-for-sale securities are carried at fair value, with the unrealized gains and losses reported in comprehensive loss. The amortized cost of debt securities in this category is adjusted for amortization of premiums and accretion of discounts to maturity. Such amortization and accretion is included in investment income. Realized gains and losses and declines in value judged to be other-than-temporary, if any, on available-for-sale securities are included in other income or expense. The cost of securities sold is based on the specific identification method. Interest and dividends on securities classified as available-for-sale are included in investment income.

Investments at December 31, 2015 and 2014 consisted of the following (in thousands):

	Years Ended December 31,	
	2015	2014
Certificates of deposit	$ 10,078	$ 17,438
Commercial paper	23,955	7,498
Corporate debt securities	323,219	174,323
Securities of government-sponsored entities	30,232	1,028
Total investments	$ 387,484	$ 200,287

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The following is a summary of investments classified as available-for-sale securities (in thousands):

	Contractual Maturity (in years)	Amortized Cost	Gross Unrealized Gains(1)	Gross Unrealized Losses(1)	Aggregate Estimated Fair Value
December 31, 2015:					
Classified as current assets:					
Certificates of deposit	Less than 1	$ 9,120	$ 1	$ (1)	$ 9,120
Commercial paper	Less than 1	23,965	1	(11)	23,955
Corporate debt securities	Less than 1	254,592	1	(414)	254,179
Securities of government-sponsored entities	Less than 1	17,762	1	(21)	17,742
Total short-term available-for-sale securities		$ 305,439	$ 4	$ (447)	$ 304,996
Classified as non-current assets:					
Certificates of deposit	1 to 2	$ 960	$	$ (2)	$ 958
Corporate debt securities	1 to 2	69,528		(488)	69,040
Securities of government-sponsored entities	1 to 2	12,534		(44)	12,490
Total long-term available-for-sale securities		$ 83,022	$	$ (534)	$ 82,488
December 31, 2014:					
Classified as current assets:					
Certificates of deposit	Less than 1	$ 9,072	$	$ (6)	$ 9,066
Commercial paper	Less than 1	7,497	1		7,498
Corporate debt securities	Less than 1	145,321	5	(123)	145,203
Securities of government-sponsored entities	Less than 1	1,029		(1)	1,028
Total short-term available-for-sale securities		$ 162,919	$ 6	$ (130)	$ 162,795
Classified as non-current assets:					
Certificates of deposit	1 to 2	$ 8,400	$	$ (28)	$ 8,372
Corporate debt securities	1 to 2	29,245		(125)	29,120
Total long-term available-for-sale securities		$ 37,645	$	$ (153)	$ 37,492

(1) Unrealized gains and losses are included in other comprehensive loss.

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The following table presents gross unrealized losses and fair value for those available-for-sale investments that were in an unrealized loss position as of December 31, 2015 and 2014, aggregated by investment category and length of time that individual securities have been in a continuous loss position (in thousands):

	Less Than 12 Months		12 Months or Greater		Total	
	Estimated Fair Value	Unrealized Losses	Estimated Fair Value	Unrealized Losses	Estimated Fair Value	Unrealized Losses
December 31, 2015:						
Certificates of deposit	$ 5,517	$ (3)	$	$	$ 5,517	$ (3)
Commercial paper	16,959	(11)			16,959	(11)
Corporate debt securities	310,160	(880)	5,521	(22)	315,681	(902)
Securities of government-sponsored entities	25,913	(65)			25,913	(65)
Total	$ 358,549	$ (959)	$ 5,521	$ (22)	$ 364,070	$ (981)
December 31, 2014:						
Certificates of deposit	$ 16,957	$ (34)	$	$	$ 16,957	$ (34)
Corporate debt securities	149,477	(248)			149,477	(248)
Securities of government-sponsored entities	1,028	(1)			1,028	(1)
Total	$ 167,462	$ (283)	$	$	$ 167,462	$ (283)

NOTE 4. FAIR VALUE MEASUREMENTS

Fair value is an exit price, representing the amount that would be received to sell an asset or paid to transfer a liability in an orderly transaction between market participants. As such, fair value is a market-based measurement that should be determined based on assumptions that market participants would use in pricing an asset or liability. As a basis for considering such assumptions, a three-tier fair value hierarchy has been established, which prioritizes the inputs used in measuring fair value as follows:

Level 1: Observable inputs such as quoted prices in active markets;

Level 2: Inputs include quoted prices for similar instruments in active markets and/or quoted prices for identical or similar instruments in markets that are not active near the measurement date; and

Level 3: Unobservable inputs in which there is little or no market data, which require the reporting entity to develop its own assumptions.

The Company classifies its cash equivalents and available for sale investments within Level 1 or Level 2. The fair value of the Company s high quality investment grade corporate debt securities is determined using proprietary valuation models and analytical tools. These valuation models and analytical tools use market pricing or prices for similar instruments that are both objective and publicly available, including matrix pricing or reported trades, benchmark yields, broker/dealer quotes, issuer spreads, two-sided markets, benchmark securities, bids and/or offers. The Company did not reclassify any investments between levels in the fair value hierarchy during the years ended December 31, 2015 and 2014.

