NEUROCRINE BIOSCIENCES INC
Form 10-K
February 08, 2019

UNITED STATES

SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

Form 10-K

(Mark One)

ANNUAL REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934
For the fiscal year ended December 31, 2018

OR

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

Commission file number: 0-22705

NEUROCRINE BIOSCIENCES, INC.

(Exact name of registrant as specified in its charter)

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

Registrant’s telephone number, including area code:

(858) 617-7600

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

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

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

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

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

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

Indicate by check mark whether the registrant has submitted electronically every Interactive Data File required to be submitted 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 such files). Yes No

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

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

Large accelerated filer	Accelerated filer
Non-accelerated filer	Smaller reporting company
	Emerging growth company

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act.

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

The aggregate market value of the common equity held by non-affiliates of the registrant as of June 30, 2018 totaled approximately $7,461,776,662 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, 2018. The identification of 10% or greater stockholders as of June 30, 2018 is based on applicable Schedule 13G and amended Schedule 13G reports. This calculation does not reflect a

determination that such parties are affiliates for any other purposes.

As of February 1, 2019, there were 90,821,267 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, 2018 are incorporated by reference into Part III of this report	III

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INGREZZA® is a registered trademark of Neurocrine Biosciences, Inc. Any other brand names or trademarks appearing in this Annual Report that are not the property of Neurocrine Biosciences, Inc. are the property of their respective holders.

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,” “intends,” “estimates,” “could,” “should,” “would,” “continue,” “seeks,” “pro forma,” or “anticipates,” o words (including their use in the negative), or by discussions of future matters such as the development of new products, technology enhancements, possible changes in legislation and other statements that are not historical. These statements include but are not limited to statements under the captions “Risk Factors,” “Management’s Discussion and Analysis of Financial Condition and Results of Operations” and “Business,” as well as other sections in this report. You should be aware that the occurrence of any of the events discussed under the heading in Part II titled “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

Overview

We were originally incorporated in California in January 1992 and reincorporated in Delaware in May 1996. We are a company focused on discovering, developing, and commercializing 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 related 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 products and product candidates.

On April 11, 2017, the United States Food and Drug Administration (FDA) approved INGREZZA® (valbenazine) capsules for the treatment of adults with tardive dyskinesia (TD). We market INGREZZA for TD in the United States (U.S.) through our specialty sales force focused primarily on physicians who treat TD patients, including psychiatrists and neurologists. The commercial launch of INGREZZA occurred on May 1, 2017.

On July 24, 2018, we were notified by AbbVie Inc. (AbbVie) that FDA approval was granted for ORILISSA® (elagolix) for the management of moderate to severe endometriosis pain in women. Discovered and developed through Phase II clinical trials by us, ORILISSA, the first FDA-approved oral medication for the management of endometriosis with associated moderate to severe pain in over a decade, began to be marketed by AbbVie in August 2018 as part of a collaboration to develop and commercialize elagolix for women’s health.

Our clinical development programs include opicapone as an adjunctive therapy to levodopa/DOPA decarboxylase inhibitors in adult Parkinson's disease patients, elagolix for uterine fibroids partnered with AbbVie, NBI-74788 for the treatment of congenital adrenal hyperplasia (CAH), and a vesicular monoamine transporter 2 (VMAT2) inhibitor and

a first-in-class central nervous system (CNS) compound each with potential use in the treatment of neurologic and psychiatric disorders.

AbbVie initiated Phase III studies of elagolix in patients with uterine fibroids in early 2016. The Phase III program included two replicate, pivotal, six-month efficacy and safety studies followed by a six-month safety and efficacy extension study. AbbVie provided positive topline efficacy data from the Phase III studies in women with uterine fibroids in the first quarter of 2018 and additional data from the six-month safety extension study in the third quarter of 2018. We believe the results from these studies will form the basis for an anticipated new drug application (NDA) submission to the FDA in the middle of 2019 for the approval of elagolix in the treatment of uterine fibroids.

We currently have three major collaborations. Two of these collaborations involve out-licensing of our proprietary technology to pharmaceutical partners. In June 2010, we announced an exclusive worldwide collaboration with AbbVie to develop and commercialize elagolix and all next-generation gonadotropin-releasing hormone (GnRH) antagonists (collectively, GnRH compounds). In March 2015, we entered into a collaboration and license agreement with Mitsubishi Tanabe Pharma Corporation (Mitsubishi Tanabe) for the development and commercialization of INGREZZA for movement disorders in Japan and other select Asian markets. The third collaboration agreement, which was entered into in February 2017, is one in which we in-licensed technology from BIAL – Portela & Ca, S.A. (BIAL) for the development and commercialization of opicapone for the treatment of human diseases and conditions, including Parkinson's disease, in the U.S. and Canada.

On January 28, 2019, we entered into a collaboration and license agreement with a clinical-stage gene therapy company, Voyager Therapeutics, Inc., or Voyager. The collaboration is focused on the development and commercialization of four programs using Voyager's proprietary gene therapy platforms. The four programs consist of Voyager's VY-AADC program for Parkinson's disease and VY-FXN01 program for Friedreich's ataxia, as well as rights to two programs to be determined by the parties in the future. The effectiveness of the agreement is subject to certain conditions, including the expiration or termination of the applicable waiting period under the Hart-Scott-Rodino Antitrust Improvements Act of 1976, as amended, and other customary closing conditions. Refer to Note 13 to the consolidated financial statements for more information on the agreement.

Our Product Pipeline

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

Program	Target Indication(s)	Status	Rights
Approved products:			
INGREZZA	Tardive Dyskinesia	Marketed	Neurocrine/Mitsubishi Tanabe (Asia-Pacific)
ORILISSA	Endometriosis	Marketed	AbbVie
Product candidates in clinical development:			
elagolix	Uterine Fibroids	Phase III	AbbVie
opicapone	Parkinson's Disease	Phase III	Neurocrine (U.S. and Canada)/BIAL
NBI-74788	Classic Congenital Adrenal Hyperplasia	Phase II	Neurocrine
New VMAT2 Inhibitor	Neurology/Psychiatry Disorders	Phase I	Neurocrine
New CNS Compound	Neurology/Psychiatry Disorders	Phase I	Neurocrine

"Marketed" indicates that we or our collaborator have received FDA regulatory approval of the product, for the specified target indication.

“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 are conducting or initiating 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.

INGREZZA (valbenazine) – VMAT2 Inhibitor

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 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, among others.

INGREZZA as a Treatment for TD. TD is defined by hyperkinetic involuntary movements which arise after months or years of treatment with dopamine receptor blocking agents, e.g. antipsychotics used for treating schizophrenia, bipolar disorder, and depression, and Reglan® (metoclopramide) for nausea and vomiting and gastric emptying in patients with gastroparesis. Features of

TD 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 U.S. alone (Kantar Health).

On April 11, 2017, INGREZZA became the first drug approved by the FDA for the treatment of TD. INGREZZA provides a once-daily dosing treatment option for TD causing reversible reduction of dopamine release at the nerve terminal by selectively inhibiting the pre-synaptic VMAT2. In vitro, INGREZZA is a highly selective inhibitor of human VMAT2 showing little or no affinity for VMAT1, other receptors, such as dopamine D2 receptors, other transporters or ion channels. INGREZZA for TD has two dosing options (40 mg and 80 mg) with 40 mg taken for the first seven days of treatment with an option of 40 mg or 80 mg thereafter depending on a patient's dosing needs. INGREZZA was generally well tolerated during our clinical trials with no apparent drug-drug interactions with the most common emergent adverse event being mild and transient somnolence.

In connection with the FDA approval of INGREZZA for TD, we committed to conduct certain post-marketing studies including Phase 1 (e.g., pharmacokinetics in volunteers with renal impairment) and Phase 4 (e.g., randomized placebo-controlled withdrawal in TD patients) studies. We expect to conduct these studies over the next four years.

Valbenazine as a Treatment for Tourette Syndrome. In the fourth quarter of 2017, we initiated T-Force GOLD, a Phase IIb study of valbenazine in pediatric patients with Tourette syndrome, a neurological disorder that consists of rapid, non-rhythmic stereotyped motor and vocal tics. T-Force GOLD was a multicenter, randomized, double-blind, placebo-controlled, parallel-group study evaluating the safety, tolerability and efficacy, with optimized dosing of once-daily valbenazine in approximately 120 pediatric patients with moderate to severe Tourette syndrome over 12 weeks of treatment. In the second quarter of 2018, we started T-Force PLATINUM, a double-blind, placebo-controlled, randomized withdrawal study of valbenazine in pediatric patients with Tourette syndrome. This study is designed to evaluate longer term efficacy and safety in patients who initial responded to open-label therapy with optimized doses of valbenazine. On December 12, 2018, we announced that topline data from the T-Force GOLD study failed to meet the primary endpoint as assessed by the placebo adjusted change from baseline in Yale Global Tic Severity Scale assessed at week 12. We continue to analyze the complete dataset from the study to determine the next steps for valbenazine in Tourette syndrome.

elagolix – GnRH Antagonist

GnRH is the endogenous peptide that binds to the GnRH receptor and 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 flushes and the loss of bone mineral density.

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

In June 2010, we entered into an exclusive worldwide collaboration with AbbVie to develop and commercialize 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 responsibility for all regulatory interactions with the FDA related to elagolix and other GnRH compounds covered by the collaboration. Following our entry into the collaboration, AbbVie undertook the development of elagolix in 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 U.S. 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 the third quarter of 2017, AbbVie submitted an NDA for elagolix for the treatment of endometriosis to the FDA. The NDA was accepted for priority review by the FDA. In July and October 2018, respectively, AbbVie announced FDA and Health Canada approval for ORILISSA, for the management of endometriosis with associated moderate to severe pain in women. AbbVie began commercialization of ORILISSA in the U.S. in August 2018.

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 U.S., 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.

AbbVie initiated Phase III studies of elagolix in patients with uterine fibroids in early 2016. The Phase III program included two replicate, pivotal, six-month efficacy and safety studies followed by a six-month safety and efficacy extension study. AbbVie evaluated 300mg of elagolix dosed twice daily both alone and in combination with hormonal add-back therapy (estradiol/norethindrone acetate). The primary endpoint in these Phase III studies was 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.

AbbVie provided positive top-line efficacy data from the two Phase III studies in women with uterine fibroids in the first quarter of 2018 and additional data from the six-month safety extension study in the third quarter of 2018. The ELARIS UF-I and UF-II studies of elagolix met all primary and ranked secondary endpoints at month six. These replicate Phase III studies were randomized, parallel, double-blind, placebo-controlled clinical trials evaluating elagolix alone or in combination with low-dose hormone (add-back) therapy in women with heavy uterine bleeding associated with uterine fibroids. The studies enrolled approximately 400 patients each for an initial six-month placebo-controlled dosing period. At the end of the six months of placebo-controlled evaluation, patients were eligible to enter an additional six-month safety extension study. The primary efficacy endpoint of the study was an assessment of the change in menstrual blood loss utilizing the alkaline hematin method comparing baseline to month six. Additional secondary efficacy endpoints were evaluated including the change in fibroid volume and hemoglobin. Bone mineral density was assessed via dual-energy x-ray absorptiometry scan at baseline, at the conclusion of dosing, and at six months post-dosing. We believe the results from these studies will form the basis for an anticipated NDA submission to the FDA in the middle of 2019 for the approval of elagolix in the treatment of uterine fibroids.

opicapone – Catechol-O-methyltransferase Inhibitor

Catechol-O-methyltransferase (COMT) inhibitors are utilized to prolong the duration of effect of levodopa, the primary treatment option for Parkinson’s disease patients. Administration of levodopa often results in adequate control of Parkinson’s symptoms, also referred to as “on-time,” however, there are periods of the day where the effects of levodopa wear off and motor symptoms worsen. These periods are considered “off-time.” Opicapone is a novel, once-daily, peripherally-acting, highly-selective COMT inhibitor utilized as adjunct therapy to levodopa/carbidopa in patients with Parkinson’s disease experiencing motor fluctuations. Opicapone works through decreasing the conversion rate of levodopa into 3-O-methyldopa, thereby reducing the off-time period in patients with Parkinson’s and extending the on-time period.

In February 2017, we entered into an exclusive license agreement with BIAL for the development and commercialization of opicapone for the treatment of human diseases and conditions, including Parkinson’s disease, in the U.S. and Canada. Under the terms of the agreement, we will be responsible for the development and

commercialization of opicapone in the U.S. and Canada.

Parkinson’s Disease. Parkinson’s disease is a chronic and progressive movement disorder that affects approximately 1 million people in the United States. The disease is characterized by a loss of neurons in the substantia nigra, the area of the brain where dopamine is produced. Dopamine production and synthesis is necessary for coordination and movement. As Parkinson’s progresses, dopamine production steadily decreases resulting in tremor, slowed movement (bradykinesia), impaired posture and balance, and speech and writing problems. There is no present cure for Parkinson’s and management consists of controlling the motor symptoms primarily through administration of levodopa therapies. While this improves the control of Parkinson’s symptoms, as the disease progresses the beneficial effects of levodopa begin to wear off, symptoms worsen, and patients experience motor fluctuations. These motor fluctuations are improved with the addition of a COMT inhibitor to levodopa.

In June 2016, the European Medicines Agency authorized ONGENTYS® (opicapone) as an adjunct therapy to preparations of levodopa/DOPA decarboxylase inhibitors in adult patients with Parkinson’s disease and end-of-dose motor fluctuations who cannot be stabilized on those combinations. This approval was based on data from a clinical development program that included 28 clinical studies of more than 900 patients treated with opicapone in 30 countries worldwide.

The two pivotal Phase III studies utilized for approval with the European Medicines Agency, BIPARK-I and BIPARK-II, demonstrated that opicapone once-daily achieved a statistically significant decrease in off-time periods for Parkinson's patients compared to placebo. The BIPARK-I study was a placebo-controlled study of approximately 600 patients that also included entacapone as an active comparator. The results of this study also showed that once-daily opicapone was non-inferior to entacapone which is dosed multiple times per day. The BIPARK-II study was a placebo-controlled study of approximately 400 patients that also showed a significant decrease in off-time periods for Parkinson's patients. In both studies, opicapone was associated with significant improvements in both patient and clinician global assessments of change. The data from these two Phase III trials also demonstrated that opicapone improved motor fluctuations in levodopa-treated patients regardless of concomitant dopamine agonist or monoamine oxidase type B inhibitors used. Opicapone was generally well tolerated and was not associated with relevant electrocardiographic or hepatic adverse events.

Both of the BIPARK Phase III trials included a one-year open-label extension where opicapone sustained the decrease in off-time and increase in on-time periods that was demonstrated during the double-blind placebo-controlled portion of the studies.

We held a meeting with the FDA in January 2018 to discuss a potential NDA submission for opicapone. Based upon the BIPARK-I and BIPARK-II pivotal Phase III studies conducted by BIAL, the FDA did not require additional Phase III trials in connection with an NDA submission for opicapone. We anticipate submitting an NDA to the FDA for opicapone in the second quarter of 2019.

NBI-74788 – Corticotropin-Releasing Factor Receptor Antagonist

Corticotropin-releasing factor$_1$ (CRF_1) is a hypothalamic hormone released directly into the hypophyseal portal vasculature which acts on the CRF_1 receptor, a G protein-coupled receptor (GPCR), 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_1 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 axis. Blockade of CRF_1 receptors at the pituitary has been shown to decrease the release of ACTH and subsequently attenuate the production and release of adrenal steroids.

Classic CAH. Classic CAH is a group of autosomal recessive genetic disorders that affects approximately 20,000-30,000 people in the U.S. 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 to 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.

NBI-74788 is a potent, selective, orally-active, CRF_1 receptor antagonist as demonstrated in a range of in vitro and in vivo assays. Blockade of CRF_1 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.

We conducted a Phase I single ascending dose study of NBI-74788 in healthy volunteers in 2017. Based on the positive results of this Phase I study, we initiated a Phase II clinical trial of NBI-74788 in adult patients with classic CAH. This clinical study is designed to be an open-label, pharmacokinetic/pharmacodynamic study assessing two ascending dose levels of 14 days dosing of NBI-74788 in up to 20 study participants. Key pharmacodynamic biomarker measurements include ACTH, 17-hydroxyprogesterone (17-OHP), androgen, and cortisol levels collected the morning following bedtime dosing on Day 1 and Day 14. We recently expanded this study to include up to 10 additional patients to further optimize dosing flexibility and convenience. Initial results from this study are expected in the first quarter of 2019.

We intend to apply for orphan drug designation for NBI-74788 in the treatment of classic CAH. Orphan drug designation is granted by the FDA to medicines intended for the treatment, diagnosis or prevention of rare diseases or disorders that affect fewer than 200,000 people in the U.S. and provides sponsors with development and commercial incentives for such designated compounds and medicines.

New VMAT2 Inhibitor

We have filed an investigational new drug application (IND) and completed dosing in the single ascending dose portion of a Phase I study designed to assess initial safety, tolerability, and pharmacokinetics of a novel, internally discovered VMAT2 inhibitor. This compound has the potential to be used in the treatment of several neurology and/or psychiatry disorders. The multiple dosing portion of this Phase 1 study is ongoing and expected to be completed during the first half of 2019.

New CNS Compound

We have filed an IND and completed dosing in a Phase I single ascending dose study for an internally discovered first-in-class CNS compound with potential use in the treatment of several neurology and/or psychiatry disorders. This study is a randomized, double-blind, single ascending dose study to evaluate the safety, tolerability, and pharmacokinetic profile of the compound in healthy participants. We are currently analyzing the data from this study to inform the design of future clinical studies for the program.

Research Programs

Our R&D focus is on addressing diseases and disorders of the central nervous and endocrine systems, which include therapeutic categories ranging from hypothalamic-pituitary-adrenal disorders to stress-related disorders and neurological/neuropsychiatric diseases. CNS and endocrinology drug therapies are among the largest therapeutic categories, accounting for over $110 billion in drug sales in the U.S. alone according to IQVIA (2018).

CNS and Neuroendocrine Disorders (Targeted by GPCRs, Solute Carrier Proteins, and Ion Channels)

GPCRs are the largest known gene superfamily of the human genome. Greater than 30% 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 7% of the current marketed drugs. We believe that 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 solute carrier proteins and 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, solute carrier proteins, 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:

Maintaining Certain Commercial Rights to Our Product Portfolio to Evolve into a Fully-Integrated Pharmaceutical Company. In April 2017, we received approval from the FDA for INGREZZA for the treatment of TD. We market INGREZZA for TD in the U.S. The commercial launch of INGREZZA occurred on May 1, 2017. We have built a specialty sales force in the U.S. of approximately 250 experienced sales professionals. This specialty sales force focuses on promotion to physicians who treat TD patients, primarily neurologists and psychiatrists. Our commercial

team is comprised of experienced professionals in marketing, access and reimbursement, managed markets, market research, commercial operations, and sales force planning and management. In addition, our commercial infrastructure includes capabilities in manufacturing, medical affairs, quality control, and compliance. We intend to retain commercial rights to certain products, including INGREZZA, that we can effectively and efficiently develop, secure regulatory approval and commercialize, which includes products with a concentrated prescriber base and well-defined patient population that can be accessed with an efficient patient and prescriber outreach program.

Advancing Life-Changing Discoveries in Neurology, Neuro-Endocrinology, and Psychiatry. 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 uterine fibroids that is partnered with AbbVie, and opicapone, a highly-selective COMT inhibitor that is an adjunct therapy to preparations of levodopa/DOPA decarboxylase inhibitors for adult patients with Parkinson’s disease and was in-licensed from BIAL. In addition, we are conducting a Phase II study of NBI-74788 in adult patients with classic CAH, a group of autosomal recessive genetic disorders. 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. By doing so, we focus our internal development resources on innovative therapies with improved probabilities of technical and commercial success.

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 product candidates, while typically retaining co-promotional rights, and at times commercial rights, in North America. For example, we have collaborated with AbbVie for the development and commercialization of ORILISSA, which has received FDA and Health Canada approval for the management of endometriosis, and with respect to our collaboration with Mitsubishi Tanabe Pharma Corporation (Mitsubishi Tanabe) for the development and commercialization of INGREZZA for movement disorders in Japan and other select Asian markets. 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, in 2018, we initiated Phase I studies for a new VMAT2 inhibitor and a new CNS compound. In 2017, based on the positive results of a Phase I study we conducted of NBI-74788 in healthy volunteers, we initiated a Phase II study of NBI-74788 in adult patients with classic CAH. We believe the creativity and productivity of our discovery research group will continue to be a critical component for our continued success.

Acquiring Rights to Complementary Drug Candidates and Technologies. We plan to continue to selectively acquire rights to products in various stages of development to take advantage of our drug development capabilities. For example, in October 2018, we entered into a research collaboration with Jnana Therapeutics, Inc. aimed at discovering novel small molecule therapeutics for multiple targets for CNS disorders. Under the terms of the agreement, we will work jointly to identify novel compounds, after which time we will be responsible for further lead optimization, and the development and commercialization of any potential therapies arising from the collaboration. In February 2017, we entered into an exclusive license agreement with BIAL for the development and commercialization of opicapone for the treatment of human diseases and conditions, including Parkinson’s disease, in the U.S. and Canada. Under the terms of the agreement, we will be responsible for the development and commercialization of opicapone in the U.S. and Canada.

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. In June 2010, we announced an exclusive worldwide collaboration with AbbVie to develop and commercialize 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 are 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 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 million related to the amortization of up-front license fees, $115 million in milestone revenue, $37 million in sponsored development revenue, and approximately $1.6 million in sales-based royalty revenue on AbbVie net sales of ORILISSA.

Mitsubishi Tanabe. In March 2015, we entered into a collaboration and license agreement with Mitsubishi Tanabe for the development and commercialization of INGREZZA 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 royalties on product sales in select territories in Asia. Under the terms of the agreement, Mitsubishi Tanabe is responsible for all development, marketing, and commercialization costs in Japan and other select Asian markets, with the exception of a single Huntington's chorea 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 INGREZZA 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 us. In such event, all INGREZZA product rights for Japan and other select Asian markets would revert to us. Since the inception of the agreement, we have recorded revenues of $19.8 million related to the up-front license fee, and $15 million in milestone revenue.

BIAL. In February 2017, we entered into an exclusive license agreement with BIAL for the development and commercialization of opicapone for the treatment of human diseases and conditions, including Parkinson's disease, in the U.S. and Canada. Under the terms of the agreement, we are responsible for the management and cost of all opicapone development and commercialization activities in the U.S. and Canada. Under the terms of the agreement, we paid BIAL an upfront license fee of $30 million. In addition, during the first quarter of 2018, the FDA provided guidance on the regulatory path forward to support an NDA for opicapone for Parkinson's disease, in which the FDA did not request that we conduct an additional Phase III study in connection with the submission of an NDA to the FDA, resulting in a $10 million event-based milestone payment to BIAL. We may also be required to pay up to an additional $105 million in milestone payments associated with the regulatory approval and net sales of products containing opicapone. In addition, we will pay BIAL a percentage of net sales (with a floor minimum) in exchange for the manufacture and supply of

opicapone drug product. Either party may terminate the agreement earlier if the other party materially breaches the agreement and does not cure the breach within a specified notice period, or upon the other party's insolvency. BIAL may terminate the agreement if we fail to use commercially reasonable efforts or fail to file an NDA for a licensed product by a specified date or under certain circumstances involving a change of control.

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 U.S. and abroad. Additionally, we have licensed from institutions the rights to issued U.S. patents, pending U.S. 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 U.S., the European Union (EU), 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 U.S., six years in Japan and ten years in the EU, measured from the date of FDA, or corresponding foreign regulatory authority, approval.

INGREZZA, our highly selective VMAT2 inhibitor is covered by U.S. Patent No. 8,039,627, which expires in 2029 (not including a potential patent term extension of up to two years) and U.S. Patent No. 8,357,697, which expires in 2027.

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).

Opicapone, a highly selective COMT inhibitor for Parkinson's disease is covered by U.S. Patent No. 8,168,793, among others, which expires in 2029 (not including a potential patent term extension of up to five years).

Manufacturing and Distribution

We currently rely on, and expect to continue to rely on, contract manufacturers to produce INGREZZA, as well as for our existing and future product candidates. We believe this outsourcing manufacturing strategy will enable us to direct our financial resources to our commercialization efforts without devoting the resources and capital required to build manufacturing facilities.

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 have also established an internal commercial supply team to manage all aspects related to the INGREZZA commercial supply chain. We have entered into long-term contracts with multiple manufacturers to ensure adequate product supply and to mitigate risk, and we expect to continue to expand and diversify our third-party manufacturing relationships during 2019.

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 products and product candidates in quantities sufficient for conducting clinical trials or for commercialization. We attempt to acquire adequate inventory of materials and/or finished product to avoid significant supply disruption.

Additionally, we have retained third-party service providers to perform a variety of functions related to the distribution of INGREZZA, including shipping, warehousing, customer service, order-taking and processing, invoicing, collections, and other distribution-related activities.

We have entered into distribution agreements for INGREZZA with a limited number of specialty pharmacies (SPs) and a specialty distributor (SD) (collectively, customers), and all of our product sales are to these customers. SPs subsequently dispense INGREZZA to patients based on the fulfillment of a prescription and the SD sells INGREZZA primarily to closed-door pharmacies and government facilities. Our agreements with SPs and the SD provide for transfer of title to the product at the time the product is delivered to the SPs or SD. Our three largest customers represented approximately 93% of our product revenue for the year ended December 31, 2018.

INGREZZA Manufacturers

We entered into a commercial supply agreement with Fabbrica Italiana Sintetici S.p.A. (F.I.S.) in March 2017, for F.I.S.'s manufacture of commercial supplies of the active pharmaceutical ingredient, or API, for INGREZZA at F.I.S.'s manufacturing site in Italy. Under the terms of the agreement, F.I.S. is responsible for manufacturing the INGREZZA API, conducting quality control, quality assurance, validation activities, stability testing, packaging, and other services related to the manufacture of the INGREZZA API. In the second quarter of 2018, we received our first order of INGREZZA API under this agreement.

The agreement requires two years' notice prior to a termination without cause, provided that no such notice may be given prior to March 2022.

We entered into a master manufacturing services agreement with Patheon UK Limited (Patheon) in November 2016, and two associated product agreements in 2017 and 2018, for Patheon's manufacture of commercial supplies of INGREZZA at its manufacturing sites. Under the terms of the agreements, we are responsible for supplying the API for INGREZZA to Patheon. Patheon is responsible for manufacturing the INGREZZA capsules, conducting quality control, quality assurance, validation activities, stability testing, packaging and providing related services for the manufacture of the INGREZZA capsules.

Pursuant to the agreements, we have agreed to order from Patheon certain annual binding minimum amounts of INGREZZA capsules based on an agreed upon pricing schedule. The agreements have an initial term ending in December 2021 and will automatically renew after the initial term for successive terms of two years, unless either party gives notice of its intention to terminate the agreements within at least 18 months prior to the end of the then current term.

Commercial Packaging Agreements

We entered into two commercial packaging agreements with third-party vendors that provide, among other things, services related to the packaging of INGREZZA, tooling purchases and repairs, analytical work, auditing of suppliers, and storage. One such vendor is located in Illinois and the other is located in Pennsylvania. We do not believe that these commercial packaging related agreements are material because our business is not substantially dependent on any individual agreement.

Marketing and Sales

During 2017, we built a specialty sales force in the U.S of experienced sales professionals. This specialty sales force focuses on educating physicians who treat TD patients, primarily neurologists and psychiatrists. Our commercial team is comprised of experienced professionals in marketing, access and reimbursement, managed markets, market research, commercial operations, and sales force planning and management. During 2018, we expanded our sales force by approximately 50% to approximately 250 experienced sales professionals to enhance our ability to develop the TD market. In addition, our commercial infrastructure includes capabilities in manufacturing, medical affairs, quality control, and compliance.

Government Regulation

Our business activities, which include the manufacture and marketing of INGREZZA as well as our other potential products currently in research and development, are subject to extensive regulation by the U.S. and other countries. Regulation by government authorities in the U.S. 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 in development 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 U.S., 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. We have a comprehensive compliance program to ensure our business practices remain compliant.

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.

Federal civil and criminal false claims laws, including the federal civil False Claims Act, and the federal civil monetary penalties law, which prohibit 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 and knowingly making, or causing to be made, a false record or statement material to a false or fraudulent claim to avoid, decrease or conceal an obligation to pay money to the federal government.

The 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 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 and 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, additional reporting requirements and oversight if we become subject to a corporate integrity agreement or similar agreement to resolve allegations of non-compliance with these laws, 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.

Development and Marketing Approval for Products

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 pharmacokinetic properties of the product in human volunteers. It is rare to evidence pharmacology in these early studies.

Phase II

Clinical trials are conducted with groups of patients afflicted with a specific disease in order to determine preliminary efficacy, optimal dosages and expanded evidence of safety.

Phase III Large-scale, multi-center, comparative clinical trials are conducted with patients afflicted with a specific disease in order to determine safety and efficacy as primary support for regulatory approval by the FDA to market a product candidate for a specific disease.

The FDA closely monitors the progress of each of the three phases of clinical trials that are conducted in the U.S. 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. Institutional Review Boards, Institutional Ethics Committees, and Data Safety Monitoring Boards may also place holds on our clinical trials or recommend that we voluntarily do so. 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 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 plan to ensure that the benefits of the drug outweigh its risks. The risk evaluation and mitigation strategy 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 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 IV 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 risk evaluation and mitigation strategy,

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 U.S. 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 U.S. The resulting prices may not be sufficient to generate an acceptable return to us or our corporate collaborators.

Orphan Drug Designation

Under the Orphan Drug Act, the FDA may grant orphan drug designation to a drug intended to treat a rare disease or condition, which is a disease or condition that affects fewer than 200,000 individuals in the U.S., or if it affects more than 200,000, there is no

reasonable expectation that sales of the drug in the U.S. will be sufficient to offset the costs of developing and making the drug available in the U.S. Orphan drug designation must be requested before submitting an NDA. Orphan drug designation does not convey any advantage in or shorten the duration of the regulatory review and approval process.

If the FDA approves a sponsor's marketing application for a designated orphan drug for use in the rare disease or condition for which it was designated, the sponsor is eligible for a seven-year period of marketing exclusivity, during which the FDA may not approve another sponsor's marketing application for a drug with the same active moiety and intended for the same use or indication as the approved orphan drug, except in limited circumstances, such as if a subsequent sponsor demonstrates its product is clinically superior. During a sponsor's orphan drug exclusivity period, competitors, however, may receive approval for drugs with different active moieties for the same indication as the approved orphan drug, or for drugs with the same active moiety as the approved orphan drug, but for different indications. Orphan drug exclusivity could block the approval of one of our products for seven years if a competitor obtains approval for a drug with the same active moiety intended for the same indication before we do, unless we are able to demonstrate that grounds for withdrawal of the orphan drug exclusivity exist, or that our product is clinically superior. Further, if a designated orphan drug receives marketing approval for an indication broader than the rare disease or condition for which it received orphan drug designation, it may not be entitled to exclusivity.

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 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 program user fee requirements for any marketed products, 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 IV 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 risk evaluation and mitigation strategies 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;
- 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 U.S. 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 U.S., 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 products or product candidates, including INGREZZA, 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 payor 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 or product candidates for which we or our collaborators receive regulatory approval for commercial sale may suffer if third-party payors fail to provide coverage and adequate reimbursement. In addition, emphasis on managed care in the U.S. has increased and we expect will continue to increase the pressure on pharmaceutical pricing. Coverage policies and third-party payor 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 U.S. 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 U.S. 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 U.S., the pharmaceutical industry has been a particular focus of these efforts and has been significantly affected by major legislative initiatives.

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 70% 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 third-party payor.

Some of the provisions of the ACA have yet to be fully implemented, and there have been legal and political challenges to certain aspects of the ACA. Since January 2017, the current presidential administration has signed two executive orders and other directives designed to delay, circumvent, or loosen certain requirements mandated by the ACA. Concurrently, Congress has considered legislation that would repeal or repeal and replace all or part of the ACA. While Congress has not passed repeal legislation, the newly enacted federal income tax law, known as the Tax

Cuts and Jobs Act, includes a provision repealing, effective January 1, 2019, the tax-based shared responsibility payment imposed by the ACA on certain individuals who fail to maintain qualifying health coverage for all or part of a year that is commonly referred to as the “individual mandate”. On January 22, 2018, the current presidential administration signed a continuing resolution on appropriations for fiscal year 2018 that delayed the implementation of certain ACA-mandated fees, including the so-called “Cadillac” tax on certain high cost employer-sponsored insurance plans, the annual fee imposed on certain health insurance providers based on market share, and the medical device excise tax on non-exempt medical devices. The Bipartisan Budget Act of 2018, or the BBA, among other things, amends the ACA, effective January 1, 2019, to close the coverage gap in most Medicare drug plans, commonly referred to as the “donut hole.” In July 2018, CMS published a final rule permitting further collections and payments to and from certain ACA qualified health plans and health insurance issuers under the ACA risk adjustment program in response to the outcome of federal district court litigation regarding the method CMS uses to

determine this risk adjustment. On December 14, 2018, a Texas U.S. District Court Judge ruled that the ACA is unconstitutional in its entirety because the "individual mandate" was repealed by Congress as part of the Tax Cuts and Jobs Act. While the Texas U.S. District Court Judge, as well as the current presidential administration and CMS, have stated that the ruling will have no immediate effect pending appeal of the decision, it is unclear how this decision, subsequent appeals, and other efforts to repeal and replace the ACA will impact the ACA.

Other legislative changes have been proposed and adopted since the ACA was enacted. These changes include aggregate reductions to Medicare payments to providers of up to 2% per fiscal year pursuant to the Budget Control Act of 2011, which began in 2013 and will remain in effect through 2027 unless additional Congressional action is taken. The American Taxpayer Relief Act of 2012, among other things, further reduced Medicare payments to several providers, including hospitals and cancer treatment centers, increased the statute of limitations period for the government to recover overpayments to providers from three to five years.

Additional changes that may affect our business include the expansion of new programs such as Medicare payment for performance initiatives for physicians under the Medicare Access and CHIP Reauthorization Act of 2015, which will be fully implemented in 2019. At this time, it is unclear how the introduction of the Medicare quality payment program will impact overall physician reimbursement.

Also, there has been heightened governmental scrutiny recently over pharmaceutical pricing practices in light of the rising cost of prescription drugs and biologics. Such scrutiny has resulted in several recent Congressional inquiries and proposed and enacted federal and state legislation designed to, among other things, bring more transparency to product pricing, review the relationship between pricing and manufacturer patient programs, and reform government program reimbursement methodologies for products. At the federal level, the current presidential administration's budget proposal for fiscal year 2019 contains further drug price control measures that could be enacted during the 2019 budget process or in other future legislation, including, for example, measures to permit Medicare Part D plans to negotiate the price of certain drugs under Medicare Part B, to allow some states to negotiate drug prices under Medicaid, and to eliminate cost sharing for generic drugs for low-income patients. Additionally, the current presidential administration released a "Blueprint" to lower drug prices and reduce out-of-pocket costs of drugs that contains additional proposals to increase manufacturer competition, increase the negotiating power of certain federal healthcare programs, incentivize manufacturers to lower the list price of their products and reduce the out of pocket costs of drug products paid by consumers. The U.S. Department of Health and Human Services has already started the process of soliciting feedback on some of these measures and, at the same, is immediately implementing others under its existing authority. For example, in September 2018, CMS announced that it will allow Medicare Advantage Plans the option to use step therapy for Part B drugs beginning January 1, 2019, and in October 2018, CMS proposed a new rule that would require direct-to-consumer television advertisements of prescription drugs and biological products, for which payment is available through or under Medicare or Medicaid, to include in the advertisement the Wholesale Acquisition Cost, or list price, of that drug or biological product. Although a number of these, and other proposed measures will require authorization through additional legislation to become effective Congress and the current presidential administration have each indicated that it will continue to seek new legislative and/or administrative measures to control drug costs. At the state level, legislatures have increasingly passed legislation and implemented regulations designed to control pharmaceutical and biological product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain product access and marketing cost disclosure and transparency measures, and, in some cases, designed to encourage importation from other countries and bulk purchasing.

Further, on May 30, 2018, the Trickett Wendler, Frank Mongiello, Jordan McLinn, and Matthew Bellina Right to Try Act of 2017, or the Right to Try Act, was signed into law. The law, among other things, provides a federal framework for certain patients to access certain investigational new drug products that have completed a Phase I clinical trial and that are undergoing investigation for FDA approval. Under certain circumstances, eligible patients can seek treatment without enrolling in clinical trials and without obtaining FDA permission under the FDA expanded access program. There is no obligation for a pharmaceutical manufacturer to make its drug products available to eligible patients as a

result of the Right to Try Act.

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 products, product candidates, or technologies obsolete or noncompetitive.

In April 2017, INGREZZA, was approved by the FDA for TD. There are currently two FDA approved drug therapies for TD; INGREZZA and AUSTEDO® (deutetrabenazine), a deuterium labeled version of XENAZINE® (tetrabenazine) and VMAT2 inhibitor that was developed by Teva Pharmaceutical Industries Ltd. (Teva). In addition, off-label treatment regimens for TD consist of utilizing various atypical antipsychotic medications (e.g., clozapine), benzodiazepines (off-label) or botulinum toxin injections to treat the movements associated with TD.

Other potential indications for our VMAT2 inhibitors include the chorea associated with Huntington's disease, tardive dystonia, and other potential diseases and disorders. Currently, AUSTEDO, XENAZINE, which is marketed by Lundbeck, and generic alternatives to XENAZINE are approved for the chorea associated with Huntington's disease.

On July 24, 2018, AbbVie, in collaboration with us, announced FDA approval for ORILISSA for the management of endometriosis with associated moderate to severe pain in women. In addition, in conjunction with our partner AbbVie, we are developing elagolix for the treatment of heavy menstrual bleeding associated with uterine fibroids. AbbVie initiated Phase III studies of elagolix in patients with uterine fibroids in early 2016. The Phase III program included two replicate, pivotal, six-month efficacy and safety studies followed by a six-month safety and efficacy extension study. AbbVie provided positive top-line efficacy data from the two Phase III studies in women with uterine fibroids in the first quarter of 2018 and additional data from the six-month safety extension study in the third quarter of 2018. We believe the results from these studies will form the basis for an anticipated NDA submission to the FDA in 2019 for the approval of elagolix in the treatment of uterine fibroids. There are no current pharmaceutical therapies approved in the U.S. for the chronic treatment of uterine fibroids. ObsEva SA has initiated a Phase IIb endometriosis study with its GnRH receptor antagonist, OBE2109, and has initiated Phase III studies of uterine fibroids patients with the same molecule. Myovant Sciences, Inc. is investigating its GnRH receptor antagonist, relugolix, in Phase III trials of endometriosis, uterine fibroids and prostate cancer patients. LUPRON DEPOT® (leuprolide), marketed by AbbVie, is approved for short-term use to improve the outcome of uterine fibroid surgery. However, approximately 250,000 hysterectomies are performed annually in the U.S. 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.