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The Company s assets which are measured at fair value on a recurring basis as of December 31, 2015 and 2014 were determined using the inputs described above (in millions):

		Fair Value Measurements Using		
	Carrying Value	Quoted Prices in Active Markets for Identical Assets (Level 1)	Significant Other Observable Inputs (Level 2)	Significant Unobservable Inputs (Level 3)
December 31, 2015:				
Classified as current assets:				
Cash and money market funds	$ 69.5	$ 69.5	$	$
Certificates of deposit	9.1	9.1		
Commercial paper	24.0		24.0	
Securities of government-sponsored entities	17.7		17.7	
Corporate debt securities	259.0		259.0	
Subtotal	379.3	78.6	300.7	
Classified as long-term assets:				
Certificates of deposit	5.7	5.7		
Securities of government-sponsored entities	12.5		12.5	
Corporate debt securities	69.0		69.0	
Total	466.5	84.3	382.2	
Less cash, cash equivalents and restricted cash	(79.0)	(74.2)	(4.8)	
Total investments	$ 387.5	$ 10.1	$ 377.4	$
December 31, 2014:				
Classified as current assets:				
Cash and money market funds	$ 28.7	$ 28.7	$	$
Certificates of deposit	9.1	9.1		
Commercial paper	7.5		7.5	
Securities of government-sponsored entities	1.5		1.5	
Corporate debt securities	147.0		147.0	
Subtotal	193.8	37.8	156.0	
Classified as long-term assets:				
Certificates of deposit	13.2	13.2		
Corporate debt securities	29.1		29.1	
Total	236.1	51.0	185.1	
Less cash, cash equivalents and restricted cash	(35.8)	(33.5)	(2.3)	
Total investments	$ 200.3	$ 17.5	$ 182.8	$

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NOTE 5. PROPERTY AND EQUIPMENT

Property and equipment, net, at December 31, 2015 and 2014 consisted of the following (in thousands):

	2015	2014
Tenant improvements	1,335	1,226
Furniture and fixtures	837	819
Equipment	28,121	29,208
	30,293	31,253
Less accumulated depreciation	(26,861)	(28,746)
Property and equipment, net	$ 3,432	$ 2,507

For each of the years ended December 31, 2015, 2014 and 2013, depreciation expense was $1.0 million, $0.8 million and $0.7 million, respectively. During 2015, 2014 and 2013, the Company recognized a gain/(loss) of approximately $9,000, ($4,000) and $37,000, respectively, related to disposal of capital equipment.

NOTE 6. ACCRUED LIABILITIES

Accrued liabilities at December 31, 2015 and 2014 consisted of the following (in thousands):

	2015	2014
Accrued employee related costs	$ 7,358	$ 6,520
Accrued development costs	7,359	1,706
Other accrued liabilities	4,317	3,282
	$ 19,034	$ 11,508

NOTE 7. COMMITMENTS AND CONTINGENCIES

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

Upon the closing of the sale of the facility and associated real property, the Company entered into a lease agreement (Lease) whereby it leased back for an initial term of 12 years its corporate headquarters comprised of two buildings located at 12790 El Camino Real (Front Building) and 12780 El Camino Real (Rear Building) in San Diego, California. The Company also entered into a series of lease amendments (Amendments), beginning in late 2008, through which it vacated the Front Building, but continues to occupy the Rear Building. The ultimate result of this real estate sale was a net gain of $39.1 million which was deferred in accordance with authoritative guidance. For the years ended December 31, 2015, 2014 and 2013, the Company recognized $3.3 million, $3.2 million and $3.1 million, respectively, of the deferred gain and will recognize the remaining $14.3 million of the deferred gain over the initial Lease term which will expire at the end of 2019.

Under the terms of the Lease and the Amendments, the Company pays base annual rent (subject to an annual fixed percentage increase), plus a 3.5% annual management fee, property taxes and other normal and necessary expenses associated with the Lease such as utilities, repairs and maintenance. In lieu of a cash security deposit under the Lease, Wells Fargo Bank, N.A. issued on the Company s behalf a letter of credit in the amount of $4.6 million, which is secured by a deposit of equal amount with the same bank. The Company also has the right to extend the Lease for two consecutive ten-year terms.

As of December 31, 2015, the Company has two sublease agreements for approximately 30,000 square feet of the Rear Building. These subleases are expected to result in approximately $1.1 million of rental income in 2016 with this sublease rental income being recorded as an

offset to rent expense. The income generated under

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these subleases is lower than the Company s financial obligation under the Lease for the Rear Building, as determined on a per square foot basis. Consequently, at the inception of such a sublease, or in association with an amendment to such sublease, the Company is required to record a cease-use liability for the net present value of the estimated difference between the expected income to be generated under the subleases and future subleases and the Lease obligation over the remaining term of the Lease for the space that is occupied by the subtenant. The subleases provide various options to extend for additional one-year renewal periods. The current terms each of these two subleases expire in February 2017 and March 2018.

The following table sets forth changes to the accrued cease-use liability during 2015 and 2014 (in thousands):

	Years Ended December 31,	
	2015	2014
Beginning balance	$ 2,678	$ 3,096
Change in estimate	(85)	
Payments	(610)	(418)
Ending balance	$ 1,983	$ 2,678

Rent Expense. Gross rent expense was $5.9 million for each of the years ended December 31, 2015, 2014 and 2013, respectively. For financial reporting purposes, the Company recognizes rent expense on a straight-line basis over the term of the lease. Accordingly, rent expense recognized in excess of rent paid is reflected as a liability in the accompanying consolidated balance sheets.

Lease Commitments. The Company leases its office and research laboratories under an operating lease with an initial term of twelve years, expiring at the end of 2019. Additionally, the Company s facility lease agreement calls for it to maintain $50 million in cash and investments at all times, or to increase the security deposit by $5 million.

As of December 31, 2015, the total estimated future annual minimum lease payments under the Company s non-cancelable building lease for the years ending after December 31, 2015 were as follows (in thousands):

	Payment Amount
2016	$ 7,606
2017	7,834
2018	8,070
2019	8,311
2020 and thereafter	
Total future minimum lease payments	$ 31,821

Product Liability. The Company s business exposes it to liability risks from its potential drug products. A successful product liability claim or series of claims brought against the Company could result in payment of significant amounts of money and divert management s attention from running the business. The Company may not be able to maintain insurance on acceptable terms, or the insurance may not provide adequate protection in the case of a product liability claim. To the extent that product liability insurance, if available, does not cover potential claims, the Company would be required to self-insure the risks associated with such claims. The Company believes that it carries reasonably adequate insurance for product liability claims.