LUPRON DEPOT, SYNAREL® (nafarelin), and depo-subQ provera104® (medroxyprogesterone), which are 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 U.S. 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.

Opicapone is a COMT inhibitor to be utilized as an adjunct therapy in the treatment of Parkinson's disease. COMT inhibitors prolong the duration of effect of levodopa which is the primary treatment option for Parkinson's disease patients. There are currently two FDA approved COMT inhibitors, COMTAN® (entacapone) originally developed by Orion Pharma and TASMAR® (tolcapone) originally developed by Hoffman-LaRoche Inc. Opicapone would compete directly with these two drugs and their generic equivalents.

NBI-74788 is currently being investigated for the treatment of 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. Both Millendo Therapeutics, with its acetyl-CoA acetyltransferase 1 inhibitor ATR-101, and Spruce Biosciences, with its CRF_1 antagonist SPR001, are in clinical development for the treatment of classic CAH.

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

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

Employees

As of December 31, 2018, we had approximately 585 full-time employees. None of our employees are represented by a collective bargaining arrangement, and we believe our relationship with our employees is good.

Insurance

We maintain product liability insurance coverage for INGREZZA and our clinical trials in amounts consistent with industry standards. However, insurance coverage is becoming increasingly expensive, and we may not be able to obtain or maintain insurance coverage at a reasonable cost or in sufficient amounts to protect us against losses due to liability.

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 (SEC) website at www.sec.gov.

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

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

We have limited marketing experience, and have only recently established our sales force, distribution and reimbursement capabilities, and we may not be able to continue to successfully commercialize INGREZZA, or any of our product candidates if they are approved in the future.

Our ability to produce INGREZZA revenues consistent with expectations ultimately depends on our ability to sell our products and secure adequate third-party reimbursement if and when they are approved by the FDA. Our limited experience in marketing and selling pharmaceutical products began with INGREZZA approval in 2017, when we hired our sales force and established our distribution and reimbursement capabilities, all of which are necessary to successfully commercialize INGREZZA. While our team members and consultants have experience marketing and selling pharmaceutical products, we may face difficulties related to managing the rapid growth of our personnel and infrastructure, and there can be no guarantee that we will be able to maintain the personnel, systems, arrangements and capabilities necessary to successfully commercialize INGREZZA or any product candidate approved by the FDA in the future. If we fail to maintain successful marketing, sales and reimbursement capabilities or fail to enter into successful marketing arrangements with third parties, our product revenues may suffer.

Use of our approved products or those of our collaborators, including INGREZZA and ORILISSA, could be associated with side effects or adverse events.

As with most pharmaceutical products, use of our approved products or those of our collaborators, including INGREZZA and ORILISSA, could be associated with side effects or adverse events which can vary in severity (from minor reactions to death) and frequency (infrequent or prevalent). Side effects or adverse events associated with the

use of our products or those of our collaborators may be observed at any time, including after a product is commercialized, and reports of any such side effects or adverse events may negatively impact demand for our or our collaborators' products or affect our or our collaborators' ability to maintain regulatory approval for such products. Side effects or other safety issues associated with the use of our approved products or those of our collaborators could require us or our collaborators to halt commercialization of these products or expose us to product liability lawsuits which will harm our business. We or our collaborators may be required by regulatory agencies to conduct additional studies regarding the safety and efficacy of our products which we have not planned or anticipated. Furthermore, there can be no assurance that we or our collaborators will resolve any issues related to any product related adverse events to the satisfaction of the FDA or any regulatory agency in a timely manner or ever, which could harm our business, prospects and financial condition.

We currently depend on single source suppliers. The loss of these suppliers, or delays or problems in the supply of INGREZZA, could materially and adversely affect our ability to successfully commercialize INGREZZA.

The manufacture of pharmaceutical products requires significant expertise and capital investment, including the development of process controls required to consistently produce the active pharmaceutical ingredients and the finished product in sufficient quantities while meeting detailed product specifications on a repeated basis. Manufacturers of pharmaceutical products may encounter difficulties in production, including difficulties with production costs and yields, process controls, quality control and quality assurance, including testing of stability, impurities and impurity levels and other product specifications by validated test methods, and compliance with strictly enforced U.S., state, and non-U.S. regulations. We depend on single source suppliers for each of the production of INGREZZA and its active pharmaceutical ingredients. If our third-party suppliers for INGREZZA encounter these or any other manufacturing, quality or compliance difficulties, we may be unable to meet commercial demand for INGREZZA, which could materially and adversely affect our ability to successfully commercialize INGREZZA. We also depend on BIAL, and its suppliers, for the production of opicapone drug substance and drug product.

In addition, if our suppliers fail or refuse to supply us with INGREZZA or its active pharmaceutical ingredient for any reason, it would take a significant amount of time and expense to qualify a new supplier. The FDA and similar international regulatory bodies must approve manufacturers of the active and inactive pharmaceutical ingredients and certain packaging materials used in pharmaceutical products. The loss of a supplier could require us to obtain regulatory clearance and to incur validation and other costs associated with the transfer of the active pharmaceutical ingredients or product manufacturing processes. If there are delays in qualifying new suppliers or facilities or a new supplier is unable to meet FDA or a similar international regulatory body's requirements for approval, there could be a shortage of INGREZZA, which could materially and adversely affect our ability to successfully commercialize INGREZZA. If BIAL is unable or refuses to supply us with opicapone drug product for any reason, we have limited opportunity to qualify a new supplier. The inability to obtain sufficient quantities of opicapone drug product could materially and adversely affect our ability to successfully commercialize opicapone.

We have no manufacturing capabilities. If third-party manufacturers of INGREZZA or any 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 commercialization of our products. We have limited 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, including INGREZZA. If we are unable to obtain or retain third-party manufacturers, we will not be able to develop or commercialize our products, including INGREZZA. 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
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drug manufacturers are subject to ongoing periodic unannounced inspection by the FDA, the U.S. Drug Enforcement Administration, and other agencies to ensure strict compliance with cGMP and other government regulations and corresponding foreign standards. We do not have control over third-party manufacturers' compliance with these regulations and standards.

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

We are subject to ongoing obligations and continued regulatory review for INGREZZA, which may result in significant additional expense and market withdrawal. Additionally, our other 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.

We received FDA regulatory approval for INGREZZA in April 2017. This approval and other regulatory approvals for any of 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. With respect to the FDA's approval of INGREZZA for TD, we are subject to certain post-marketing requirements and commitments. Failure to comply with these post-marketing requirements and commitments could result in withdrawal of our marketing approval for INGREZZA. In addition, with respect to INGREZZA, and any product candidate that the FDA or a comparable foreign regulatory authority approves, 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 (especially for a product, such as INGREZZA, which has been administered in only a limited patient population to date), 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.

The FDA's policies may change, and additional government regulations may be enacted that could prevent, limit or delay regulatory approval of any of our product candidates or future indications for currently approved products. 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 on a sustained basis.

If physicians and patients do not accept INGREZZA or any of our other products, or our sales and marketing efforts are not effective, we may not generate sufficient revenue.

The commercial success of INGREZZA or any of our other products, if approved for marketing, will depend upon the acceptance of those products as safe and effective by the medical community and patients.

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

- the timing of receipt of marketing approvals for indications;
- the safety and efficacy of the products;
- the pricing of our 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 distribution support, and, to date, although we have hired experienced sales and marketing professionals, we have very limited sales and marketing experience. We may face difficulties related to managing the growth of our sales and marketing organization, and it is possible that the rapid expansion in our sales and marketing team may have a short-term negative effect on our external sales and marketing efforts given the need to devote significant time to the training and integration of these personnel. If our sales and marketing efforts are not effective and the medical community and patients do not ultimately accept our products as being safe, effective, superior and/or cost-effective, we may not generate sufficient revenue.

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 FDA or similar foreign regulatory authority may not allow an IND application or foreign equivalent filings required to initiate human clinical studies for our drug candidates or the FDA may require additional preclinical studies as a condition of the initiation of Phase I clinical studies, or additional clinical studies for progression from Phase I to Phase II, or Phase II to Phase III, or for 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. For example, any of the clinical, regulatory or operational events described above could change our planned clinical and regulatory activities for the opicapone program in Parkinson’s disease and/or our NBI-74788 program for the treatment of CAH. Additionally, any of these events described above could result in suspension of a program and/or obviate any filings for necessary regulatory approvals.

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.

Even if the clinical trials are successfully completed, we cannot guarantee that the FDA or foreign regulatory authorities will interpret the results as we do, and more trials could be required before we submit our product candidates for approval. To the extent that the results of the trials are not satisfactory to the FDA or foreign regulatory authorities for support of a marketing application, approval of our product candidates may be significantly delayed, or we may be required to expend significant additional resources, which may not be available to us, to conduct additional trials in support of potential approval of our product candidates.

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 with the exceptions of INGREZZA, which has been approved by the FDA for TD, and ORILISSA (partnered with AbbVie), which has been approved by the FDA for the management of moderate to severe endometriosis pain in women. Only a small number of research

and development programs ultimately result in commercially successful drugs. Potential products that appear to be promising at early stages of development may not reach the market for a number of reasons. These reasons include the possibilities that the potential products may:

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

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

We depend on our current collaborators for the development and commercialization of our products and product candidates that we out-license and in-license and may need to enter into future collaborations to develop and commercialize certain of our product candidates.

Our strategy for fully developing and commercializing ORILISSA 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 ORILISSA.

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

- does not successfully commercialize ORILISSA for endometriosis;
- fails to gain regulatory approval of elagolix;
    - for uterine fibroids, and if applicable, successfully launch and commercialize elagolix for that indication;
- does not conduct its collaborative activities in a timely manner;
- does not devote sufficient time and resources to our partnered program;
- terminates its agreement with us;
- develops, either alone or with others, products that may compete with elagolix;
- disputes our respective allocations of rights to any products or technology developed during our collaboration; or
- merges 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 INGREZZA 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 out-licensing 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.

In February 2017, we entered into a license agreement with BIAL for the development and commercialization of opicapone for the treatment of human diseases and conditions, including Parkinson’s disease, in the U.S. and Canada. Under the terms of the agreement, we are responsible for the management of all opicapone development and commercialization activities; however, we will depend on BIAL to supply all drug product and investigation medicinal product for our development and commercialization activities. In addition, pursuant to the license agreement, the parties have established a joint steering committee with overall coordination and strategic oversight over activities under the agreement and to provide a forum for regular exchange of information, and BIAL has the right to co-promote licensed products during certain periods of time and to engage in certain marketing-related activities in cooperation with us. Accordingly, our strategy for developing and commercializing opicapone is dependent upon maintaining our current collaboration with BIAL. Because of our reliance on BIAL for certain aspects related to the development and commercialization of opicapone, any disagreement with BIAL, or BIAL’s decision to not devote sufficient time and resources to our collaboration or to not conduct activities in a timely manner, could substantially delay and/or prohibit our ability to develop and commercialize opicapone.

These issues and possible disagreements with AbbVie, Mitsubishi Tanabe, BIAL, 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.

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

We do not and will not have access to all information regarding ORILISSA, including potentially material information about commercialization plans, medical information strategies, clinical trial design and execution, safety reports from clinical trials, safety reports, regulatory affairs, process development, manufacturing 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 ORILISSA 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 commercialization efforts related to ORILISSA, or the status of the clinical development or regulatory approval pathway of other product candidates licensed to it, we may make operational and/or investment decisions that we would not have made had we been fully informed, which may materially and adversely affect our business and operations.

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, including INGREZZA, 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 U.S. 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. In addition, communications from government officials regarding health care costs and pharmaceutical pricing could have a negative impact on our stock price, even if such communications do not ultimately impact coverage or reimbursement decisions for our products.

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 INGREZZA or any other product candidate for which we obtain marketing approval. 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.

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. 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. For example, BIAL may terminate our license agreement, pursuant to which we have rights to develop and commercialize opicapone, if we fail to use commercially reasonable efforts, fail to submit an NDA for a licensed product by a specified date, or otherwise breach the license agreement. In addition, if we were to violate any of the terms of our licenses, we could become subject to damages. 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.

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 our 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 could face liability if a regulatory authority determines that we are promoting INGREZZA, or any of our product candidates that receives regulatory approval, 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 U.S. 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. We intend to comply with the requirements and restrictions of the FDA and other regulatory agencies with respect to our promotion of our products, including INGREZZA, 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 civil 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.

Our indebtedness and liabilities could limit the cash flow available for our operations, expose us to risks that could adversely affect our business, financial condition and results of operations.

To date, we have sold $517.5 million aggregate principal amount of 2.25% convertible senior notes due May 15, 2024 (2024 Notes). We may also incur additional indebtedness to meet future financing needs. Our indebtedness could have significant negative consequences for our security holders and our business, results of operations and financial condition by, among other things:

- increasing our vulnerability to adverse economic and industry conditions;
- limiting our ability to obtain additional financing;
- requiring the dedication of a substantial portion of our cash flow from operations to service our indebtedness, which will reduce the amount of cash available for other purposes;
- limiting our flexibility to plan for, or react to, changes in our business;
- diluting the interests of our existing stockholders as a result of issuing shares of our common stock upon conversion of the 2024 Notes; and
- placing us at a possible competitive disadvantage with competitors that are less leveraged than us or have better access to capital.

Our business may not generate sufficient funds, and we may otherwise be unable to maintain sufficient cash reserves, to pay amounts due under the 2024 Notes and any additional indebtedness that we may incur. In addition, our cash needs may increase in the future. In addition, any future indebtedness that we may incur may contain financial and other restrictive covenants that limit our ability to operate our business, raise capital or make payments under our other indebtedness. If we fail to comply with these covenants or to make payments under our indebtedness when due, then we would be in default under that indebtedness, which could, in turn, result in that and our other indebtedness becoming immediately payable in full.

The conditional conversion feature of the 2024 Notes, if triggered, may adversely affect our financial condition, operating results, or liquidity.

In the event the conditional conversion feature of the 2024 Notes is triggered, holders of 2024 Notes will be entitled to convert their 2024 Notes at any time during specified periods at their option. If one or more of the holders of the 2024 Notes elects to convert their notes, unless we satisfy our conversion obligation by delivering only shares of our common stock, we would be required to settle all or a portion of our conversion obligation through the payment of cash, which could adversely affect our liquidity. The conditional convertibility of the 2024 Notes will be monitored at each quarterly reporting date and analyzed dependent upon market prices of our common stock during the prescribed measurement periods.

We have a history of losses and expect to increase our expenses 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 approximately $1.2 billion as of December 31, 2018.

In April 2017, we received FDA approval of INGREZZA for TD, and in July 2018, our partner AbbVie received FDA approval for ORILISSA for management of moderate to severe endometriosis pain in women. However, we have not yet obtained regulatory approvals for any other product candidates. Even if we succeed in commercializing INGREZZA or developing and commercializing any of our other product candidates, we may not be profitable. We also expect to continue to incur significant operating and capital expenditures as we:

- commercialize INGREZZA for TD;
- 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, sales and marketing personnel.

We expect to increase our expenses and other investments in the coming years as we fund our operations, in-licensing or acquisition opportunities, and capital expenditures. While we were profitable for the year ended December 31, 2018, our future operating results and profitability may fluctuate from period to period due to the factors described above, and we will need to generate significant revenues to achieve and maintain profitability and positive cash flow on a sustained basis. We may not be able to generate these revenues, and we may never achieve profitability on a sustained basis in the future. Our failure to maintain or increase profitability on a sustained basis could negatively impact the market price of our common stock.

We have recently increased the size of our organization and will need to continue to increase the size of our organization. We may encounter difficulties with managing our growth, which could adversely affect our results of operations.

As of December 31, 2018, we had approximately 585 full-time employees. Although we have substantially increased the size of our organization, we may need to add additional qualified personnel and resources, especially now that we

have a commercial sales force. Our current infrastructure may be inadequate to support our development and commercialization efforts and expected growth. Future growth will impose significant added responsibilities on members of management, including the need to identify, recruit, maintain and integrate additional employees, and may take time away from running other aspects of our business, including development and commercialization of our product candidates.

Our future financial performance and our ability to commercialize INGREZZA and any other product candidates that receive regulatory approval will depend, in part, on our ability to manage any future growth effectively. In particular, as we commercialize INGREZZA, we will need to support the training and ongoing activities of our sales force and will likely need to continue to expand the size of our employee base for managerial, operational, financial and other resources. To that end, we must be able to successfully:

- manage our development efforts effectively;
- integrate additional management, administrative and manufacturing personnel;

- further develop our marketing and sales organization; and
- maintain sufficient administrative, accounting and management information systems and controls.

We may not be able to accomplish these tasks or successfully manage our operations and, accordingly, may not achieve our research, development, and commercialization goals. Our failure to accomplish any of these goals could harm our financial results and prospects.

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.

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 or impact our commercialization of INGREZZA or any product candidate approved by the FDA.

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, including the successful commercialization of INGREZZA or any product candidate approved by the FDA. Furthermore, recruiting and retaining qualified scientific personnel to perform research and development work in the future, along with personnel with experience marketing and selling pharmaceutical products, is critical to our success. We may be unable to attract and retain personnel on acceptable terms given the competition among biotechnology, pharmaceutical and health care companies, universities and non-profit research institutions for experienced scientists and individuals with experience marketing and selling pharmaceutical products. We may face particular retention challenges in light of the recent rapid growth in our personnel and infrastructure and the perceived impact of those changes upon our corporate culture. In addition, we rely on a significant number of consultants to assist us in formulating our research and development strategy and our commercialization strategy. Our consultants may have commitments to, or advisory or consulting agreements with, other entities that may limit their availability to us.

If the market opportunities for our products and product candidates are smaller than we believe they are, our revenues may be adversely affected and our business may suffer.

Certain of the diseases that INGREZZA and our product candidates are being developed to address are in underserved and underdiagnosed populations. Our projections of both the number of people who have these diseases, as well as the subset of people with these diseases who will seek treatment utilizing our products or product candidates, may not be accurate. If our estimates of the prevalence or number of patients potentially on therapy prove to be inaccurate, the market opportunities for INGREZZA and our product candidates may be smaller than we believe they are, our prospects for generating expected revenue may be adversely affected and our business may suffer.

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 financial results are unpredictable and may fluctuate, for among other reasons, due to commercial sales of INGREZZA, royalties from out-licensed products, the impact of Medicare Part D coverage, 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. In addition, we recently received regulatory approval from the FDA for INGREZZA in TD and our revenues will be

dependent on our ability to sell INGREZZA and to secure adequate third-party reimbursement. 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 financial results in a quarter. While we were profitable for the year ended December 31, 2018, our future operating results and profitability may fluctuate from period to period, and even if we become profitable on a quarterly or annual basis, we may not be able to sustain or increase our profitability. Moreover, as our company and our market capitalization have grown, our financial performance has become increasingly subject to quarterly and annual comparisons with the expectations of securities analysts or investors. The failure of our financial results to meet these expectations, either in a single quarterly or annual period over a sustained period time, could cause our stock price to decline.

U.S. federal income tax reform could adversely affect our business and financial condition.