Licensing and Research Agreements. The Company has entered into inlicensing agreements with various universities and research organizations, which are generally cancelable at the option of the Company with terms ranging from 0-180 days written notice. Under the terms of these agreements, the Company has received licenses to research tools, know-how and technology claimed, in certain patents or patent applications. The Company is

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required to pay fees, milestones and/or royalties on future sales of products employing the technology or falling under claims of a patent, and some of the agreements require minimum royalty payments. Some of the agreements also require the Company to pay expenses arising from the prosecution and maintenance of the patents covering the inlicensed technology. The Company continually reassesses the value of the license agreements and cancels them when research efforts are discontinued on these programs. If all inlicensed and research candidates are successfully developed, the Company may be required to pay milestone payments of approximately $17 million over the lives of these agreements, in addition to royalties on sales of the affected products at rates ranging up to 5%. Due to the uncertainties of the development process, the timing and probability of the milestone and royalty payments cannot be accurately estimated.

Litigation. From time to time, the Company may be subject to legal proceedings and claims in the ordinary course of business. On December 1, 2015, Icahn School of Medicine at Mount Sinai (Mount Sinai) filed a complaint against the Company in the United States District Court for the Southern District of New York: *Icahn School of Medicine at Mount Sinai v. Neurocrine Biosciences, Inc.*, Case No. 1:15-cv-09414. In the complaint, Mount Sinai alleges that the Company, by entering into an exclusive worldwide collaboration with AbbVie to develop and commercialize next-generation gonadotropin-releasing hormone antagonists, breached its license agreement with Mount Sinai dated August 27, 1999. Mount Sinai is seeking unspecified monetary damages, future sublicensing fees and attorney s fees. The Company believes that it has meritorious defenses to the claims made in the complaint and intend to vigorously defend itself against such claims, but is not able to predict the ultimate outcome of this action.

The Company is not aware of any other proceedings or claims that it believes will have, individually or in the aggregate, a material adverse effect on its business, financial condition or results of operations.

NOTE 8. SHARE-BASED COMPENSATION

Share-Based Compensation Plans. In May 2011, the Company adopted the Neurocrine Biosciences, Inc. 2011 Equity Incentive Plan (the 2011 Plan) pursuant to which 13.5 million shares of Company common stock are authorized for issuance. The 2011 Plan provides for the grant of stock options that qualify as incentive stock options under Section 422 of the Internal Revenue Code of 1986, as amended (the Code), nonstatutory stock options, restricted stock awards, restricted stock unit awards (RSUs), stock appreciation rights, performance stock awards, performance-based restricted stock units (PRSUs) and other forms of equity compensation.

The Company also issues stock options under the Neurocrine Biosciences, Inc. Inducement Plan to certain executive level employees. During 2015 and 2014, 120,000 and 160,000 stock options, respectively, and during 2015 50,000 RSUs were granted pursuant to such inducement plan. These stock option grants have a four year vesting period and the RSUs have a three year cliff vesting. The Company currently has approximately 0.3 million in stock options and RSUs outstanding under this inducement plan.

As of December 31, 2015, approximately 6.2 million remained available for future grant awards under the 2011 Plan. Only share awards made under the 2011 Plan that are subsequently cancelled due to forfeiture or expiration are returned to the share pool available for future grants.

The Company issues new shares upon the exercise of stock options, the issuance of stock bonus awards and vesting of RSUs and PRSUs, and has 12.8 million shares of common stock reserved for such issuance as of December 31, 2015.

Vesting Provisions of Share-Based Compensation. Stock options generally have terms from seven to ten years from the date of grant, and generally vest over a three to four-year period. The maximum contractual term for all options granted from the 2011 Plan is ten years. RSUs granted under the 2011 Plan generally have vesting periods of four years. PRSUs granted under the 2011 Plan vest based on the achievement of certain pre-defined Company-specific performance criteria and expire five years from the grant date.

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Share-Based Compensation. The compensation cost that has been included in the statement of comprehensive loss for all share-based compensation arrangements is as follows (in thousands):

	Years Ended December 31,		
	2015	2014	2013
General and administrative expense	$ 15,281	$ 5,167	$ 3,516
Research and development expense	13,111	5,215	3,303
Share-based compensation expense	$ 28,392	$ 10,382	$ 6,819

Authoritative guidance requires that cash flows resulting from tax deductions in excess of the cumulative compensation cost recognized for options exercised be classified as cash inflows provided by financing activities and cash outflows used in operating activities. Due to the Company s net tax loss position, no tax benefits have been recognized in the consolidated statements of cash flows.

Stock Options. The exercise price of all options granted during the years ended December 31, 2015, 2014 and 2013 was equal to the closing price of the Company s common stock on the date of grant. The estimated fair value of each option award granted was determined on the date of grant using the Black-Scholes option-pricing valuation model with the following weighted-average assumptions for option grants during the three years ended December 31, 2015:

	Years Ended December 31,		
	2015	2014	2013
Risk-free interest rate	1.7%	2.2%	1.4%
Expected volatility of common stock	66%	71%	76%
Dividend yield	0.0%	0.0%	0.0%
Expected option term	6.6 years	7.2 years	7.3 years

The Company estimates the fair value of stock options using a Black-Scholes option-pricing model on the date of grant. The fair value of equity instruments that are ultimately expected to vest, net of estimated forfeitures, are recognized and amortized on a straight-line basis over the requisite service period. The Black-Scholes option-pricing model incorporates various and highly sensitive assumptions including expected volatility, expected term and interest rates. The expected volatility is based on the historical volatility of the Company s common stock over the most recent period commensurate with the estimated expected term of the Company s stock options. The expected option term is estimated based on historical experience as well as the status of the employee. For example, directors and officers have a longer expected option term than all other employees. The risk-free rate for periods within the contractual life of the option is based upon observed interest rates appropriate for the expected term of the Company s employee stock options. The Company has never declared or paid dividends and has no plans to do so in the foreseeable future.