On December 22, 2017, U.S. federal income tax legislation was signed into law (H.R. 1, "An Act to provide for reconciliation pursuant to titles II and V of the concurrent resolution on the budget for fiscal year 2018", informally titled the Tax Cuts and Jobs Act, or the Tax Act). The Tax Act, among other things, contains significant changes to corporate taxation, including reduction of the corporate tax rate from a top marginal rate of 35% to a flat rate of 21%, repeal of the alternative minimum tax for corporations, limitation of the tax deduction for interest expense to 30% of adjusted earnings (except for certain small businesses), limitation of the deduction for net operating losses to 80% of current year taxable income and elimination of net operating loss carrybacks, one time taxation of offshore earnings at reduced rates regardless of whether they are repatriated, elimination of U.S. tax on foreign earnings (subject to certain important exceptions), immediate deductions for certain new investments instead of deductions for depreciation expense over time, and modifying or repealing many business deductions and credits. Notwithstanding the reduction in the corporate income tax rate, the overall impact of the Tax Act is uncertain and our business and financial condition could be adversely affected. In addition, it is uncertain if and to what extent various states will conform to the Tax Act. The impact of the Tax Act on holders of our common stock is also uncertain and could be adverse. We urge our stockholders to consult with their legal and tax advisors with respect to this legislation and the potential tax consequences of investing in or holding our common stock.

Our ability to use net operating loss carryforwards and certain other tax attributes may be limited.

Our net operating loss, or NOL, carryforwards generated in tax years ending on or prior to December 31, 2017, are only permitted to be carried forward for 20 years under applicable U.S. tax law. Under the Tax Act, our federal NOLs generated in tax years ending after December 31, 2017, may be carried forward indefinitely, but the deductibility of such federal NOLs generated in tax years beginning after December 31, 2017, is limited. It is uncertain if and to what extent various states will conform to the Tax Act. In addition, under Sections 382 and 383 of the Internal Revenue Code of 1986, as amended, and corresponding provisions of state law, if a corporation undergoes an "ownership change," which is generally defined as a greater than 50% change, by value, in its equity ownership over a three-year period, the corporation's ability to use its pre-change NOL carryforwards and other pre-change tax attributes to offset its post-change income or taxes may be limited. We do not believe we have experienced any previous ownership changes, but the determination is complex and there can be no assurance we are correct. Furthermore, we may experience ownership changes in the future as a result of subsequent shifts in our stock ownership, some of which may be outside of our control.

As a result, our pre-2018 NOL carryforwards may expire prior to being used and our NOL carryforwards generated thereafter will be subject to a percentage limitation and, if we undergo an ownership change (or if we previously underwent such an ownership change), our ability to use all of our pre-change NOLs and other pre-change tax attributes (such as research tax credits) to offset our post-change income or taxes may be limited. Similar provisions of state tax law may also apply to limit our use of accumulated state tax attributes. In addition, at the state level, there may be periods during which the use of NOLs is suspended or otherwise limited, which could accelerate or permanently increase state taxes owed. As a result, we may be unable to use all or a material portion of our NOLs and other tax attributes, which could adversely affect our future cash flows.

Our effective tax rate may fluctuate, and we may incur obligations in tax jurisdictions in excess of accrued amounts.

Our effective tax rate is derived from a combination of applicable tax rates in the various places that we operate. In preparing our financial statements, we estimate the amount of tax that will become payable in each of such places. Nevertheless, our effective tax rate may be different than experienced in the past due to numerous factors, including passage of the newly enacted federal income tax law, changes in the mix of our profitability from state to state, the results of examinations and audits of our tax filings, our inability to secure or sustain acceptable agreements with tax authorities, changes in accounting for income taxes and changes in tax laws. Any of these factors could cause us to experience an effective tax rate significantly different from previous periods or our current expectations and may

result in tax obligations in excess of amounts accrued in our financial statements.

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. Furthermore, especially as we and our market capitalization have grown, the price of our common stock has been increasingly affected by quarterly and annual comparisons with the valuations and recommendations of the analysts who cover our business. If our results do not meet these analysts' forecasts, the expectations of our investors or the financial guidance we provide to investors in any period, which is based on assumptions that may be incorrect or that may change from quarter to quarter, the market price of our common stock could decline. Over the course of the last 12 months, the price of our common stock has ranged from approximately $127.00 per share to approximately $65.00 per share. The market price of our common stock may fluctuate in response to many factors, including:

- sales of INGREZZA and ORILISSA;
- the status and cost of our post-marketing commitments for INGREZZA;
- the results of our clinical trials;

- reports of safety issues related to INGREZZA or ORILISSA;
- 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;
- additions or departures of key personnel;
- fluctuations in our operating results;
- potential litigation matters;
- government regulation;
- government and third-party payor coverage and reimbursement;
- failure of any of our product candidates, if approved, to achieve commercial success; and
- public concern as to the safety of our drugs.

If we cannot raise additional funding, we may be unable to complete development of our product candidates or establish commercial and manufacturing capabilities in the future.

We may require additional funding to effectively commercialize INGREZZA, to continue our research and product development programs, to conduct preclinical studies and clinical trials, for operating expenses, to pursue regulatory approvals for our product candidates, for the costs involved in filing and prosecuting patent applications and enforcing or defending patent claims, if any, and the cost of product in-licensing and any possible acquisitions. In addition, 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, the cost of product in-taking and possible acquisitions, fully commercialize products and operate the company to the full extent currently planned. If we cannot obtain adequate funds, we may be required to curtail significantly our commercial plans or 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:

- the commercial success of INGREZZA and/or ORILISSA;
- debt service obligations on the 2024 Notes;
- continued scientific progress in our R&D and clinical 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 any future 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, for so long as we continue to satisfy the requirements to be deemed a well-known seasoned issuer, we can utilize a shelf registration statement currently on file with the SEC, to allow us to issue an unlimited number of securities from time to time. In addition, during the second quarter of 2017, we issued the 2024 Notes and 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.

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 sales, 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.

Risks Related to Our Industry

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 U.S., 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 U.S. 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 and state 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 provided 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, Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act of 2010, or collectively 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;
- 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 70% 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.

Some of the provisions of the ACA have yet to be fully implemented, and there have been legal and political challenges to certain aspects of the ACA. Since January 2017, two executive orders and other directives designed to delay, circumvent, or loosen certain requirements mandated by the ACA have been put into place. Concurrently, Congress has considered legislation that would repeal or repeal and replace all or part of the ACA. While Congress has not passed repeal legislation, the Tax Cuts and Jobs Act includes a provision repealing, effective January 1, 2019, the tax-based shared responsibility payment imposed by the ACA on certain individuals who fail to maintain qualifying health coverage for all or part of a year that is commonly referred to as the "individual mandate". On January 22, 2018, a continuing resolution was enacted on appropriations for fiscal year 2018 that delayed the implementation of certain ACA-mandated fees, including the so-called "Cadillac" tax on certain high cost employer-sponsored insurance plans, the annual fee imposed on certain health insurance providers based on market share, and the medical device excise tax on non-exempt medical devices. The Bipartisan Budget Act of 2018, or the BBA, among other things, amends the ACA, effective January 1, 2019, to close the coverage gap in most Medicare drug plans, commonly referred to as the "donut hole". In July 2018, the Centers for Medicare and Medicaid Services, or CMS, published a final rule permitting further collections and payments to and from certain ACA-qualified health plans and health insurance issuers under the ACA risk adjustment program in response to the outcome of federal district court litigation regarding the method CMS uses to determine this risk adjustment. On December 14, 2018, a Texas U.S. District Court Judge ruled that the ACA is unconstitutional in its entirety because the "individual mandate" was repealed by Congress as part of the Tax Cuts and Jobs Act. While the Texas U.S. District Court Judge, as well as the current presidential administration and CMS, have stated that the ruling will have no immediate effect pending appeal of the decision, it is unclear how this decision, subsequent appeals, and other efforts to repeal and replace the ACA will impact the ACA and our business.

Other legislative changes have been proposed and adopted since the ACA was enacted. These changes include aggregate reductions to Medicare payments to providers of up to 2% per fiscal year pursuant to the Budget Control Act of 2011, which began in 2013 and, due to subsequent legislative amendments to the statute, including the BBA, will remain in effect through 2027 unless additional Congressional action is taken. The American Taxpayer Relief Act of 2012, among other things, further reduced Medicare payments to several providers, including hospitals and cancer treatment centers, increased the statute of limitations period for the government to recover overpayments to providers from three to five years.

Additional changes that may affect our business include the expansion of new programs such as Medicare payment for performance initiatives for physicians under the Medicare Access and CHIP Reauthorization Act of 2015, which will be fully implemented in 2019. At this time, it is unclear how the introduction of the Medicare quality payment program will impact overall physician reimbursement.

Also, there has been heightened governmental scrutiny recently over pharmaceutical pricing practices in light of the rising cost of prescription drugs and biologics. Such scrutiny has resulted in several recent Congressional inquiries and proposed and enacted federal and state legislation designed to, among other things, bring more transparency to product pricing, review the relationship between pricing and manufacturer patient programs, and reform government program reimbursement methodologies for products. At the federal level, the current presidential administration's budget proposal for fiscal year 2019 contains further drug price control measures that could be enacted during the 2019 budget process or in other future legislation, including, for example, measures to permit Medicare Part D plans to negotiate the price of certain drugs under Medicare Part B, to allow some states to negotiate drug prices under Medicaid, and to eliminate cost sharing for generic drugs for low-income patients. Further, the current presidential administration released a "Blueprint" to lower drug prices and reduce out of pocket costs of drugs that contains

additional proposals to increase manufacturer competition, increase the negotiating power of certain federal healthcare programs, incentivize manufacturers to lower the list price of their products and reduce the out of pocket costs of drug products paid by consumers. The U.S. Department of Health and Human Services has already started the process of soliciting feedback on certain of these measures and, additionally, is immediately implementing others under its existing authority. For example, in September 2018, CMS announced that it will allow Medicare Advantage Plans the option to use step therapy for Part B drugs beginning January 1, 2019, and in October 2018, CMS proposed a new rule that would require direct-to-consumer television advertisements of prescription drugs and biological products, for which payment is available through or under Medicare or Medicaid, to include in the advertisement the Wholesale Acquisition Cost, or list price, of that drug or biological product. Although a number of these, and other potential, proposals will require authorization through additional legislation to become effective, Congress and the executive branch have each indicated that it will continue to seek new legislative and/or administrative measures to control drug costs. At the state level, legislatures have increasingly passed legislation and implemented regulations designed to control pharmaceutical and biological product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain product access and marketing cost disclosure and transparency measures, and, in some cases, designed to encourage importation from other countries and bulk purchasing.

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 sustained profitability or commercialize our drugs.

Additionally, on May 30, 2018, the Trickett Wendler, Frank Mongiello, Jordan McLinn, and Matthew Bellina Right to Try Act of 2017 was signed into law. The law, among other things, provides a federal framework for certain patients to access certain investigational new drug products that have completed a Phase I clinical trial and that are undergoing investigation for FDA approval. Under certain circumstances, eligible patients can seek treatment without enrolling in clinical trials and without obtaining FDA permission under the FDA expanded access program. There is no obligation for a drug manufacturer to make its drug products available to eligible patients as a result of the Right to Try Act.

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 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 products and product candidates from academic institutions, government agencies, research institutions and biotechnology and pharmaceutical companies.

Competition may also arise from, among other things:

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

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

We are commercializing and performing research on or developing products for the treatment of several disorders including endometriosis, TD, uterine fibroids, essential tremor, classic congenital adrenal hyperplasia, pain, and other neurological and endocrine-related diseases and disorders, and there are a number of competitors to our products and product candidates. If one or more of our competitors' products or programs are successful, the market for our products may be reduced or eliminated. For example, in August 2017, Teva received approval for AUSTEDO to treat TD.

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 U.S. and internationally.

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

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

In addition, although we own a number of patents, the issuance of a patent is not conclusive as to its validity or enforceability, and third parties may challenge the validity or enforceability of our patents. We cannot assure you how much protection, if any, will be given to our patents if we attempt to enforce them and they are challenged in court or in other proceedings. It is possible that a competitor may successfully challenge our patents or that challenges will result in limitations of their coverage. Moreover, competitors may infringe our patents or successfully avoid them through design innovation. To prevent infringement or unauthorized use, we may need to file infringement claims, which are expensive and time-consuming. In addition, in an infringement proceeding a court may decide that a patent of ours is not valid or is unenforceable or may refuse to stop the other party from using the technology at issue on the grounds that our patents do not cover its technology. Interference proceedings declared by the U.S. 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 U.S.

If we fail to obtain or maintain orphan drug designation or other regulatory exclusivity for some of our product candidates, our competitive position would be harmed.

A product candidate that receives orphan drug designation can benefit from a streamlined regulatory process as well as potential commercial benefits following approval. Currently, this designation provides market exclusivity in the U.S. and the EU for seven years and ten years, respectively, if a product is the first such product approved for such orphan indication. This market exclusivity does not, however, pertain to indications other than those for which the drug was specifically designated in the approval, nor does it prevent other types of drugs from receiving orphan designations or approvals in these same indications. Further, even after an orphan drug is approved, the FDA can subsequently approve the same drug for the same condition if the FDA concludes that the new drug is clinically superior to the orphan product or a market shortage occurs.

In the EU, orphan exclusivity may be reduced to six years if the drug no longer satisfies the original designation criteria or can be lost altogether if the marketing authorization holder consents to a second orphan drug application or cannot supply enough drug, or when a second applicant demonstrates its drug is “clinically superior” to the original orphan drug. We may not be successful obtaining orphan drug designations for any indications and, even if we succeed, such orphan drug designations may fail to result in or maintain orphan drug exclusivity upon approval, which would harm our competitive position.

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, or by employees of our commercial partners 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, to maintain the confidentiality of our trade secrets or the trade secrets of our commercial partners, 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. Any action against our employees, independent contractors, principal investigators, consultants, commercial partners or vendors for violations of these laws could result in significant civil, criminal, and administrative penalties, fines, and imprisonment.

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 current and future sales, marketing, patient co-payment assistance 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 civil and criminal false claims laws, including the federal civil False Claims Act, and civil monetary penalties laws, 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;
- 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 physicians and their immediate family members; and
- analogous state, local, 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; state and local laws that require the registration of pharmaceutical sales representatives; state and local "drug takeback" laws and regulations; 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.

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, additional reporting requirements and oversight if we become subject to a corporate integrity agreement or similar agreement to resolve allegations of non-compliance with these laws, 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 once commercialized outside the U.S. 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, including INGREZZA, 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 $25 million per occurrence and $25 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. Upon FDA approval of INGREZZA we expanded our insurance coverage to include product liability insurance related to the sale of INGREZZA in the amount of $25 million per occurrence and $25 million in the aggregate. However, we may be unable to obtain commercially reasonable product liability insurance for any products approved in the future 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. Furthermore, regardless of the eventual outcome of a product liability claim, any product liability claim against us may decrease demand for our approved products, including INGREZZA, damage our reputation, result in regulatory investigations that could require costly recalls or product modifications, cause clinical trial participants to withdrawal, result in costs to defend the related litigation, decrease our revenue, and divert management’s attention from managing our business.

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.

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

We are increasingly dependent on information technology systems and infrastructure, including mobile technologies, to operate our business. In the ordinary course of our business, we collect and store confidential and sensitive electronic 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 electronic information remains secure and is perceived to be secure. The size and complexity of our information technology systems, and those of third-party vendors with whom we contract, and the volume of data we retain, make

such systems potentially vulnerable to breakdown, malicious intrusion, security breaches and other cyber-attacks. Information security risks have significantly increased in recent years in part due to the proliferation of new technologies and the increased sophistication and activities of organized crime, hackers, terrorists and other external parties, including foreign state actors. A security breach or privacy violation that leads to disclosure or modification of or prevents access to personally identifiable information or other protected information could harm our reputation, compel us to comply with federal and/or state breach notification laws and foreign law equivalents, subject us to mandatory corrective action, require us to verify the correctness of database contents and otherwise subject us to liability under laws and regulations that protect personal data, resulting in increased costs or loss of revenue. Similarly, the loss of clinical trial data from completed or ongoing or planned clinical trials could result in delays in our regulatory approval efforts and significantly increase our costs to recover or reproduce the data. If we are unable to prevent such security breaches or privacy violations or implement satisfactory remedial measures, our operations could be disrupted, and we may suffer loss of reputation, financial loss and other regulatory penalties because of lost or misappropriated information. In addition, these breaches and other inappropriate access can be difficult to detect, and any delay in identifying them may lead to increased harm of the type described above. Moreover, the prevalent use of mobile devices that access confidential information increases the risk of data security breaches, which could lead to the loss of confidential information, trade secrets or other intellectual property. As cyber threats continue to evolve, we may be required to expend significant additional resources to continue to modify or

enhance our protective measures or to investigate and remediate any information security vulnerabilities. While we have implemented security measures to protect our data security and information technology systems, such measures may not prevent such events. Significant disruptions of our information technology systems or breaches of data security could have a material adverse effect on our business, financial condition and results of operations.

Compliance with global privacy and data security requirements could result in additional costs and liabilities to us or inhibit our ability to collect and process data globally, and the failure to comply with such requirements could have a material adverse effect on our business, financial condition or results of operations.

The regulatory framework for the collection, use, safeguarding, sharing, transfer and other processing of information worldwide is rapidly evolving and is likely to remain uncertain for the foreseeable future. For example, the EU's General Data Protection Regulation, or GDPR, imposes strict obligations on the processing of personal data, including personal health data, and the free movement of such data. The GDPR applies to any company established in the EU as well as any company outside the EU that processes personal data in connection with the offering of goods or services to individuals in the EU or the monitoring of their behavior. The GDPR enhances data protection obligations for processors and controllers of personal data, including, for example, obligations relating to: processing health and other sensitive data; obtaining consent of individuals; providing notice to individuals regarding data processing activities; responding to data subject requests; taking certain measures when engaging third-party processors; notifying data subjects and regulators of data breaches; implementing safeguards to protect the security and confidentiality of personal data; and transferring personal data to countries outside the EU, including the U.S. The GDPR imposes substantial fines for breaches of data protection requirements, which can be up to four percent of global revenue or 20 million euros, whichever is greater, and it also confers a private right of action on data subjects for breaches of data protection requirements. The GDPR and other changes in laws or regulations associated with the enhanced protection of certain types of sensitive data, such as healthcare data or other personal information from our clinical trials, could require us to change our business practices or lead to government enforcement actions, private litigation or significant penalties against us and could have a material adverse effect on our business, financial condition or results of operations.

ITEM 1B. UNRESOLVED STAFF COMMENTS

None.

ITEM 2. PROPERTIES

We lease our corporate headquarters, which are located in San Diego, California, and consist of 140,000 square feet of laboratory and office space located at 12780 El Camino Real, 45,000 square feet of office space located at 12777 High Bluff Drive, and 7,500 square feet of office space located at 12790 El Camino Real.

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

ITEM 3. LEGAL PROCEEDINGS

The information set forth under Note 12 "Commitments and Contingencies" to our consolidated financial statements included in Part II, Item 8 of this Annual Report on Form 10-K is incorporated herein by reference.

ITEM 4. MINE SAFETY DISCLOSURES

None.