Authoritative guidance requires forfeitures to be estimated at the time of grant and revised, if necessary, in subsequent periods if actual forfeitures differ from those estimates. Pre-vesting forfeitures for awards with monthly vesting terms were estimated to be 0% in 2015 based on historical experience. Pre-vesting forfeitures for awards with annual vesting terms were also estimated at 0% in 2015 based on historical employee turnover experience. The effect of past restructurings has been excluded from the historical review of employee turnover. The effect of pre-vesting forfeitures for awards has historically been negligible on the Company s recorded expense. The Company s determination of fair value is affected by the Company s stock price as well as a number of assumptions that require judgment. The weighted-average fair values of options granted during the years ended December 31, 2015, 2014 and 2013, estimated as of the grant date using the Black-Scholes option valuation model, were $23.24, $12.57 and $6.55, respectively.

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A summary of the status of the Company s stock options as of December 31, 2015, 2014 and 2013 and of changes in options outstanding under the plans during the three years ended December 31, 2015 is as follows (in thousands, except for weighted average exercise price data):

	2015		2014		2013	
	Options	Weighted Average Exercise Price	Options	Weighted Average Exercise Price	Options	Weighted Average Exercise Price
Outstanding at January 1	5,750	$ 9.31	5,853	$ 7.54	6,166	$ 7.62
Granted	1,159	37.21	1,089	18.41	771	9.24
Exercised	(1,315)	5.01	(1,135)	6.50	(904)	5.96
Canceled	(87)	46.08	(57)	56.83	(180)	25.68
Outstanding at December 31	5,507	$ 15.63	5,750	$ 9.31	5,853	$ 7.54

Options outstanding at December 31, 2015 have a weighted average remaining contractual term of 6.8 years.

For the year ended December 31, 2015, share-based compensation expense related to stock options was $13.6 million. As of December 31, 2015, there was approximately $28.0 million of unamortized compensation cost related to stock options, which is expected to be recognized over a weighted average remaining vesting period of approximately 2.6 years. As of December 31, 2015, there were approximately 3.8 million options exercisable with a weighted average exercise price of $10.44 and a weighted-average remaining contractual term of 6.1 years. The total intrinsic value, which is the amount by which the exercise price was exceeded by the sale price of the Company s common stock on the date of sale, of stock option exercises during the years ended December 31, 2015, 2014, and 2013 was $43.6 million, $14.3 million and $6.0 million, respectively. As of December 31, 2015, the total intrinsic value of options outstanding and exercisable was $225.4 million and $177.0 million, respectively. Cash received from stock option exercises for the years ended December 31, 2015, 2014 and 2013 was $6.3 million, $5.6 million and $5.3 million, respectively.

Restricted Stock Units. The fair value of RSUs is based on the closing sale price of the Company s common stock on the date of issuance. The total number of RSUs expected to vest is adjusted by estimated forfeiture rates, which has been based on historical experience of equity awards and historical employee turnover experience. The effect of pre-vesting forfeitures for awards has historically been negligible on the Company s recorded expense and was estimated at 0% in 2015. The effect of past restructurings has been excluded from the historical review of employee turnover. For the year ended December 31, 2015, 2014 and 2013, share-based compensation expense related to RSUs was $6.0 million, $2.6 million, and $0.8 million, respectively. As of December 31, 2015, there was approximately $16.2 million of unamortized compensation cost related to RSUs, which is expected to be recognized over a weighted average remaining vesting period of approximately 2.7 years.

The total intrinsic value of RSUs converted into common shares during the years ended December 31, 2015, 2014 and 2013 was $5.7 million, $1.7 million, and $0, respectively. The RSUs, at the election of eligible employees, may be subject to deferred delivery arrangement. The total intrinsic value of RSUs outstanding at December 31, 2015 was $51.5 million based on the Company s closing stock price on that date.

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A summary of the status of the Company s RSUs as of December 31, 2015, 2014 and 2013 and of changes in RSUs outstanding under the plans for the three years ended December 31, 2015 is as follows (in thousands, except for weighted average grant date fair value per unit):

	2015		2014		2013	
	Number of Units	Weighted Average Grant Date Fair Value per Unit	Number of Units	Weighted Average Grant Date Fair Value per Unit	Number of Units	Weighted Average Grant Date Fair Value per Unit
Outstanding at January 1	669	$ 15.01	373	$ 8.65		$
Granted	448	33.62	389	19.59	379	8.65
Cancelled	(16)	20.83			(6)	8.65
Converted into common shares	(191)	14.24	(93)	8.65		
Outstanding at December 31	910	$ 24.23	669	$ 15.01	373	$ 8.65

Performance-Based Restricted Stock Units. During the years ended December 31, 2015 and 2014, the Company granted 50,000 and 475,000 PRSUs, respectively, that vest based on the achievement of certain pre-defined Company-specific performance criteria and expire approximately five years from the grant date. Because the performance based criteria for vesting for the PRSUs was not immediately probable, no associated expense was recorded for the PRSUs during the year ended December 31, 2014. During 2015, the Company recognized approximately $8.8 million in expense related to PRSUs as it became probable that the pre-defined performance conditions would be met mainly due to the Phase III results of the Kinect 3 clinical study. At December 31, 2015, the total unrecognized estimated compensation expense related to these PRSUs was $2.2 million and will be recognized ratably over the remaining expected performance period. The total intrinsic value of PRSUs converted into common shares during the year ended December 31, 2015 was $14.9 million. The total intrinsic value of PRSUs outstanding at December 31, 2015 was $12.0 million based on the Company s closing stock price on that date.

NOTE 9. STOCKHOLDERS EQUITY

Equity Financing

In February 2015, the Company completed a public offering of common stock in which the Company sold approximately 8.0 million shares of its common stock at an offering price of $36.00 per share. The shares were sold pursuant to an automatic shelf registration statement filed with the Securities and Exchange Commission (SEC). The net proceeds generated from this transaction, after underwriting discounts and commissions and offering costs, were approximately $270.7 million.

In February 2014, the Company completed a public offering of common stock in which the Company sold 8.0 million shares of its common stock at an offering price of $17.75 per share. The shares were sold pursuant to a shelf registration statement previously filed with the SEC. The net proceeds generated from this transaction, after underwriting discounts and commissions and offering costs, were approximately $133.2 million.

Shelf Registration Statement

In February 2014, the Company filed an automatic shelf registration statement which immediately became effective by rule of the SEC. For so long as the Company continues to satisfy the requirements to be deemed a well-known seasoned issuer, this shelf registration statement allows the Company to issue an unlimited number of shares of its common stock from time to time. As of December 31, 2015, the Company had sold approximately 16.0 million shares of its common stock under this shelf registration statement.

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NOTE 10. INCOME TAXES

Under the FASB s accounting guidance related to uncertain tax positions, among other things, the impact of an uncertain income tax position on the income tax return must be recognized at the largest amount that is more-likely-than-not to be sustained upon audit by the relevant taxing authority. An uncertain income tax position will not be recognized if it has less than a 50% likelihood of being sustained. Additionally, the guidance provides guidance on derecognition, classification, interest and penalties, accounting in interim periods, disclosure and transition.

The Company s policy is to recognize interest and/or penalties related to income tax matters in income tax expense. The Company had no accrual for interest or penalties on the Company s consolidated balance sheets at December 31, 2015 or December 31, 2014, and has not recognized interest and/or penalties in the statement of comprehensive loss for the year ended December 31, 2015.

The Company is subject to taxation in the United States and various state jurisdictions. The Company s tax years for 1998 (federal)/2002 (California) and forward are subject to examination by the United States and California tax authorities due to the carry forward of unutilized net operating losses and R&D credits.

At December 31, 2015, the Company had deferred tax assets of $382.4 million. Due to uncertainties surrounding the Company s ability to generate future taxable income to realize these assets, a full valuation has been established to offset the net deferred tax asset. Additionally, the future utilization of the Company s net operating loss and R&D credit carry forwards to offset future taxable income may be subject to an annual limitation, pursuant to Internal Revenue Code Sections 382 and 383, as a result of ownership changes that could occur in the future. The Company has determined that no ownership changes have occurred through December 31, 2015.

At December 31, 2015, the Company had Federal and California income tax net operating loss carry forwards of approximately $736.0 million and $567.3 million, respectively. The Federal tax loss carry forwards will begin to expire in 2021, unless previously utilized.

The California net operating loss carry forwards will expire as follows (in thousands):

Year	Amount
2016	116,600
2017	51,900
2018	140,600
2028 and beyond	258,100

In addition, the Company has Federal and California R&D tax credit carry forwards of $38.2 million and $27.2 million, respectively. The Federal R&D tax credit carry forwards begin expiring in 2018 and will continue to expire unless utilized. The California R&D tax credit carryforwards carry forward indefinitely. The Company also has Federal Alternative Minimum Tax credit carryforwards of approximately $213,000, which will carry forward indefinitely. At December 31, 2015, approximately $77.0 million of the net operating loss carry forwards relate to stock option exercises, which will result in an increase to additional paid-in capital and a decrease in income taxes payable at the time when the tax loss carryforwards are utilized.

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Significant components of the Company s deferred tax assets as of December 31, 2015 and 2014 are listed below. A valuation allowance of $382.4 million and $367.1 million at December 31, 2015 and 2014, respectively, has been recognized to offset the deferred tax assets as realization of such assets is uncertain. Amounts are shown as of December 31 as of each respective year (in thousands):

	2015	2014
Deferred tax assets:		
Net operating losses	$ 257,900	$ 260,600
Research and development credits	33,500	29,000
Capitalized research and development	58,900	45,700
Share-based compensation expense	10,900	6,900
Deferred revenue	4,300	800
Deferred gain on sales leaseback	5,000	7,200
Intangibles	6,900	10,600
Cease-use expense	700	1,100
Fixed assets	400	500
Other	3,900	4,700
Total deferred tax assets	382,400	367,100
Valuation allowance	(382,400)	(367,100)
Net deferred tax assets	$	$

The provision for income taxes on earnings subject to income taxes differs from the statutory Federal rate at December 31, 2015, 2014 and 2013, due to the following (in thousands):

	2015	2014	2013
Federal income taxes at 35%	$ (31,126)	$ (21,190)	$ (16,131)
State income tax, net of Federal benefit	2	(3,410)	(2,611)
Tax effect on non-deductible expenses	172	10	7
Share-based compensation expense	201	91	215
Change in tax rate	10,773		
Expired tax attributes	5,594	315	151
Research credits	(6,638)	(1,882)	(3,458)
Change in valuation allowance	15,029	25,366	20,504
Uncertain tax positions	5,940	621	1,283
Other	53	79	40
	$	$	$

The following table summarizes the activity related to our unrecognized tax benefits (in thousands):

	2015	2014	2013
Balance as of the beginning of the year	$ 23,854	$ 23,131	$ 21,672
Increases related to prior year tax positions	6,636	47	543
Increases related to current year tax positions	2,584	676	916
Expiration of the statute of limitations for the assessment of taxes			
Balance as of the end of the year	$ 33,074	$ 23,854	$ 23,131

The Company, under authoritative guidance, excluded those deferred tax assets that are not more likely than not to be sustained under the technical merits of the tax position. These unrecognized tax benefits totaled $6.6 and $2.6 million for prior year tax positions and current year tax positions, respectively, as reflected in the tabular rollforward above.

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As of December 31, 2015, the Company had $26.2 million of unrecognized tax benefits that, if recognized and realized, would effect the effective tax rate.

In the next twelve months, the Company does not expect a significant change in their unrecognized tax benefits.

NOTE 11. RETIREMENT PLAN

The Company has a 401(k) defined contribution savings plan (401(k) Plan). The 401(k) Plan is for the benefit of all qualifying employees and permits voluntary contributions by employees up to 60% of base salary limited by the IRS-imposed maximum. Employer contributions were $0.4 million, $0.3 million and $0.3 million for the years ended December 31, 2015, 2014 and 2013, respectively.