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, 2018		
1st Quarter	$92.98	$74.12
2nd Quarter	$106.26	$74.34
3rd Quarter	$126.98	$96.98
4th Quarter	$125.59	$64.72
Year Ended December 31, 2017		
1st Quarter	$47.43	$38.38
2nd Quarter	$55.38	$39.21
3rd Quarter	$61.51	$44.75
4th Quarter	$78.05	$57.71

As of February 1, 2019, there were approximately 51 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 2018.

Stock Performance Graph and Cumulative Total Return*

The graph below shows the cumulative total stockholder return assuming the investment of $100 on December 31, 2013 (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 Securities and Exchange Commission (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.

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.

(in thousands, except per share data)	2018	2017	2016	2015	2014
STATEMENT OF COMPREHENSIVE INCOME (LOSS) DATA					
Revenues:					
Product sales, net	$409,608	$116,626	$—	$—	$—
Collaboration revenue	41,632	45,000	15,000	19,769	—
Total revenues	451,240	161,626	15,000	19,769	—
Operating expenses:					
Cost of sales	4,889	1,254	—	—	—
Research and development	160,524	121,827	94,291	81,491	46,425
Sales, general and administrative	248,932	169,906	68,081	32,480	17,986
Total operating expenses	414,345	292,987	162,372	113,971	64,411
Income (loss) from operations	36,895	(131,361)	(147,372)	(94,202)	(64,411)
Other (expense) income:					
Interest expense	(30,530)	(19,523)	—	—	—
Investment income and other, net	15,476	8,342	6,282	5,273	3,869
Total other (expense) income	(15,054)	(11,181)	6,282	5,273	3,869
Income (loss) before provision for income taxes	21,841	(142,542)	(141,090)	(88,929)	(60,542)
Provision for income taxes	730	—	—	—	—
Net income (loss)	$21,111	$(142,542)	$(141,090)	$(88,929)	$(60,542)
Net income (loss) per share:					
Basic	$0.23	$(1.62)	$(1.63)	$(1.05)	$(0.81)
Diluted	$0.22	$(1.62)	$(1.63)	$(1.05)	$(0.81)
Shares used in calculation of net income (loss) per share:					
Weighted average common shares outstanding, basic	90,235	88,089	86,713	84,496	74,577
Weighted average common shares outstanding, diluted	95,386	88,089	86,713	84,496	74,577
BALANCE SHEET DATA					
Cash, cash equivalents and investments	$866,941	$763,290	$350,840	$461,679	$231,301
Working capital	649,544	500,493	280,028	358,359	182,539
Total assets	993,151	817,591	365,086	474,785	243,033
Convertible senior notes	388,496	369,618	—	—	—
Accumulated deficit	(1,177,755)	(1,198,866)	(1,056,324)	(915,234)	(826,305)
Total stockholders' equity	480,765	372,138	314,877	424,454	208,699

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 commercialization of our product and product candidates, 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 are a company focused on discovering, developing, and commercializing 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 related 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 products and product candidates.

On April 11, 2017, the United States Food and Drug Administration (FDA) approved INGREZZA® (valbenazine) capsules for the treatment of adults with tardive dyskinesia (TD). We market INGREZZA for TD in the United States (U.S.) through our specialty sales force focused primarily on physicians who treat TD patients, including psychiatrists and neurologists. The commercial launch of INGREZZA occurred on May 1, 2017.

On July 24, 2018, we were notified by AbbVie Inc. (AbbVie) that FDA approval was granted for ORILISSA® (elagolix) for the management of moderate to severe endometriosis pain in women. Discovered and developed through Phase II clinical trials by us, ORILISSA, the first FDA-approved oral medication for the management of endometriosis with associated moderate to severe pain in over a decade, began to be marketed by AbbVie in August 2018 as part of a collaboration to develop and commercialize elagolix for women's health.

Our clinical development programs include opicapone as an adjunctive therapy to levodopa/DOPA decarboxylase inhibitors in adult Parkinson's disease patients, elagolix for uterine fibroids partnered with AbbVie, NBI-74788 for the treatment of congenital adrenal hyperplasia (CAH), and a vesicular monoamine transporter 2 (VMAT2) inhibitor and a first-in-class central nervous system (CNS) compound each with potential use in the treatment of neurologic and psychiatric disorders.

AbbVie initiated Phase III studies of elagolix in patients with uterine fibroids in early 2016. The Phase III program included two replicate, pivotal, six-month efficacy and safety studies followed by a six-month safety and efficacy extension study. AbbVie provided positive topline efficacy data from the Phase III studies in women with uterine fibroids in the first quarter of 2018 and additional data from the six-month safety extension study in the third quarter of 2018. We believe the results from these studies will form the basis for an anticipated new drug application (NDA) submission to the FDA in the middle of 2019 for the approval of elagolix in the treatment of uterine fibroids.

We currently have three major collaborations. Two of these collaborations involve out-licensing of our proprietary technology to pharmaceutical partners. In June 2010, we announced an exclusive worldwide collaboration with AbbVie to develop and commercialize elagolix and all next-generation gonadotropin-releasing hormone (GnRH) antagonists (collectively, GnRH Compounds). In March 2015, we entered into a collaboration and license agreement with Mitsubishi Tanabe Pharma Corporation (Mitsubishi Tanabe) for the development and commercialization of

INGREZZA for movement disorders in Japan and other select Asian markets. The third collaboration agreement, which was entered into in February 2018, is one in which we in-licensed technology from BIAL – Portela & Ca, S.A. (BIAL) for the development and commercialization of opicapone for the treatment of human diseases and conditions, including Parkinson's disease, in the U.S. and Canada.

On January 28, 2019, we entered into a collaboration and license agreement with a clinical-stage gene therapy company, Voyager Therapeutics, Inc., or Voyager. The collaboration is focused on the development and commercialization of four programs using Voyager's proprietary gene therapy platforms. The four programs consist of Voyager's VY-AADC program for Parkinson's disease and VY-FXN01 program for Friedreich's ataxia, as well as rights to two programs to be determined by the parties in the future. The effectiveness of the agreement is subject to certain conditions, including the expiration or termination of the applicable waiting period under the Hart-Scott-Rodino Antitrust Improvements Act of 1976, as amended, and other customary closing conditions. Refer to Note 13 to the consolidated financial statements for more information on the agreement.

We have funded our operations primarily through private and public offerings of our common stock, debt securities, and payments received under collaboration agreements. While we independently develop many of our product candidates, we entered into collaborations for several of our programs and intend to rely on our product revenues and existing and future collaborations to meet our funding requirements. While we were profitable for the year ended December 31, 2018, our future operating results and profitability may fluctuate from period to period as product candidates are advanced through the various stages of clinical development and as we proceed with the commercial launch of INGREZZA and other potential future pipeline products. As of December 31, 2018, we had an accumulated deficit of approximately $1.2 billion.

Results of Operations

Revenues

The following table presents our revenues by category during the periods presented:

	Year Ended December 31,		
(in thousands)	2018	2017	2016
Revenues:			
INGREZZA product sales, net	$409,608	$116,626	$—
Collaboration revenue	41,632	45,000	15,000
Total revenues	$451,240	$161,626	$15,000

Product Sales, net

In April 2017, the FDA approved INGREZZA for the treatment of TD. INGREZZA became available for prescription in late April 2017. Net product sales were $409.6 million for 2018 and $116.6 million for 2017. There were no net product sales for 2016.

Collaboration Revenue

In July 2018, we were notified by AbbVie that FDA approval was granted for ORILISSA for the management of moderate to severe endometriosis pain in women, resulting in the achievement of a $40 million event-based milestone, which we recognized as revenue in the third quarter of 2018. We also recognized sales-based royalties of approximately $1.6 million for 2018, which are payable to us by AbbVie on quarterly net sales of ORILISSA.

In October 2017, AbbVie’s NDA submission for elagolix in endometriosis was accepted as filed by the FDA, resulting in the achievement of a $30 million event-based milestone, which we recognized as revenue in the fourth quarter of 2017. We also recognized $15 million in development event-based payments as revenue in 2017, resulting from Mitsubishi Tanabe’s initiation of Phase II/III development of INGREZZA in TD in Asia.

In 2016, we recognized $15 million in event-based revenue as a result of AbbVie initiating Phase III clinical studies of elagolix in patients with uterine fibroids.

Operating Expenses

Cost of Sales

Cost of sales was $4.9 million for 2018 and $1.3 million for 2017. Cost of sales for product sold in 2018 and 2017 excluded costs that were previously charged to R&D expense prior to FDA approval of INGREZZA for TD. This reduced cost drug product had a positive impact on our cost of sales and related product gross margins for 2018 and 2017. In the first quarter of 2019, we will begin to incur a higher cost of sales that includes the cost of INGREZZA active pharmaceutical ingredients produced following FDA approval. There was no cost of sales for 2016.

Research and Development

R&D expenditures include costs related to preclinical and clinical trials, scientific personnel, equipment, consultants, sponsored research, share-based compensation, and allocated facility and depreciation 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 the following 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. In-process R&D expenses and collaboration payments include upfront and milestone payments made in connection with strategic licensing arrangements we have entered into with third parties. Personnel expenses include salaries and wages, share-based compensation, payroll taxes, and benefits for those individuals involved in ongoing R&D efforts. Other R&D expenses primarily represent lab supply expenses and scientific consulting expenses.

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

(in millions)	Year Ended December 31, 2018	2017	2016
External development expense:			
VMAT2	$37.5	$20.9	$32.4
CRF_1	9.8	3.9	2.5
Other	5.6	3.4	1.0
Total external development expense	52.9	28.2	35.9
In-process R&D expenses and collaboration payments	15.0	30.0	—
R&D personnel expense	62.0	42.2	34.1
R&D facility and depreciation expense	8.1	5.8	6.3
Other R&D expense	22.5	15.6	18.0
Total R&D expense	$160.5	$121.8	$94.3

R&D expense increased $38.7 million, from $121.8 million in 2017 to $160.5 million in 2018, primarily due to the ongoing progression of our product candidate pipeline and increased personnel expenses on higher headcount, including increased non-cash share-based compensation of $11.7 million, which included a non-recurring charge of $7.7 million related to the modification of certain options and RSUs. In-process R&D expenses and collaboration payments decreased from $30 million in 2017 to $15 million in 2018, primarily due to a $20 million decrease in payments to BIAL. Excluding the decrease in payments to BIAL, R&D expense for 2018 increased $58.7 million compared to 2017.

R&D expense increased $27.5 million, from $94.3 million in 2016 to $121.8 million in 2017, primarily due to a $30 million payment to BIAL to in-license opicapone.

Sales, General and Administrative

Sales, general and administrative (SG&A) expense increased $79.0 million, from $169.9 million in 2017 to $248.9 million in 2018, primarily due to our commercial launch for INGREZZA in April 2017 and the subsequent sales force expansion in the third quarter of 2018, which included higher personnel related costs of $32.0 million compared to 2017, including increased non-cash share-based compensation of $3.9 million.

SG&A expense increased to $101.8 million, from $68.1 million in 2016 to $169.9 million in 2017, primarily due to our commercial launch for INGREZZA in April 2017, an increase of $56.7 million in personnel related costs, including increased non-cash share-based compensation of $8.2 million, and an increase of $36.6 million in external costs resulting from market research, patient support, commercial launch activities, and other professional services.

Other (Expense) Income

Other expense, net, increased $3.9 million, from $11.2 million in 2017 to $15.1 million in 2018, due to higher interest expense in 2018 resulting from our issuance of $517.5 million of 2.25% convertible senior notes due May 15, 2024 (2024 Notes) in May 2017.

Other expense, net, increased $17.5 million, from an income position of $6.3 million in 2016 to an expense position of $11.2 million in 2017, due to the incurrence of interest expense resulting from our issuance of the 2024 Notes in May 2017.

Provision for Income Taxes

Our provision for income taxes for 2018 was $0.7 million for estimated current state income taxes. As of December 31, 2018, we have recorded a full valuation allowance against our net deferred tax assets as realization is uncertain. As a result, our tax expense varies from the statutory tax rate primarily due to the change in the valuation recorded for the year, net of other permanent book/tax differences, tax credits generated, and impacts of changes in tax laws. We did not record a provision for income taxes for 2017 or 2016.

Net Income (Loss)

Net income for 2018 was $21.1 million, or $0.22 diluted net income per share, compared to a net loss of $142.5 million, or $1.62 net loss per share, for 2017 and a net loss of $141.1 million, or $1.63 net loss per share, for 2016. The change from 2017 to 2018 was primarily the result of increased INGREZZA net product sales, offset by ongoing support for the commercial launch of INGREZZA for TD and progression of our clinical pipeline. The change from 2016 to 2017 was primarily the result of increased operating expenses due to the in-licensing of opicapone and costs associated with the commercial launch of INGREZZA for TD, offset by increased revenues primarily driven by sales of INGREZZA.

Liquidity and Capital Resources

At December 31, 2018, our cash, cash equivalents, and investments totaled $866.9 million compared to $763.3 million at December 31, 2017.

Net cash provided by operating activities in 2018 was $101.4 million, compared to net cash used in operating activities of $94.3 million in 2017 and $106.2 million in 2016. The significant change to positive cash flow generated from operations from 2017 to 2018 was primarily driven by increased INGREZZA net product sales and the achievement of the $40.0 million event-based milestone related to the FDA's approval of ORILISSA. The net loss from 2017 increased by $1.4 million over 2016 levels but included increased non-cash share-based compensation of $14.1 million and the amortization of the debt discount of approximately $10.9 million resulting from our issuance of the 2024 Notes in May 2017.

Net cash used in investing activities was $242.9 million in 2018 and $251.3 million in 2017, compared to net cash provided by investing activities of $113.0 million in 2016. The change in net cash used in investing activities resulted primarily from timing differences in investment purchases, sales and maturities of investments, fluctuation of our portfolio-mix between cash equivalents and short-term and long-term investment holdings, and an increase in additions to our property and equipment, which in 2018 consisted predominantly of tenant improvements to our corporate facilities.

Net cash provided by financing activities was $29.5 million in 2018, $516.6 million in 2017, and $2.4 million in 2016. The change in cash provided by financing activities was primarily due to net proceeds of approximately $502.8 million from our issuance of the 2024 Notes in May 2017. Proceeds from stock option exercises were approximately $29.5 million in 2018, $13.9 million in 2017, and $2.4 million in 2016.

Shelf Registration Statement. In February 2017, we filed an automatic shelf registration statement which immediately became effective by rule of the Securities and Exchange Commission (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 securities from time to time. We sold no securities under this shelf registration statement in 2018 or 2017.

Convertible Debt. In May 2017, we issued the 2024 Notes. Refer to Note 5 to the consolidated financial statements for more information on the 2024 Notes.

Off-Balance Sheet Arrangements

As of December 31, 2018, we did not have any off-balance sheet arrangements.

Critical Accounting Policies and Estimates

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 of America (GAAP). 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 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:

Product Revenue Recognition

Our net product sales consist of U.S. sales of INGREZZA and are recognized when the customer obtains control of our product in an amount that reflects the consideration we expect to receive from the customer in exchange for that product. If the consideration promised under the associated contract includes a variable amount, we estimate the consideration we expect to receive for transferring the good to the customer. There are two methods for determining the amount of variable consideration: (i) the expected value method, which is the sum of probability-weighted amounts in a range of possible consideration amounts, and; (ii) the mostly likely amount method, which identifies the single most likely amount in a range of possible consideration amounts.

Revenue from product sales is recorded at the net sales (transaction) price, which includes an estimate of variable consideration for which reserves are established and which results from contractual discounts, returns, chargebacks, rebates, co-pay assistance, and other allowances relating to sales of our products. The following represent our significant categories of sales discounts and allowances:

Trade Discounts and Allowances: We generally provide customers with discounts, that include prompt payment, discounts for sales data, and other off-invoice discounts that are explicitly stated in the associated contracts and are recorded as a reduction of revenue in the period the related product revenue is recognized.

Product Returns: We offer our customers limited product return rights for damages and shipment errors provided it is within a very limited period after the original shipping date as set forth in the applicable individual distribution agreement. We do not allow product returns for product that has been dispensed to a patient or for drug expiration. We receive real-time shipping and inventory reports from our customers and have the ability to control the amount of product that is sold to our customers. Product returns to date have not been significant and we have not considered it necessary to record a reserve for product returns.

Government Rebates: We are subject to discount obligations under state Medicaid programs and Medicare prescription drug coverage gap program. We estimate our Medicaid and Medicare prescription drug coverage gap rebates based upon a range of possible outcomes that are probability-weighted for the estimated payor mix. These reserves are recorded in the same period the related revenue is recognized, resulting in a reduction of product revenue and the establishment of a current liability that is included in accrued expenses on the consolidated balance sheet. Our liability for these rebates consists of invoices received for claims from prior quarters that have not been paid or for which an invoice has not yet been received, estimates of claims for the current quarter, and estimated future claims that will be made for product that has been recognized as revenue, but remains in the distribution channel inventories at the end of each reporting period.

Provider Chargebacks and Discounts: Chargebacks for fees and discounts to providers represent the estimated obligations resulting from contractual commitments to sell products to qualified healthcare providers at prices lower than the list prices charged to customers who directly purchase the product from us. Customers charge us for the difference between what they pay for the product and the ultimate selling price to the qualified healthcare providers. These reserves are established in the same period that the related revenue is recognized, resulting in a reduction of product revenue and accounts receivable. Chargeback amounts are generally determined at the time of resale to the qualified healthcare provider by customers, and we generally issue credits for such amounts following the customer’s notification to us of the resale. Reserves for chargebacks consist of credits that we expect to issue for units that remain in the distribution channel inventories at each reporting period end that we expect will be sold to qualified healthcare providers.

Co-Payment Assistance: We offer co-payment assistance to commercially insured patients meeting certain eligibility requirements. The calculation of the accrual for co-pay assistance is based on an estimate of claims and the cost per claim that we expect to receive associated with product that has been recognized as revenue but remains in the distribution channel inventories at the end of each reporting period.

Share-Based Compensation

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.

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, 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. For actual forfeitures, we recognize the adjustment to compensation expense in the period the forfeitures occur.

Additional Information

Refer to Note 1 to the consolidated financial statements for information on accounting pronouncements that have impacted or are expected to materially impact our consolidated financial condition, results of operations, or cash flows.

Factors That May Affect Future Financial Condition and Liquidity

We anticipate increases in expenditures as we execute on our commercialization plan for INGREZZA and continue our R&D activities. Our strategies to develop some of our programs may include collaborative agreements with major pharmaceutical companies and sales of our securities in both public and private offerings. Such collaborative agreements may include a partial recovery of our research costs through license fees, contract research funding, and milestone revenues and such collaborators may be 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 collaborative arrangements of this nature, in whole or in part, and how such arrangements would affect our capital requirements.

Our in-license, research, and clinical development agreements are generally cancelable with written notice within 180 days or less. In addition to the minimum annual payments due under certain in-license and research agreements, including a $30 million upfront license fee paid to BIAL in February 2017, we may be required to pay up to approximately $105 million in milestone payments, plus sales royalties, in the event that all scientific research, development and commercialization milestones under these agreements are achieved.

The funding necessary to execute our business strategies is subject to numerous uncertainties, which may adversely affect our liquidity and capital resources. Marketing of approved pharmaceuticals and 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. In the pharmaceutical industry, total R&D spend for a drug candidate that successfully completes all stages of R&D and is commercialized may exceed $2 billion. Further, it can take in excess of ten years to complete all stages of R&D for a 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 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.