NOTE 12. SELECTED QUARTERLY FINANCIAL DATA (UNAUDITED)

The following is a summary of the quarterly results of the Company for the years ended December 31, 2015 and 2014 *(unaudited, in thousands, except for per share data)*:

	Year Ended December 31,				
	First Quarter	Second Quarter	Third Quarter	Fourth Quarter	Year Ended December 31
2015:					
Revenues	$ 19,769	$	$	$	$ 19,769
Operating expenses	22,057	25,322	35,844	30,748	113,971
Net loss	(1,192)	(23,987)	(34,435)	(29,315)	(88,929)
Net loss per share:					
Basic and Diluted	$ (0.01)	$ (0.28)	$ (0.40)	$ (0.34)	$ (1.05)
Shares used in the calculation of net loss per share:					
Basic and Diluted	80,349	85,518	85,856	86,184	84,496
2014:					
Revenues	$	$	$	$	$
Operating expenses	12,725	14,361	16,857	20,468	64,411
Net loss	(11,842)	(13,381)	(15,875)	(19,444)	(60,542)
Net loss per share:					
Basic and Diluted	$ (0.17)	$ (0.18)	$ (0.21)	$ (0.26)	$ (0.81)
Shares used in the calculation of net loss per share:					
Basic and Diluted	70,260	75,879	75,948	76,139	74,577

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ITEM 9. ***CHANGES IN AND DISAGREEMENTS WITH ACCOUNTANTS ON ACCOUNTING AND FINANCIAL DISCLOSURE***
Not applicable.

ITEM 9A. ***CONTROLS AND PROCEDURES***
We maintain disclosure controls and procedures that are designed to ensure that information required to be disclosed in our Exchange Act reports is recorded, processed, summarized and reported within the timelines specified in the SEC s rules and forms, and that such information is accumulated and communicated to our management, including our Chief Executive Officer and Chief Financial Officer, as appropriate, to allow timely decisions regarding required disclosure. In designing and evaluating the disclosure controls and procedures, management recognized that any controls and procedures, no matter how well designed and operated, can only provide reasonable assurance of achieving the desired control objectives, and in reaching a reasonable level of assurance, management necessarily was required to apply its judgment in evaluating the cost-benefit relationship of possible controls and procedures.

As required by SEC Rule 13a-15(b), we carried out an evaluation, under the supervision and with the participation of our management, including our Chief Executive Officer and Chief Financial Officer, of the effectiveness of the design and operation of our disclosure controls and procedures as of the end of the year covered by this report. Based on the foregoing, our Chief Executive Officer and Chief Financial Officer concluded that our disclosure controls and procedures were effective at the reasonable assurance level.

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Management s Report on Internal Control Over Financial Reporting

Internal control over financial reporting refers to the process designed by, or under the supervision of, our Chief Executive Officer and Chief Financial Officer, and effected by our board of directors, management and other personnel, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles, and includes those policies and procedures that:

(1) Pertain to the maintenance of records that in reasonable detail accurately and fairly reflect the transactions and dispositions of our assets;

(2) Provide reasonable assurance that transactions are recorded as necessary to permit preparation of financial statements in accordance with generally accepted accounting principles, and that our receipts and expenditures are being made only in accordance with authorization of our management and directors; and

(3) Provide reasonable assurance regarding prevention or timely detection of unauthorized acquisition, use or disposition of our assets that could have a material effect on the financial statements.

Internal control over financial reporting cannot provide absolute assurance of achieving financial reporting objectives because of its inherent limitations. Internal control over financial reporting is a process that involves human diligence and compliance and is subject to lapses in judgment and breakdowns resulting from human failures. Internal control over financial reporting also can be circumvented by collusion or improper management override. Because of such limitations, there is a risk that material misstatements may not be prevented or detected on a timely basis by internal control over financial reporting. However, these inherent limitations are known features of the financial reporting process. Therefore, it is possible to design into the process safeguards to reduce, though not eliminate, this risk. Management is responsible for establishing and maintaining adequate internal control over financial reporting for the company.

Management has used the framework set forth in the report entitled Internal Control-Integrated Framework (2013 framework) published by the Committee of Sponsoring Organizations of the Treadway Commission (2013 framework), known as COSO, to evaluate the effectiveness of our internal control over financial reporting. Based on this assessment, management has concluded that our internal control over financial reporting was effective as of December 31, 2015. Ernst & Young, LLP, our independent registered public accounting firm, has issued an attestation report on our internal control over financial reporting as of December 31, 2015, which is included herein.

There has been no change in our internal control over financial reporting during our most recent fiscal quarter that has materially affected, or is reasonably likely to materially affect, our internal control over financial reporting.

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Report of Independent Registered Public Accounting Firm

The Board of Directors and Stockholders of

Neurocrine Biosciences, Inc.

We have audited Neurocrine Biosciences, Inc. s internal control over financial reporting as of December 31, 2015, based on criteria established in Internal Control-Integrated Framework issued by the Committee of Sponsoring Organizations of the Treadway Commission (2013 framework) (the COSO criteria). Neurocrine Biosciences, Inc. s management is responsible for maintaining effective internal control over financial reporting, and for its assessment of the effectiveness of internal control over financial reporting included in the accompanying Management s Report on Internal Control Over Financial Reporting. Our responsibility is to express an opinion on the company s internal control over financial reporting based on our audit.

We conducted our audit in accordance with the standards of the Public Company Accounting Oversight Board (United States). Those standards require that we plan and perform the audit to obtain reasonable assurance about whether effective internal control over financial reporting was maintained in all material respects. Our audit included obtaining an understanding of internal control over financial reporting, assessing the risk that a material weakness exists, testing and evaluating the design and operating effectiveness of internal control based on the assessed risk, and performing such other procedures as we considered necessary in the circumstances. We believe that our audit provides a reasonable basis for our opinion.

A company s internal control over financial reporting is a process designed to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles. A company s internal control over financial reporting includes those policies and procedures that (1) pertain to the maintenance of records that, in reasonable detail, accurately and fairly reflect the transactions and dispositions of the assets of the company; (2) provide reasonable assurance that transactions are recorded as necessary to permit preparation of financial statements in accordance with generally accepted accounting principles, and that receipts and expenditures of the company are being made only in accordance with authorizations of management and directors of the company; and (3) provide reasonable assurance regarding prevention or timely detection of unauthorized acquisition, use, or disposition of the company s assets that could have a material effect on the financial statements.