Other than INGREZZA, which has been approved by the FDA for the treatment of TD, and ORILISSA (partnered with AbbVie), which has been approved by the FDA for the management of moderate to severe endometriosis pain in women, our product candidates have not yet achieved FDA regulatory approval, which is required before we can market them as therapeutic products in the U.S. 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, clinical trials, and post-marketing studies 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 currently have limited experience in marketing and selling pharmaceutical products. If we fail to maintain successful marketing, sales, and reimbursement capabilities, or fail to enter into successful arrangements with third parties, our product revenues may suffer. 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:

- the commercial success of INGREZZA and/or ORILISSA;
- debt service obligations on the 2024 Notes;
- continued scientific progress in our R&D and clinical 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 any future 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 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 or commercialization activities as planned.

We may require additional funding to effectively commercialize INGREZZA, to continue our research and product development programs, to conduct preclinical studies and clinical trials, for operating expenses, to pursue regulatory approvals for our product candidates, for the costs involved in filing and prosecuting patent applications and enforcing or defending patent claims, if any, the cost of product in-licensing and any possible acquisitions, and we may require additional funding to establish manufacturing and marketing capabilities in the future. We may seek to access the public or private equity markets whenever conditions are favorable. 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 securities from time to time. In addition, we issued $517.5 million of convertible debt in May 2017 and we have previously financed capital purchases and may continue to pursue opportunities to obtain additional debt financing in the future. 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, products 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 approved products will generate revenues sufficient to enable us to earn a profit.

Contractual Obligations

Our contractual obligations as of December 31, 2018, are as follows:

(in millions)	Total	2019	2020	2021	2022	2023 and Thereafter
Contractual obligations:						
2024 Notes and related interest [1]	$581.4	$11.6	$11.6	$11.6	$11.6	$ 535.0
Operating leases [2]	101.9	7.4	8.4	8.6	8.9	68.6
Total contractual obligations	$683.3	$19.0	$20.0	$20.2	$20.5	$ 603.6

(1) Amounts for the 2024 Notes and related interest in the table above assume that we will hold the 2024 Notes until maturity.

(2) Amounts for operating leases presented in the table above reflect future minimum rental commitments under non-cancelable operating leases as of December 31 for each of the periods presented.

2024 Notes and Related Interest. In May 2017, we completed a private placement of $517.5 million in aggregate principal amount of 2.25% convertible senior notes scheduled to mature on May 15, 2024, unless earlier converted, redeemed, or repurchased. We may not redeem the 2024 Notes prior to May 15, 2021. On or after this date, at our election, we may redeem all, or any portion, of the 2024 Notes under certain circumstances. The 2024 Notes do not contain any financial or operating covenants or any restrictions on the payment of dividends, the issuance of other indebtedness, or the issuance or repurchase of securities by us. There are customary events of default with respect to the 2024 Notes, including that upon certain events of default, 100% of the principal and accrued and unpaid interest on the 2024 Notes will automatically become due and payable. Refer to Note 5 to the consolidated financial statements for more information on the 2024 Notes.

Operating Leases. We lease our corporate headquarters, which consist of laboratory and office space located San Diego, California, under various operating lease agreements. In addition to minimum rental commitments, these operating leases may require us to pay additional amounts for taxes, insurance, maintenance, and other operating expenses. The non-cancelable lease terms for these operating leases expire at various dates between 2020 and 2029 and do not include renewal options. Refer to Note 10 to the consolidated financial statements for more information on the major facilities that we occupy under lease arrangements.

ITEM 7A. QUANTITATIVE AND QUALITATIVE DISCLOSURES ABOUT MARKET RISK

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, 2018, 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.

ITEM 8. FINANCIAL STATEMENTS AND SUPPLEMENTARY DATA
NEUROCRINE BIOSCIENCES, INC.

INDEX TO THE CONSOLIDATED FINANCIAL STATEMENTS

Report of Independent Registered Public Accounting Firm

To the Shareholders and the Board of Directors of

Neurocrine Biosciences, Inc.

Opinion on the Financial Statements

We have audited the accompanying consolidated balance sheets of Neurocrine Biosciences, Inc. (the “Company”) as of December 31, 2018 and 2017, the related consolidated statements of operations and comprehensive income (loss), stockholders’ equity, and cash flows, for each of the three years in the period ended December 31, 2018 and the related notes (collectively referred to as the “consolidated financial statements”). In our opinion, the consolidated financial statements present fairly, in all material respects, the financial position of the Company at December 31, 2018 and 2017, and the results of its operations and its cash flows for each of the three years in the period ended December 31, 2018, 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) (PCAOB), the Company’s internal control over financial reporting as of December 31, 2018, 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 7, 2019 expressed an unqualified opinion thereon.

Basis for Opinion

These financial statements are the responsibility of the Company’s management. Our responsibility is to express an opinion on the Company’s financial statements based on our audits. We are a public accounting firm registered with the PCAOB and are required to be independent with respect to the Company in accordance with the U.S. federal securities laws and the applicable rules and regulations of the Securities and Exchange Commission and the PCAOB.

We conducted our audits in accordance with the standards of the PCAOB. Those standards require that we plan and perform the audit to obtain reasonable assurance about whether the financial statements are free of material misstatement, whether due to error or fraud. Our audits included performing procedures to assess the risks of material misstatement of the financial statements, whether due to error or fraud, and performing procedures that respond to those risks. Such procedures included examining, on a test basis, evidence regarding the amounts and disclosures in the financial statements. Our audits also included evaluating the accounting principles used and significant estimates made by management, as well as evaluating the overall presentation of the financial statements. We believe that our audits provide a reasonable basis for our opinion.

/s/ Ernst & Young LLP

We have served as the Company’s auditor since 1992.

San Diego, California

February 7, 2019

NEUROCRINE BIOSCIENCES, INC.

CONSOLIDATED BALANCE SHEETS

(in thousands, except share and per share data)	December 31, 2018	2017
ASSETS		
Current assets:		
Cash and cash equivalents	$141,714	$254,712
Short-term investments, available-for-sale	509,199	261,217
Accounts receivable	56,240	31,127
Inventory	10,864	1,024
Other current assets	19,760	6,839
Total current assets	737,777	554,919
Property and equipment, net	33,869	10,811
Long-term investments, available-for-sale	216,028	247,361
Restricted cash	5,477	4,500
Total assets	$993,151	$817,591
LIABILITIES AND STOCKHOLDERS' EQUITY		
Current liabilities:		
Accounts payable and accrued liabilities	$86,377	$53,520
Other current liabilities	1,856	906
Total current liabilities	88,233	54,426
Deferred gain on sale of real estate	7,312	8,043
Deferred revenue	10,231	10,231
Deferred rent	18,114	3,135
Convertible senior notes	388,496	369,618
Total liabilities	512,386	445,453
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; 220,000,000 shares authorized; issued and outstanding shares were 90,797,087 and 88,793,903 at December 31, 2018 and 2017, respectively	91	89
Additional paid-in capital	1,660,361	1,572,765
Accumulated other comprehensive loss	(1,932)	(1,850)
Accumulated deficit	(1,177,755)	(1,198,866)
Total stockholders' equity	480,765	372,138
Total liabilities and stockholders' equity	$993,151	$817,591

See accompanying notes to consolidated financial statements.

NEUROCRINE BIOSCIENCES, INC.

CONSOLIDATED STATEMENTS OF OPERATIONS

AND COMPREHENSIVE INCOME (LOSS)

	Year Ended December 31,		
(in thousands, except per share data)	2018	2017	2016
Revenues:			
Product sales, net	$409,608	$116,626	$—
Collaboration revenue	41,632	45,000	15,000
Total revenues	451,240	161,626	15,000
Operating expenses:			
Cost of sales	4,889	1,254	—
Research and development	160,524	121,827	94,291
Sales, general and administrative	248,932	169,906	68,081
Total operating expenses	414,345	292,987	162,372
Income (loss) from operations	36,895	(131,361)	(147,372)
Other (expense) income:			
Interest expense	(30,530)	(19,523)	—
Investment income and other, net	15,476	8,342	6,282
Total other (expense) income	(15,054)	(11,181)	6,282
Income (loss) before provision for income taxes	21,841	(142,542)	(141,090)
Provision for income taxes	730	—	—
Net income (loss)	$21,111	$(142,542)	$(141,090)
Net income (loss) per share:			
Basic	$0.23	$(1.62)	$(1.63)
Diluted	$0.22	$(1.62)	$(1.63)
Shares used in the calculation of net income (loss) per share:			
Weighted average common shares outstanding, basic	90,235	88,089	86,713
Weighted average common shares outstanding, diluted	95,386	88,089	86,713
Other comprehensive income (loss):			
Net income (loss)	$21,111	$(142,542)	$(141,090)
Unrealized (loss) gain on available-for-sale securities	(82)	(1,532)	659
Comprehensive income (loss)	$21,029	$(144,074)	$(140,431)

See accompanying notes to consolidated financial statements.

NEUROCRINE BIOSCIENCES, INC.

CONSOLIDATED STATEMENTS OF STOCKHOLDERS' EQUITY

(in thousands)	Common Stock Shares	Amount	Additional Paid in Capital	Accumulated Other Comprehensive (Loss) Gain	Accumulated Deficit	Total Stockholders' Equity
BALANCE AT DECEMBER 31, 2015	86,263	$ 86	$1,340,579	$ (977)	$(915,234)	$ 424,454
Net loss	—	—	—	—	(141,090)	(141,090)
Unrealized gains on available-for-sale investments	—	—	—	659	—	659
Share-based compensation expense	—	—	28,464	—	—	28,464
Issuance of common stock for vested restricted stock units	284	—	—	—	—	—
Issuance of common stock for stock option exercises	336	1	2,389	—	—	2,390
BALANCE AT DECEMBER 31, 2016	86,883	$ 87	$1,371,432	$ (318)	$(1,056,324)	$ 314,877
Net loss	—	—	—	—	(142,542)	(142,542)
Unrealized losses on available-for-sale investments	—	—	—	(1,532)	—	(1,532)
Share-based compensation expense	—	—	42,522	—	—	42,522
Issuance of common stock for vested restricted stock units	562	1	—	—	—	1
Issuance of common stock for stock option exercises	1,349	1	13,863	—	—	13,864
Equity component of convertible debt, net of issuance costs	—	—	144,948	—	—	144,948
BALANCE AT DECEMBER 31, 2017	88,794	$ 89	$1,572,765	$ (1,850)	$(1,198,866)	$ 372,138
Net income	—	—	—	—	21,111	21,111
Unrealized losses on available-for-sale investments	—	—	—	(82)	—	(82)
Share-based compensation expense	—	—	58,068	—	—	58,068
Issuance of common stock for vested restricted stock units	429	—	—	—	—	—

Issuance of common stock for stock option exercises	1,574	2	29,528	—	—	29,530
BALANCE AT DECEMBER 31, 2018	90,797	$ 91	$1,660,361	$ (1,932)	$(1,177,755)	$ 480,765

See accompanying notes to consolidated financial statements.

NEUROCRINE BIOSCIENCES, INC.

CONSOLIDATED STATEMENTS OF CASH FLOWS

(in thousands)	Year Ended December 31, 2018	2017	2016
CASH FLOWS FROM OPERATING ACTIVITIES			
Net income (loss)	$21,111	$(142,542)	$(141,090)
Reconciliation of net income (loss) to net cash provided by (used in) operating activities:			
Depreciation and amortization	4,024	2,400	1,453
Amortization of debt discount	17,552	10,937	—
Amortization of debt issuance costs	1,326	848	—
Amortization of premiums on investments	1,449	1,756	3,520
Share-based compensation expense	58,068	42,522	28,464
Deferred rent	351	1,203	(294)
Gain on sales of assets, net	(760)	(2,104)	(3,431)
Cease-use expense	—	(544)	(584)
Change in operating assets and liabilities:			
Accounts receivable	(25,113)	(31,127)	—
Inventory	(3,524)	(1,024)	—
Reimbursements for tenant improvements	8,701	—	—
Accounts payable and accrued liabilities	24,223	27,338	4,398
Other current assets and liabilities, net	(6,044)	(3,994)	1,383
Net cash provided by (used in) operating activities	101,364	(94,331)	(106,181)
CASH FLOWS FROM INVESTING ACTIVITIES			
Purchases of investments	(545,962)	(583,408)	(298,776)
Sales and maturities of investments	327,825	339,088	415,826
Purchases of property and equipment	(24,812)	(6,940)	(4,108)
Proceeds from sales of property and equipment	34	7	13
Net cash (used in) provided by investing activities	(242,915)	(251,253)	112,955
CASH FLOWS FROM FINANCING ACTIVITIES			
Issuance of common stock	29,530	13,865	2,390
Proceeds from issuance of senior convertible notes, net	—	502,781	—
Net cash provided by financing activities	29,530	516,646	2,390
Net change in cash, cash equivalents, and restricted cash	(112,021)	171,062	9,164
Cash, cash equivalents, and restricted cash at beginning of the period	259,212	88,150	78,986
Cash, cash equivalents, and restricted cash at end of the period	$147,191	$259,212	$88,150
SUPPLEMENTAL DISCLOSURES			
Cash paid for interest	$11,644	$6,242	$—
Non-cash capital expenditures	$2,318	$—	$—

See accompanying notes to consolidated financial statements.

NEUROCRINE BIOSCIENCES, INC.

NOTES TO THE CONSOLIDATED FINANCIAL STATEMENTS

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. Neurocrine Continental, Inc., is a Delaware corporation and a wholly owned subsidiary of the Company. The Company also has two wholly-owned Irish subsidiaries, Neurocrine Therapeutics, Ltd. and Neurocrine Europe, Ltd. both of which were formed in December 2014 and are inactive. The Company discovers, develops, and commercializes 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 related diseases and disorders.

The Company discovered, developed, and markets INGREZZA® (valbenazine), the first United States Food and Drug Administration (FDA)-approved product indicated for the treatment of adults with tardive dyskinesia (TD), an involuntary movement disorder. Discovered and developed through Phase II clinical trials by the Company, ORILISSA® (elagolix), the first FDA-approved oral medication for the management of endometriosis associated with moderate to severe pain in over a decade, is marketed by AbbVie Inc. (AbbVie) as part of a collaboration to develop and commercialize elagolix for women’s health. The Company’s clinical development programs include opicapone as an adjunctive therapy to levodopa/DOPA decarboxylase inhibitors in Parkinson's disease patients, elagolix for uterine fibroids partnered with AbbVie, NBI-74788 for the treatment of congenital adrenal hyperplasia (CAH), and a vesicular monoamine transporter 2 (VMAT2) inhibitor and a first-in-class central nervous system (CNS) compound each with potential use in the treatment of neurologic and psychiatric disorders.

Principles of Consolidation. The consolidated financial statements include the accounts of Neurocrine as well as its wholly owned subsidiaries. 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.

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

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

Accounts Receivable. Accounts receivable are recorded net of customer allowances for prompt payment discounts, chargebacks, and any allowance for doubtful accounts. The Company estimates the allowance for doubtful accounts based on existing contractual payment terms, actual payment patterns of its customers, and individual customer

circumstances. To date, an allowance for doubtful accounts has not been required.

Fair Value of Financial Instruments. Certain financial instruments, including cash, cash equivalents, accounts receivable, accounts payable, and accrued liabilities are carried at cost, which the Company believes approximates fair value because of the short-term nature of these instruments. The $517.5 million of 2.25% convertible senior notes due May 15, 2024 (2024 Notes) were recorded at the estimated value of a similar non-convertible instrument on the date of issuance and accretes to the face value of the 2024 Notes over their 7-year term. The fair value of the 2024 Notes is estimated utilizing market quotations from an over-the-counter trading market and approximated 119% and 128% of the face value of the 2024 Notes at December 31, 2018 and 2017, respectively.

Inventory. Inventory is stated at the lower of cost or estimated net realizable value. The Company currently uses actual costing to determine the cost basis for its inventory. Inventory is valued on a first-in, first-out basis and consists primarily of third-party manufacturing costs. The Company capitalizes inventory costs associated with its products upon regulatory approval when, based on management’s judgment, future commercialization is considered probable and the future economic benefit is expected to be realized; otherwise, such costs are expensed.

Prior to FDA approval of INGREZZA, all costs related to its manufacture were included in R&D expense in the period incurred. Historically, the Company's physical inventory included active pharmaceutical ingredients produced prior to FDA approval of INGREZZA and accordingly had no cost basis as the cost associated with producing this material was expensed in the period incurred. Costs associated with the manufacture of bulk drug product, finished bottling, and other labeling activities that occurred post FDA approval of INGREZZA are included in the inventory value.

The Company reduces its inventory to net realizable value for potential excess, dated, or obsolete inventory based on an analysis of forecasted demand compared to quantities on hand and any firm purchase orders, as well as product shelf life. To date, such reserves have not been significant.

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 3 to 7 years. Leasehold improvements are depreciated over the shorter of their estimated useful lives or the remaining lease term. Depreciation expense was $4.0 million for 2018, $2.4 million for 2017, and $1.5 million for 2016.

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.

Revenue Recognition. The Company recognizes revenue when the customer obtains control of the product in an amount that reflects the consideration the Company expects to receive from the customer in exchange for that product. To determine revenue recognition, the Company performs the following five steps: (i) identify the contract(s) with a customer; (ii) identify the performance obligations in the contract; (iii) determine the transaction price; (iv) allocate the transaction price to the performance obligations in the contract; and (v) recognize revenue when (or as) the Company satisfies the performance obligation. The Company only applies the five-step model to contracts when it is probable that the Company will collect the consideration it is entitled to in exchange for the good transferred to the customer. Once a contract is determined to be within the scope of Accounting Standards Codification 606, Revenue from Contracts with Customers (Topic 606), at contract inception, the Company assesses the goods promised within the contract to determine those that are performance obligations and assesses whether each promised good is distinct. The Company then recognizes as revenue the amount of the transaction price that is allocated to the respective performance obligation when (or as) the performance obligation is satisfied.

Product Sales, Net. The Company's product sales consist of sales of INGREZZA in the U.S. INGREZZA was approved by the FDA on April 11, 2017 and the Company commenced shipments of INGREZZA to specialty pharmacies (SPs) and a specialty distributor (SD) (collectively, customers) in April 2017. The SPs dispense product to a patient based on the fulfillment of a prescription and the SD sells product to closed-door pharmacies and government facilities. The Company's agreements with the customers provide for transfer of title to the product at the time the product is delivered to the customers. In addition, except for limited circumstances, the customers have no right of product return. Product sales are recognized when the customers obtain control of the Company's product, typically upon delivery to the customers.

Revenue from product sales are recorded at the net sales price (transaction price), which includes an estimate of variable consideration for which reserves are established and which results from contractual discounts, returns, chargebacks, rebates, co-pay assistance, and other allowances relating to sales of the Company's products. These reserves are based on the amounts earned or to be claimed on the related sales and are classified as reductions of accounts receivable (if the amounts are payable to the customers) or a current liability (if the amounts are payable to parties other than the customers). Where appropriate, these estimates take into consideration a range of possible

outcomes that are probability-weighted for relevant factors such as the Company's historical experience, current contractual and statutory requirements, specific known market events and trends, industry data, and forecasted customer buying and payment patterns. Overall, these reserves reflect the Company's best estimates of the amount of consideration to which it is entitled based on the terms of the contract. The amount of variable consideration that is included in the transaction price may be constrained and is included in the net sales price only to the extent that it is probable that a significant reversal in the amount of the cumulative revenue recognized will not occur in a future period. Actual amounts of consideration ultimately received may differ from the Company's estimates. If actual results in the future vary from the Company's estimates, the Company will adjust these estimates, which would affect net product revenue and earnings in the period such variances become known.

Shipping and handling costs related to the Company's product sales are included in sales, general and administrative expenses.

Collaborative and Other Revenue. The Company enters into collaboration and licensing agreements under which it licenses certain rights to its product candidates to third parties. The terms of these arrangements typically include payment to the Company of one or more of the following: non-refundable, up-front license fees; development, regulatory, and commercial milestone payments; payments for manufacturing supply services; and royalties on net sales of licensed products.

As part of the accounting for these arrangements, the Company develops assumptions that require judgment to determine the stand-alone selling price for each performance obligation identified in the contract. The Company uses key assumptions to determine the stand-alone selling price, which may include forecasted revenues, development timelines, reimbursement rates for personnel costs, discount rates, and probabilities of technical and regulatory success.

Royalty Revenue: For arrangements that include sales-based royalties, including milestone payments based on the level of sales, and the license is deemed to be the predominant item to which the royalties relate, the Company recognizes revenue at the later of (i) when the related sales occur, or (ii) when the performance obligation to which some or all of the royalty has been allocated has been satisfied (or partially satisfied). Sales-based royalties for ORILISSA are calculated as a percentage of AbbVie net sales as defined in the Company's agreement with AbbVie. Each quarterly period, sales-based royalties are recorded based on estimated quarterly net sales of ORILISSA. Differences between actual results and estimated amounts are adjusted for in the period in which they become known, which typically follows the quarterly period in which the estimate was made.

Licenses of Intellectual Property: If the license to the Company's intellectual property embedded within a collaboration and/or licensing arrangement is determined to be distinct from the other performance obligations identified in the arrangement, the Company recognizes revenues from non-refundable, up-front fees allocated to the license when the license is transferred to the licensee and the licensee is able to use and benefit from the license. For licenses that are bundled with other promises, the Company utilizes judgment to assess the nature of the combined performance obligation to determine whether the obligation is satisfied over time or at a point in time and, if over time, the appropriate method of measuring progress for purposes of recognizing revenue from non-refundable, up-front fees. The Company evaluates the measure of progress each reporting period and, if necessary, adjusts the measure of performance and related revenue recognition.

The Company receives payments from its licensees based on billing schedules established in each agreement. Up-front payments and fees are recorded as deferred revenue upon receipt, or when due, and may require deferral of revenue recognition to a future period until the Company performs its obligations under these arrangements. Amounts are recorded as accounts receivable when the Company's right to consideration is unconditional.

Milestone Payments: At the inception of each arrangement that includes development, commercialization, and regulatory milestone payments, the Company evaluates whether the milestones are considered probable of being reached and estimates the amount to be included in the transaction price using the most likely amount method. Performance milestone payments represent a form of variable consideration. If it is probable that a significant revenue reversal would not occur, the associated milestone value is included in the transaction price. Milestone payments that are not within the Company's control or that of the licensee, such as regulatory approvals, are not considered probable of being achieved until those approvals are received. The transaction price is then allocated to each performance obligation on a relative stand-alone selling price basis, for which the Company recognizes revenue as or when the performance obligations under the contract are satisfied. At the end of each subsequent reporting period, the Company re-evaluates the probability of achievement of such development milestones and any related constraint, and if necessary, adjusts its estimate of the overall transaction price. Any such adjustments are recorded on a cumulative catch-up basis, which would affect milestone and license fees revenues and earnings in the period of adjustment.

Manufacturing Supply Services: Arrangements that include a promise for future supply of drug substance or drug product for either clinical development or commercial supply at the licensee's discretion are generally considered as

options. The Company assesses if these options provide a material right to the licensee and if so, they are accounted for as separate performance obligations.

Concentration of Credit Risk. The Company does not currently have any of its own manufacturing facilities, and therefore it depends on an outsourced manufacturing strategy for the production of INGREZZA for commercial use and for the production of its product candidates for clinical trials. The Company has contracts in place with one third-party manufacturer that is approved for the commercial production of INGREZZA's capsules at 2 separate sites and one third-party manufacturer that is approved for the production of INGREZZA's active pharmaceutical ingredient. Although there are potential sources of supply other than the Company's existing suppliers, any new supplier would be required to qualify under applicable regulatory requirements.

The Company has entered into distribution agreements with a limited number of SPs and SDs, and all of the Company's product sales are to these customers. The Company's 3 largest customers represented 93% of the Company's product revenue for the year ended December 31, 2018 and 2017 and substantially all of the Company's accounts receivable balance at December 31, 2018 and 2017.

Financial instruments that potentially subject the Company to concentrations of credit risk consist primarily of cash, cash equivalents, investments, and accounts receivables. The Company 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.

Cost of Sales. Cost of sales includes third-party manufacturing, transportation, freight, and indirect overhead costs associated with the manufacture and distribution of INGREZZA, sales-based license costs on AbbVie net sales of ORILISSA, as defined in the Company's agreement with AbbVie, and period costs resulting from certain inventory manufacturing services and variances and adjustment charges. A portion of the costs associated with the manufacture of INGREZZA sold to date was expensed as R&D prior to the FDA's approval of INGREZZA and is therefore excluded from cost of sales during this period.

Research and Development Expenses. R&D expenses consist 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 consulting 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, in-licenses, and third-party funded research arrangements.

Advertising Expense. In connection with the FDA approval and commercial launch of INGREZZA in April 2017, the Company began to incur advertising costs, which are expensed when services are performed, or goods are delivered. The Company incurred advertising costs related to its marketed product, INGREZZA, of $20.5 million in 2018 and $10.1 million in 2017.

Share-Based Compensation. The Company grants stock options to purchase its common stock to eligible employees and directors and also grants certain employees restricted stock units (RSUs) and performance-based restricted stock units (PRSUs). Additionally, the Company allows employees to participate in an employee stock purchase plan (ESPP).

The Company estimates the fair value of stock options and shares to be issued under the ESPP 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 3 to 4 years; however, certain provisions in the Company's equity compensation plans provide for shorter vesting periods under certain circumstances. The fair value of shares to be issued under the ESPP are recognized and amortized on a straight-line basis over the purchase period, which is generally 6 months. Additionally, the Company granted certain PRSUs that vest upon the achievement of certain pre-defined company-specific performance-based criteria. Expense related to these PRSUs is generally recognized ratably over the expected performance period once the pre-defined performance-based criteria for vesting becomes probable.

Net Income (Loss) Per Share. Basic net income (loss) per share is computed using the weighted average number of common shares outstanding during the period. Diluted net income per share is computed using the weighted average number of common and potentially dilutive shares outstanding during the period, including the potentially dilutive shares resulting from the conversion of the 2024 Notes, and excluding the effect of stock options and restricted stock outstanding for periods when their effect is anti-dilutive, using the treasury stock method.

Convertible debt instruments that may be settled entirely or partly in cash (such as the 2024 Notes) may, in certain circumstances where the borrower has the ability and intent to settle in cash, be accounted for under the treasury stock method. The Company issued the 2024 Notes with a combination settlement feature, which the Company has the ability and intent to use upon conversion of the notes, to settle the principal amount of debt for cash and the excess of the principal portion in shares of its common stock. As a result, of the approximately 6.8 million shares underlying the

2024 Notes, only the shares required to settle the excess of the principal portion would be considered dilutive under the treasury stock method. Further, approximately 0.3 million PRSUs have been excluded from the calculation of diluted net income per share as the performance condition has not been achieved. In loss periods, basic net loss per share and diluted net loss per share are identical because the otherwise dilutive potential common shares become anti-dilutive and are therefore excluded.

Recently Adopted Accounting Pronouncements.

In May 2014, the Financial Accounting Standards Board (FASB) issued Account Standards Update (ASU) No. 2014-09, “Revenue from Contracts with Customers (Topic 606)”, which supersedes all existing revenue recognition requirements, including most industry-specific guidance. This new standard amends the guidance for the recognition of revenue from contracts with customers to transfer goods and services. The FASB subsequently issued additional, clarifying standards to address issues arising from implementation of the new revenue recognition standard. The Company adopted this standard on January 1, 2018, using the modified retrospective method, and applied the standard only to contracts that were not completed prior to January 1, 2018. The adoption of the new revenue standard did not change the Company’s revenue recognition. As the Company did not identify any accounting changes that impacted the amount of reported revenues with respect to product revenues, or revenue from collaboration and license agreements, no adjustment to retained earnings was required upon adoption.

In November 2016, the FASB issued ASU 2016-18, “Statement of Cash Flows (Topic 230): Restricted Cash”, which clarifies the presentation of restricted cash and restricted cash equivalents in the statements of cash flows. Under this ASU, restricted cash and restricted cash equivalents are included with cash and cash equivalents when reconciling the beginning and end-of-period total amounts presented on the statements of cash flows. This ASU is intended to reduce diversity in practice in the classification and presentation of changes in restricted cash on the statement of cash flows. This ASU requires that the statement of cash flows explain the change in total cash and equivalents and amounts generally described as restricted cash or restricted cash equivalents when reconciling the beginning and end-of-period total amounts. This ASU also requires a reconciliation between the total of cash and equivalents and restricted cash presented on the statement of cash flows and the cash and equivalents balance presented on the balance sheet. This amended guidance was retrospectively adopted on January 1, 2018 and requires that cash, cash equivalents, and restricted cash reported on the consolidated statements of cash flows now includes restricted cash of $5.5 million as of December 31, 2018 and $4.5 million as of December 31, 2017, as well as previously reported cash and cash equivalents.

Recently Issued Accounting Pronouncements

In February 2016, the FASB issued ASU No. 2016-02, “Leases (Topic 842)”, which requires lessees to recognize leases on the balance sheet and disclose key information about leasing arrangements. Topic 842 establishes a right-of-use (ROU) model that requires a lessee to recognize a ROU asset and lease liability on the balance sheet for all leases with a term longer than 12 months. Topic 842 also requires disclosures to meet the objective of enabling users of financial statements to assess the amount, timing, and uncertainty of cash flows arising from leases.

Topic 842 is effective for the Company beginning January 1, 2019, using a modified retrospective approach, with early adoption permitted. An entity may choose to use either the effective date or the beginning of the earliest comparative period presented in the financial statements as the date of initial application. The Company expects to adopt Topic 842 on January 1, 2019, using a modified retrospective approach, and to choose the effective date as the date of initial application. Consequently, financial information will not be updated, and the disclosures required under Topic 842 will not be provided for dates and periods prior to January 1, 2019.

Topic 842 provides a number of optional practical expedients and accounting policy elections. The Company expects to elect the package of practical expedients requiring no reassessment of whether any expired or existing contracts are or contain leases, the lease classification of any expired or existing leases, or initial direct costs for any existing leases. Further, the Company expects to elect accounting policies not to apply the recognition requirements under Topic 842 to any of the Company’s short-term leases, instead recognizing the lease payments in profit or loss on a straight-line basis over the lease term, and to account for each separate lease and associated nonlease components as a single lease component for all of its leases.

The Company expects Topic 842 will have a material effect on its consolidated balance sheets. However, the Company does not expect Topic 842 will have a material effect on its consolidated statements of operations and comprehensive income (loss) or consolidated statements of cash flows. While the Company continues to assess all of the effects of adoption, the most significant effects relate to (1) the recognition of right-of-use (ROU) assets of approximately $49 million and lease liabilities of approximately $69 million, primarily resulting from leases of office and laboratory space; (2) the recognition of an existing deferred gain on a sale of real estate of approximately $8 million as a cumulative-effect adjustment to equity; (3) the derecognition of deferred rent of approximately $20 million for certain lease incentives received; and (4) significant new disclosure requirements.

In June 2018, the FASB issued ASU 2018-07, “Compensation-Stock Compensation (Topic 718): Improvements to Nonemployee Share-Based Payment Accounting”, which expands the scope of Topic 718 to include share-based payment transactions for acquiring goods and services from nonemployees and applies to all share-based payment transactions in which a grantor acquires goods or services to be used or consumed in a grantor’s own operations by issuing share-based payment awards. This ASU does not apply to share-based payments used to effectively provide

financing to the issuer or awards granted in conjunction with selling goods or services to customers as part of a contract accounted for under Topic 606. This update is effective for public business entities for fiscal years beginning after December 15, 2018, including interim periods within that fiscal year. The Company does not expect this update will have a material impact on its consolidated financial statements and related disclosures.

NOTE 2. SIGNIFICANT COLLABORATIVE RESEARCH AND DEVELOPMENT AGREEMENTS

Mitsubishi Tanabe Pharma Corporation. During 2015, the Company entered into a collaboration and license agreement with Mitsubishi Tanabe Pharma Corporation (Mitsubishi Tanabe) for the development and commercialization of INGREZZA for movement disorders in Japan and other select Asian markets. Mitsubishi Tanabe made an up-front license fee of $30 million and has agreed to make payments 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 and the Company would be entitled to a percentage of sales of INGREZZA in Japan and other select Asian markets for the longer of ten years or the life of the related patent rights. Further, the collaboration effort between the parties to advance INGREZZA towards commercialization in Japan and other select Asian markets is governed by joint steering and development committees with representatives from both parties. 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 INGREZZA product rights for Japan and other select Asian markets would revert to the Company.

The Company assessed this arrangement in accordance with Topic 606 and identified the following performance obligations: (i) INGREZZA technology license and existing know-how; and (ii) development activities to initiate a clinical trial of INGREZZA for Huntington’s chorea, at an estimated cost of approximately $12 million, should Mitsubishi Tanabe request. The Company has the option to participate on the joint steering committee, but since participation is at its option it was deemed to not be a performance obligation. The option for Mitsubishi Tanabe to engage the Company to manufacture and supply pharmaceutical products, not at a discount, was not considered a material right and therefore not a performance obligation. Based on these assessments, the Company identified the license and the development activities as the only performance obligations at the inception of the agreement, which were both deemed to be distinct.

To evaluate the appropriate transaction price, the Company determined that the up-front amount constituted the entirety of the consideration to be included in the transaction price and to be allocated to the performance obligations based on the Company’s best estimate of their relative stand-alone selling prices. For the license, the stand-alone selling price was calculated using an income approach model and included the following key assumptions: the development timeline, revenue forecast, discount rate, and probabilities of technical and regulatory success. The relative selling price of the Company’s development activities to initiate a clinical trial of INGREZZA for Huntington’s chorea was based on an assessment of costs to perform the study, based upon a peer company analysis for similar studies. The Company believes a change in the assumptions used to determine its stand-alone selling price for the license most likely would not have a significant effect on the allocation of consideration received (or receivable) to the performance obligations.

At execution, the transaction price included only the $30 million up-front consideration received. None of the development or regulatory milestones have been included in the transaction price, as all milestone amounts were fully constrained. As part of its evaluation of the constraint, the Company considered numerous factors, including that achievement of the milestones is outside of its control and contingent upon success in future clinical trials and the licensee’s efforts. Any consideration related to sales-based milestones (including royalties) will be recognized when the related sales occur as they were determined to relate predominantly to the license granted to Mitsubishi Tanabe and therefore have also been excluded from the transaction price. The Company will re-evaluate the transaction price in each reporting period and as uncertain events are resolved or other changes in circumstances occur.

To date, the Company has recognized revenue under this agreement of $19.8 million associated with the delivery of a technology license and existing know-how, and $15 million in development event-based payments resulting from Mitsubishi Tanabe's initiation of Phase II/III development of INGREZZA in tardive dyskinesia (TD) in Asia. 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. No revenue was recognized under the Mitsubishi Tanabe agreement for 2018 or 2016. In 2017, the Company recognized $15 million in development event-based payments resulting from Mitsubishi Tanabe's initiation of Phase II/III development of INGREZZA in TD in Asia.

AbbVie. In June 2010, the Company announced an exclusive worldwide collaboration with AbbVie, to develop and commercialize elagolix and all next-generation gonadotropin-releasing factor (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 $115 million has been earned as of December 31, 2018, and up to an additional $50 million in commercial event-based payments.

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.

The Company evaluated the terms of this agreement under Topic 606 and determined that there is one performance obligation, the exclusive worldwide license with rights to develop, manufacture, and commercialize elagolix. At execution, the transaction price included only the $75 million up-front consideration received. None of the development or regulatory milestones were included in the transaction price, as all milestone amounts were fully constrained. As part of the Company's evaluation of the constraint, the Company considered numerous factors, including that achievement of the milestones is outside of its control and contingent upon success in future clinical trials and the licensee's efforts. Any consideration related to sales-based milestones (including royalties) will be recognized when the related sales occur as they were determined to relate predominantly to the license granted to AbbVie and therefore have also been excluded from the transaction price. The Company will re-evaluate the transaction price in each reporting period and as uncertain events are resolved or other changes in circumstances occur.

On July 24, 2018, AbbVie received approval from the FDA for ORILISSA for the management of moderate to severe endometriosis pain in women, resulting in the achievement of a $40 million event-based milestone, which the Company recognized as revenue for 2018. The Company also recognized sales-based royalties on AbbVie net sales of ORILISSA of approximately $1.6 million for 2018. In 2017, event-based revenue of $30 million was recognized based on AbbVie's new drug application (NDA) submission for elagolix in endometriosis being accepted by the FDA. In 2016, event-based revenue of $15 million was recognized related to AbbVie's initiation of Phase III development of elagolix in uterine fibroids.

BIAL – Portela & Ca, S.A. In February 2017, the Company entered into an exclusive license agreement with BIAL – Portela & Ca, S.A. (BIAL) for the development and commercialization of opicapone for the treatment of human diseases and conditions, including Parkinson's disease, in the U.S. and Canada. The Company paid BIAL an upfront license fee of $30 million, which was expensed in 2017 as in-process R&D. During the first quarter of 2018, the FDA provided guidance on the regulatory path forward to support an NDA for opicapone for Parkinson's Disease, in which the FDA did not request that the Company conduct an additional Phase III study, resulting in a $10 million event-based milestone payment to BIAL, which was expense as incurred. The Company may be required to pay up to an additional $105 million in milestone payments associated with the regulatory approval and net sales of opicapone. Prior to FDA approval of opicapone, the Company may also be required to pay up to an additional $10 million in milestones based on certain regulatory and clinical results and FDA acceptance of the Company's NDA submission for opicapone. Upon commercialization of opicapone, the Company agreed to determine certain annual sales forecasts. In the event the Company fails to meet the minimum sales requirements for a particular year, it would be required to pay BIAL an amount equal to the difference between the actual net sales and minimum sales requirements for such year. In the event the Company fails to meet the minimum sales requirements for any two years, BIAL may terminate the agreement.

Under the terms of the agreement, the Company is responsible for the management and cost of all opicapone development and commercialization activities in the U.S. and Canada. Further, unless terminated earlier, the agreement will continue on a licensed product-by-product and country-by-country basis until a generic product in respect of such licensed product under the agreement is sold in a country and sales of such generic product are greater than a specified percentage of total sales of such licensed product in such country. Upon the Company's written request prior to the estimated expiration of the term in respect of a licensed product, the parties shall negotiate a good faith continuation of BIAL's supply of such licensed product after the term. After the term, and if BIAL is not supplying a certain licensed product, the Company shall pay BIAL a trademark royalty based on the net sales of such licensed

product. Either party may terminate the agreement earlier if the other party materially breaches the agreement and does not cure the breach within a specified notice period, or upon the other party's insolvency. BIAL may terminate the agreement if the Company fails to use commercially reasonable efforts or to submit an NDA for a licensed product by a specified date or under certain circumstances involving a change of control of the Company. In certain circumstances where BIAL elects to terminate the agreement in connection with the Company's change of control, BIAL shall pay the Company a termination fee. The Company may terminate the agreement at any time for any reason upon six months written notice to BIAL if prior to the first NDA approval in the U.S., and upon 9 months written notice to BIAL if such notice is given after the first NDA approval in the U.S. If the Company's termination request occurs prior to the first NDA approval in the U.S., it shall pay BIAL a termination fee except under certain conditions specified in the agreement.