Because of its inherent limitations, internal control over financial reporting may not prevent or detect misstatements. Also, projections of any evaluation of effectiveness to future periods are subject to the risk that controls may become inadequate because of changes in conditions, or that the degree of compliance with the policies or procedures may deteriorate.

In our opinion, Neurocrine Biosciences, Inc. maintained, in all material respects, effective internal control over financial reporting as of December 31, 2015, based on the COSO criteria.

We also have audited, in accordance with the standards of the Public Company Accounting Oversight Board (United States), the consolidated balance sheets of Neurocrine Biosciences, Inc. as of December 31, 2015 and 2014, and the related consolidated statements of comprehensive loss, stockholders equity and cash flows for each of the three years in the period ended December 31, 2015 of Neurocrine Biosciences, Inc. and our report dated February 11, 2016 expressed an unqualified opinion thereon.

/s/ Ernst & Young LLP

San Diego, California

February 11, 2016

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ITEM 9B. ***OTHER INFORMATION***

None.

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PART III

ITEM 10. ***DIRECTORS, EXECUTIVE OFFICERS AND CORPORATE GOVERNANCE***

Information required by this item will be contained in our Definitive Proxy Statement for our 2016 Annual Meeting of Stockholders, to be filed pursuant to Regulation 14A with the Securities and Exchange Commission within 120 days of December 31, 2015. Such information is incorporated herein by reference.

We have adopted a code of ethics that applies to our Chief Executive Officer, Chief Financial Officer, and to all of our other officers, directors, employees and agents. The code of ethics is available at the Corporate Governance section of the Investors page on our website at www.neurocrine.com. We intend to disclose future amendments to, or waivers from, certain provisions of our code of ethics on the above website within four business days following the date of such amendment or waiver.

ITEM 11. ***EXECUTIVE COMPENSATION***

Information required by this item will be contained in our Definitive Proxy Statement for our 2016 Annual Meeting of Stockholders, to be filed pursuant to Regulation 14A with the Securities and Exchange Commission within 120 days of December 31, 2015. Such information is incorporated herein by reference.

ITEM 12. ***SECURITY OWNERSHIP OF CERTAIN BENEFICIAL OWNERS AND MANAGEMENT AND RELATED STOCKHOLDER MATTERS***

Information required by this item will be contained in our Definitive Proxy Statement for our 2016 Annual Meeting of Stockholders, to be filed pursuant to Regulation 14A with the Securities and Exchange Commission within 120 days of December 31, 2015. Such information is incorporated herein by reference.

ITEM 13. ***CERTAIN RELATIONSHIPS AND RELATED TRANSACTIONS, AND DIRECTOR INDEPENDENCE***

Information required by this item will be contained in our Definitive Proxy Statement for our 2016 Annual Meeting of Stockholders, to be filed pursuant to Regulation 14A with the Securities and Exchange Commission within 120 days of December 31, 2015. Such information is incorporated herein by reference.

ITEM 14. ***PRINCIPAL ACCOUNTANT FEES AND SERVICES***

Information required by this item will be contained in our Definitive Proxy Statement for our 2016 Annual Meeting of Stockholders, to be filed pursuant to Regulation 14A with the Securities and Exchange Commission within 120 days of December 31, 2015. Such information is incorporated herein by reference.

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PART IV

ITEM 15. ***EXHIBITS, FINANCIAL STATEMENT SCHEDULES***
(a) Documents filed as part of this report.

1. List of Financial Statements. The following are included in Item 8 of this report:

Report of Independent Registered Public Accounting Firm

Consolidated Balance Sheets as of December 31, 2015 and 2014

Consolidated Statements of Comprehensive Loss for the years ended December 31, 2015, 2014 and 2013

Consolidated Statements of Stockholders Equity for the years ended December 31, 2015, 2014 and 2013

Consolidated Statements of Cash Flows for the years ended December 31, 2015, 2014 and 2013

Notes to the Consolidated Financial Statements (includes unaudited Selected Quarterly Financial Data)

2. List of all Financial Statement schedules. All schedules are omitted because they are not applicable or the required information is shown in the Financial Statements or notes thereto.

3. List of Exhibits required by Item 601 of Regulation S-K. See part (b) below.

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

Exhibit Number	**Description**
3.1	Certificate of Incorporation(11)
3.2	Certificate of Amendment to Certificate of Incorporation(11)
3.3	Bylaws, as amended(11)
4.1	Form of Common Stock Certificate(1)
10.1**	Neurocrine Biosciences, Inc. 2003 Incentive Stock Plan, as amended and form of stock option agreement and restricted stock unit agreement.(7)
10.2**	Form of Indemnity Agreement entered into between the Company and its officers and directors.(5)
10.3**	Employment Commencement Nonstatutory Stock Option Agreement dated October 31, 2005 between the Company and Christopher O Brien.(4)
10.4	Amended and Restated Lease dated November 1, 2011 between the Company and Kilroy Realty, L.P.(8)
10.5	Letter of Credit dated December 3, 2007, issued by Wells Fargo Bank, N.A. for the benefit of Kilroy Realty, L.P., as amended on November 20, 2014.(13)
10.6**	Amended and Restated Employment Agreement effective August 1, 2007 between the Company and Kevin C. Gorman, Ph.D.(3)
10.7	License agreement dated August 27, 1999 between the Company and the Mount Sinai School of Medicine of the City University of New York.(9)

10.8**	Amended and Restated Employment Agreement effective August 1, 2007 between the Company and Timothy P. Coughlin.(3)
10.9**	Amended and Restated Employment Agreement effective August 6, 2007 between the Company and Christopher F. O Brien M.D.(6)

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Exhibit Number	Description
10.10**	Amended and Restated Employment Agreement effective August 23, 2007 between the Company and Dimitri E. Grigoriadis, Ph.D.(6)
10.11**	Amended and Restated Employment Agreement effective August 14, 2007 between the Company and Haig Bozigian, Ph.D.(6)
10.12**	2011 Equity Incentive Plan, as amended, Form of Stock Option Grant Notice and Option Agreement for use thereunder, and Form of Restricted Stock Unit Grant Notice and Restricted Stock Unit Agreement for use thereunder.(12)
10.13*	Collaboration Agreement dated June 15, 2010, by and between Abbott International Luxembourg S.a.r.l. and the Company as amended on August 31, 2011.
10.14**	Form of Amendment to Employment Agreement for executive officers.(10)
10.15**	Neurocrine Biosciences, Inc. Inducement Plan, as amended, Form of Stock Option Grant Notice and Option Agreement for use thereunder.(2)
10.16	Collaboration and License Agreement dated March 31, 2015 between Mitsubishi Tanabe Pharma Corporation and the Company.(14)
10.17	First Amendment to Collaboration and License Agreement Dated August 31, 2011 between the Company and Abbott International Luxemburg S.a.r.l.(15)
21.1	Subsidiaries of the Company
23.1	Consent of Independent Registered Public Accounting Firm
31.1	Certification of Chief Executive Officer pursuant to Rules 13a-14 and 15d-14 promulgated under the Securities Exchange Act of 1934
31.2	Certification of Chief Financial Officer pursuant to Rules 13a-14 and 15d-14 promulgated under the Securities Exchange Act of 1934
32***	Certifications of Chief Executive Officer and Chief Financial Officer pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002
101.INS	XBRL Instance Document.
101.SCH	XBRL Taxonomy Extension Schema Document.
101.CAL	XBRL Taxonomy Extension Calculation Linkbase Document.
101.DEF	XBRL Taxonomy Extension Definition Linkbase Document.
101.LAB	XBRL Taxonomy Extension Label Linkbase Document.
101.PRE	XBRL Taxonomy Extension Presentation Linkbase Document.

(1) Incorporated by reference to the Company s Registration Statement on Form S-1 (Registration No. 333-03172)
(2) Incorporated by reference to the Company s Quarterly Report on Form 10-Q filed on July 29, 2015
(3) Incorporated by reference to the Company s Quarterly Report on Form 10-Q filed on August 3, 2007
(4) Incorporated by reference to the Company s Current Report on Form 8-K filed on November 1, 2005
(5) Incorporated by reference to the Company s Current Report on Form 8-K filed on September 1, 2009
(6) Incorporated by reference to the Company s Annual Report on Form 10-K filed on February 11, 2008
(7) Incorporated by reference to the Company s Quarterly Report on Form 10-Q filed on July 30, 2009
(8) Incorporated by reference to the Company s Current Report on Form 8-K filed on January 18, 2012
(9) Incorporated by reference to the Company s Quarterly Report on Form 10-Q filed on July 26, 2013
(10) Incorporated by reference to the Company s Annual Report on Form 10-K filed on February 10, 2011
(11) Incorporated by reference to Exhibit 3.1 to the Company s Current Report on Form 8-K dated October 2, 2015, and Exhibits 3.1, 3.2 and 3.3 to the Company s Annual Report on From 10-K filed on February 8, 2013

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(12) Incorporated by reference to the Company s Current Report on Form 8-K filed on June 1, 2015
(13) Incorporated by reference to the Company s Annual Report on Form 10-K filed on February 9, 2015
(14) Incorporated by reference to the Company s Quarterly Report on Form 10-Q filed on April 30, 2015
(15) Incorporated by reference to the Company s Quarterly Report on Form 10-Q filed on October 31, 2011.
* Confidential treatment has been granted with respect to certain portions of the exhibit.
** Management contract or compensatory plan or arrangement.
*** These certifications are being furnished solely to accompany this annual report pursuant to 18 U.S.C. Section 1350, and are not being filed for purposes of Section 18 of the Securities Exchange Act of 1934 and are not to be incorporated by reference into any filing of Neurocrine Biosciences, Inc., whether made before or after the date hereof, regardless of any general incorporation language in such filing.

Except as specifically noted above, the Company s Annual Reports on Form 10-K, Quarterly Reports on Form 10-Q and Current Reports on Form 8-K have a Commission File Number of 000-22705.

(c) Financial Statement Schedules. See Item 15(a)(2) above.

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SIGNATURES

Pursuant to the requirements of Section 13 or 15(d) of the Securities Exchange Act of 1934, the Registrant has duly caused this report to be signed on its behalf by the undersigned, thereunto duly authorized.

NEUROCRINE BIOSCIENCES, INC.

A Delaware Corporation

By: /s/ Kevin C. Gorman
Kevin C. Gorman
President and Chief Executive Officer
Date: February 11, 2016

Pursuant to the requirements of the Securities Exchange Act of 1934, this report has been signed by the following persons on behalf of the Registrant and in the capacities and on the dates indicated:

Signature	Title	Date
/s/ Kevin C. Gorman	President, Chief Executive Officer	February 11, 2016
Kevin C. Gorman	and Director	
	(Principal Executive Officer)	
/s/ Timothy P. Coughlin	Chief Financial Officer	February 11, 2016
Timothy P. Coughlin	(Principal Financial and Accounting Officer)	
/s/ William H. Rastetter	Chairman of the Board of Directors	February 11, 2016
William H. Rastetter		
/s/ Gary A. Lyons	Director	February 11, 2016
Gary A. Lyons		
/s/ W. Thomas Mitchell	Director	February 11, 2016
W. Thomas Mitchell		
/s/ Joseph A. Mollica	Director	February 11, 2016
Joseph A. Mollica		
/s/ George J. Morrow	Director	February 11, 2016
George J. Morrow		
/s/ Corinne H. Nevinny	Director	February 11, 2016

Corinne H. Nevinny		
/s/ Richard F. Pops	Director	February 11, 2016
Richard F. Pops		
/s/ Alfred W. Sandrock, Jr.	Director	February 11, 2016
Alfred W. Sandrock, Jr.		
/s/ Stephen A. Sherwin	Director	February 11, 2016
Stephen A. Sherwin		