NOTE 3. INVESTMENTS

Available-for-sale securities are carried at fair value, with the unrealized gains and losses reported in comprehensive income (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 are included in investment income. Realized gains and losses and declines in value judged to be other-than-temporary, if any, on available-for-sale securities are included in investment income and other, net. 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 and other, net.

Investments at December 31, 2018 and 2017 consisted of the following:

	December 31,	
(in thousands)	2018	2017
Commercial paper	$94,572	$75,362
Corporate debt securities	544,978	414,815
Securities of government-sponsored entities	85,677	18,401
Total investments	$725,227	$508,578

The following is a summary of investments classified as available-for-sale securities:

(in thousands)	Contractual Maturity (in years)	Amortized Cost	Gross Unrealized Gains	Gross Unrealized Losses	Aggregate Estimated Fair Value
December 31, 2018:					
Classified as current assets:					
Commercial paper	Less than 1	$94,617	$ —	$ (45)	$94,572
Corporate debt securities	Less than 1	395,385	—	(1,598)	393,787
Securities of government-sponsored entities	Less than 1	20,887	8	(55)	20,840
Total short-term available-for-sale securities		$510,889	$ 8	$ (1,698)	$509,199
Classified as non-current assets:					
Corporate debt securities	1 to 2	$151,594	$ 66	$ (469)	$151,191
Securities of government-sponsored entities	1 to 2	64,676	162	(1)	64,837
Total long-term available-for-sale securities		$216,270	$ 228	$ (470)	$216,028
December 31, 2017:					
Classified as current assets:					
Commercial paper	Less than 1	$75,396	$ 1	$ (35)	$75,362
Corporate debt securities	Less than 1	178,776	—	(400)	178,376
Securities of government-sponsored entities	Less than 1	7,503	—	(24)	7,479
Total short-term available-for-sale securities		$261,675	$ 1	$ (459)	$261,217
Classified as non-current assets:					
Corporate debt securities	1 to 2	$237,749	$ —	$ (1,310)	$236,439
Securities of government-sponsored entities	1 to 2	11,004	—	(82)	10,922
Total long-term available-for-sale securities		$248,753	$ —	$ (1,392)	$247,361

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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, 2018 and 2017, aggregated by investment category and length of time that individual securities have been in a continuous loss position:

	Less Than 12 Months		12 Months or Greater		Total	
(in thousands)	Estimated Fair Value	Unrealized Losses	Estimated Fair Value	Unrealized Losses	Estimated Fair Value	Unrealized Losses
December 31, 2018:						
Commercial paper	$51,927	$ (45)	$—	$ —	$51,927	$ (45)
Corporate debt securities	274,696	(746)	234,798	(1,321)	509,494	(2,067)
Securities of government-sponsored entities	4,999	(1)	10,947	(55)	15,946	(56)
Total	$331,622	$ (792)	$245,745	$ (1,376)	$577,367	$ (2,168)
December 31, 2017:						
Commercial paper	$62,602	$ (35)	$—	$ —	$62,602	$ (35)
Corporate debt securities	386,728	(1,660)	28,087	(50)	414,815	(1,710)
Securities of government-sponsored entities	10,922	(82)	7,479	(24)	18,401	(106)
Total	$460,252	$ (1,777)	$35,566	$ (74)	$495,818	$ (1,851)

At each reporting date, the Company performs an evaluation of impairment to determine if any unrealized losses are other-than-temporary. Factors considered in determining whether a loss is other-than-temporary include the length of time and extent to which fair value has been less than the cost basis, the financial condition of the issuer, and the Company's intent and ability to hold the investment until recovery of its amortized cost basis. The Company intends, and has the ability, to hold its investments in unrealized loss positions until their amortized cost basis has been recovered. Based on its evaluation, the Company determined that its unrealized losses were not other-than-temporary at December 31, 2018 and 2017.

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 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, 2018 and 2017.

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The Company's assets, which are measured at fair value on a recurring basis as of December 31, 2018 and 2017, were determined using the inputs described above:

		Fair Value Measurements Using		
(in millions)	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, 2018:				
Classified as current assets:				
Cash and money market funds	$ 141.7	$ 141.7	$ —	$ —
Commercial paper	94.6	—	94.6	—
Securities of government-sponsored entities	20.8	—	20.8	—
Corporate debt securities	393.8	—	393.8	—
Subtotal	650.9	141.7	509.2	—
Classified as long-term assets:				
Cash and money market funds	1.5	1.5	—	—
Certificates of deposit	4.0	4.0	—	—
Securities of government-sponsored entities	64.8	—	64.8	—
Corporate debt securities	151.2	—	151.2	—
Total	872.4	147.2	725.2	—
Less cash, cash equivalents and restricted cash	(147.2)	(147.2)	—	—
Total investments	$ 725.2	$ —	$ 725.2	$ —
December 31, 2017:				
Classified as current assets:				
Cash and money market funds	$ 170.2	$ 170.2	$ —	$ —
Commercial paper	159.9	—	159.9	—
Securities of government-sponsored entities	7.5	—	7.5	—
Corporate debt securities	178.4	—	178.4	—
Subtotal	516.0	170.2	345.8	—
Classified as long-term assets:				
Cash and money market funds	1.5	1.5	—	—
Certificates of deposit	3.0	3.0	—	—
Securities of government-sponsored entities	10.9	—	10.9	—
Corporate debt securities	236.4	—	236.4	—
Total	767.8	174.7	593.1	—
Less cash, cash equivalents and restricted cash	(259.2)	(174.6)	(84.6)	—
Total investments	$ 508.6	$ 0.1	$ 508.5	$ —

The fair value of the 2024 Notes, calculated utilizing market quotations from an over-the-counter trading market for these notes (Level 2), was approximately $616.1 million as of December 31, 2018 and $662.1 million as of December 31, 2017. Refer to Note 5 to the consolidated financial statements for more information on the 2024 Notes.

NOTE 5. CONVERTIBLE SENIOR NOTES

On May 2, 2017, the Company completed a private placement of $517.5 million in aggregate principal amount of 2.25% convertible senior notes due 2024 and entered into an indenture agreement that sets forth the details of all the terms and conditions of the 2024 Notes (2024 Indenture). The 2024 Notes accrue interest at a fixed rate of 2.25% per year, payable semiannually in arrears on May 15 and November 15 of each year, beginning on November 15, 2017. The 2024 Notes mature on May 15, 2024. The net proceeds from the issuance of the 2024 Notes were approximately $502.8 million, after deducting commissions and the offering expenses payable by the Company.

Holders of the 2024 Notes may convert the 2024 Notes at any time prior to the close of business on the business day immediately preceding May 15, 2024, only under the following circumstances:

(i) during any calendar quarter commencing after the calendar quarter ending on September 30, 2017 (and only during such calendar quarter), if the last reported sale price of the Company’s common stock for at least 20 trading days (whether or not consecutive) during a period of 30 consecutive trading days ending on the last trading day of the immediately preceding calendar quarter is greater than 130% of the conversion price on each applicable trading day;

(ii) during the 5 business-day period immediately after any 5 consecutive trading-day period (the measurement period) in which the trading price (as defined in the 2024 Indenture) per $1,000 principal amount of the 2024 Notes for each trading day of the measurement period was less than 98% of the product of the last reported sale price of the Company's common stock and the conversion rate on each such trading day;

(iii) upon the occurrence of specified corporate events, including a merger or a sale of all or substantially all of the Company's assets; or

(iv) if the Company calls the 2024 Notes for redemption, until the close of business on the business day immediately preceding the redemption date.

On or after January 15, 2024, until the close of business on the scheduled trading day immediately preceding May 15, 2024, holders may convert their 2024 Notes at any time.

Upon conversion, holders will receive the principal amount of their 2024 Notes and any excess conversion value, calculated based on the per share volume-weighted average price (VWAP) for each of the 30 consecutive trading days during the observation period. For both the principal and excess conversion value, holders may receive cash, shares of the Company's common stock or a combination of cash and shares of its common stock, at the Company's option.

It is the Company's intent and policy to settle conversions through combination settlement, which essentially involves repayment of an amount of cash equal to the "principal portion" and delivery of the "share amount" in excess of the principal portion in shares of common stock or cash. In general, for each $1,000 in principal, the "principal portion" of cash upon settlement is defined as the lesser of $1,000, and the conversion value during the 25-day observation period as described in the indenture for the notes. The conversion value is the sum of the daily conversion value which is the product of the effective conversion rate divided by 25 days and the daily VWAP of the Company's common stock. The "share amount" is the cumulative "daily share amount" during the observation period, which is calculated by dividing the daily VWAP into the difference between the daily conversion value (i.e., conversion rate x daily VWAP) and $1,000.

The initial conversion rate for the 2024 Notes is 13.1711 shares of common stock per $1,000 principal amount, which is equivalent to an initial conversion price of approximately $75.92 per share of the Company's common stock. At the initial conversion rate, settlement of the 2024 Notes for shares of the Company's common stock would approximate 6.8 million shares. The conversion rate will be subject to adjustment in some events but will not be adjusted for any accrued and unpaid interest. The initial conversion price of the 2024 Notes represented a premium of approximately 42.5% to the closing sale price of $53.28 per share of the Company's common stock on the Nasdaq Global Select Market on April 26, 2017, the date the Company priced the private offering of the 2024 Notes.

In the event of conversion, holders would forgo all future interest payments, any unpaid accrued interest and the possibility of further stock price appreciation. Upon the receipt of conversion requests, the settlement of the 2024 Notes will be paid pursuant to the terms of the 2024 Indenture. In the event that all of the 2024 Notes are converted, the Company would be required to repay the $517.5 million in principal value and any conversion premium in any combination of cash and shares of its common stock (at the Company's option).

On or after, but not prior to May 15, 2021, the Company may redeem for cash all or part of the 2024 Notes if the last reported sale price (as defined in the 2024 Indenture) of its common stock has been at least 130% of the conversion price then in effect for at least 20 trading days (whether or not consecutive) during any 30 consecutive trading-day period ending on, and including, the trading day immediately before the date which the Company provides notice of redemption. The redemption price will equal the sum of (i) 100% of the principal amount of the 2024 Notes being redeemed, plus (ii) accrued and unpaid interest, including additional interest, if any, to, but excluding, the redemption date. No sinking fund is provided for the 2024 Notes.

If the Company undergoes a fundamental change, as defined in the 2024 Indenture, subject to certain conditions, holders of the 2024 Notes may require the Company to repurchase for cash all or part of their 2024 Notes at a repurchase price equal to 100% of the principal amount of the 2024 Notes to be repurchased, plus accrued and unpaid interest to, but excluding, the fundamental change repurchase date. In addition, if a ‘‘make-whole fundamental change’’

(as defined in the 2024 Indenture) occurs prior to January 15, 2024, the Company will, in certain circumstances, increase the conversion rate for a holder who elects to convert the 2024 Notes in connection with the make-whole fundamental change.

The 2024 Notes are the Company’s general unsecured obligations that rank senior in right of payment to all of its indebtedness that is expressly subordinated in right of payment to the 2024 Notes, and equal in right of payment to the Company’s unsecured indebtedness.

While the 2024 Notes are currently classified as long-term on the Company's consolidated balance sheets, the future convertibility and resulting balance sheet classification of this liability will be monitored at each quarterly reporting date and will be analyzed dependent upon market prices of the Company's common stock during the prescribed measurement periods. In the event that the holders of the 2024 Notes have the election to convert the 2024 Notes at any time during the prescribed measurement period, the 2024 Notes would then be considered a current obligation and classified as such.

As of December 31, 2018, the fair value of the 2024 Notes, which was estimated utilizing market quotations from an over-the-counter trading market, approximated 119% of their face value.

An entity must separately account for the liability and equity components of convertible debt instruments (such as the 2024 Notes) that may be settled entirely or partially in cash upon conversion in a manner that reflects the issuer's economic interest cost. The liability component of the instrument was valued in a manner that reflects the market interest rate for a similar nonconvertible instrument at the date of issuance. The initial carrying value of the liability component of $368.3 million was calculated using a 7.5% assumed borrowing rate. The equity component of $149.2 million, representing the conversion option, was determined by deducting the fair value of the liability component from the par value of the 2024 Notes and is recorded in additional paid-in capital on the consolidated balance sheet at the issuance date. That equity component is treated as a discount on the liability component of the 2024 Notes, which is amortized over the 7-year term of the 2024 Notes using the effective interest rate method. The equity component is not re-measured as long as it continues to meet the conditions for equity classification.

The Company allocated the total transaction costs of approximately $14.7 million related to the issuance of the 2024 Notes to the liability and equity components of the 2024 Notes based on their relative values. Transaction costs attributable to the liability component are amortized to interest expense over the seven-year term of the 2024 Notes, and transaction costs attributable to the equity component are netted with the equity component in stockholders' equity.

The 2024 Notes do not contain any financial or operating covenants or any restrictions on the payment of dividends, the issuance of other indebtedness or the issuance or repurchase of securities by the Company. The 2024 Indenture contains customary events of default with respect to the 2024 Notes, including that upon certain events of default, 100% of the principal and accrued and unpaid interest on the 2024 Notes will automatically become due and payable.

Convertible senior notes, net of discounts and deferred financing costs consisted of the following:

	December 31,	
(in thousands)	2018	2017
Principal	$517,500	$517,500
Deferred financing costs	(8,326)	(9,652)
Debt discount, net	(120,678)	(138,230)
Net carrying amount	$388,496	$369,618

NOTE 6. OTHER BALANCE SHEET DETAILS

Inventory consisted of the following:

December 31,

(in thousands)	2018	2017
Raw materials	$7,855	$—
Work in process	2,208	491
Finished goods	801	533
Total inventory	$10,864	$1,024

Property and equipment, net, consisted of the following:

	December 31,	
(in thousands)	2018	2017
Tenant improvements	$19,857	$2,019
Furniture and fixtures	2,968	1,303
Scientific equipment	28,163	26,248
Computer equipment	11,152	8,821
	62,140	38,391
Less accumulated depreciation	(28,271)	(27,580)
Property and equipment, net	$33,869	$10,811

Accounts payable and accrued liabilities consisted of the following:

	December 31,	
(in thousands)	2018	2017
Accrued employee related costs	$27,341	$24,901
Accounts payable	13,801	5,648
Accrued development costs	7,069	4,799
Other accrued liabilities	38,166	18,172
Total accounts payable and accrued liabilities	$86,377	$53,520

NOTE 7. NET INCOME (LOSS) PER SHARE

Net income (loss) per share was calculated as follows:

	Year Ended December 31,		
(in thousands, except per share data)	2018	2017	2016
Net income (loss) - basic and diluted	$21,111	$(142,542)	$(141,090)
Weighted-average common shares outstanding:			
Basic	90,235	88,089	86,713
Effect of dilutive securities:			
Employee stock purchase program	11	—	—
Stock options	3,228	—	—
Restricted stock units	564	—	—
2024 Notes	1,348	—	—
Diluted	95,386	88,089	86,713
Net income (loss) per share:			
Basic	$0.23	$(1.62)	$(1.63)
Diluted	$0.22	$(1.62)	$(1.63)

Shares which have been excluded from diluted per share amounts because their effect would have been anti-dilutive include the following:

	Year Ended December 31,		
(in thousands)	2018	2017	2016
Stock options and restricted stock units	887	7,436	6,995

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 19 million shares of Company's 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. In May 2018, the Company adopted the Neurocrine Biosciences, Inc. ESPP pursuant to which 300,000 shares of the Company's common stock are authorized for issuance. No purchases have occurred under the ESPP during the year ended December 31, 2018.

The Company also issues stock options and RSUs under the Neurocrine Biosciences, Inc. Inducement Plan (Inducement Plan) to certain employees. The Company granted 70,000 stock options and 20,000 RSUs pursuant to the Inducement Plan in 2018 and granted 410,000 stock options and 12,500 RSUs pursuant to the Inducement Plan in 2017. The Company did not grant any stock options or RSUs pursuant to the Inducement Plan during 2016. These stock option grants have a 4-year vesting period and the RSUs generally have vesting periods of 3 to 4 years. The Company currently has 245,162 in stock options and RSUs outstanding under this Inducement Plan.

As of December 31, 2018, approximately 6.8 million shares of common stock remained available for the future grant of 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 the vesting of RSUs and PRSUs, and has 7.2 million shares of common stock reserved for such issuances as of December 31, 2018.

Vesting Provisions of Share-Based Compensation. Stock options generally have terms from 7 to 10 years from the date of grant, and generally vest over a 3 to 4-year period. The maximum contractual term for all options granted from the 2011 Plan is 10 years. RSUs granted under the 2011 Plan generally have vesting periods of 4 years. PRSUs granted under the 2011 Plan vest based on the achievement of certain pre-defined Company-specific performance criteria and expire 4 to 5 years from the grant date.

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

	Year Ended December 31,		
(in thousands)	2018	2017	2016
Sales, general and administrative expense	$31,847	$27,951	$16,770
Research and development expense	26,221	14,571	11,694
Share-based compensation expense	$58,068	$42,522	$28,464

Stock Options. The exercise price of all stock options granted during the years ended December 31, 2018, 2017 and 2016 was equal to the closing price of the Company's common stock on the date of grant. The estimated fair value of each stock 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, 2018:

	Year Ended December 31,		
(in thousands)	2018	2017	2016
Risk-free interest rate	2.5 %	2.0 %	1.4 %
Expected volatility of common stock	59.5%	58.0 %	60.0 %
Dividend yield	0.0 %	0.0 %	0.0 %
Expected option term	4.7 years	5.7 years	5.6 years

The Company estimates the fair value of stock options using a Black-Scholes option-pricing model on the date of grant. The fair values of equity instruments 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, 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.

The Company's determination of fair value is affected by its stock price as well as a number of assumptions that require judgment. The weighted-average fair values of stock options granted during the years ended December 31, 2018, 2017 and 2016, estimated as of the grant date using the Black-Scholes option-pricing model, were $43.42, $25.11 and $21.49, respectively.

A summary of the status of the Company's stock options as of December 31, 2018, 2017 and 2016 and of changes in options outstanding under the plans during the three years ended December 31, 2018 is as follows:

	2018		2017		2016	
(in thousands, except weighted average data)	Options	Weighted Average Exercise Price	Options	Weighted Average Exercise Price	Options	Weighted Average Exercise Price
Outstanding at January 1	6,356	$ 28.83	6,112	$ 20.01	5,507	$ 15.63
Granted	1,040	84.97	1,807	46.55	1,077	40.19
Exercised	(1,592)	18.95	(1,353)	10.41	(341)	7.60
Canceled	(58)	64.67	(210)	43.05	(131)	34.35
Outstanding at December 31	5,746	$ 41.38	6,356	$ 28.83	6,112	$ 20.01

Stock options outstanding at December 31, 2018 had a weighted average remaining contractual term of 6.7 years.

For the year ended December 31, 2018, 2017 and 2016 share-based compensation expense related to stock options was $35.4 million, $28.2 million, and $18.4 million, respectively. As of December 31, 2018, there was approximately $55.4 million of unamortized compensation cost related to stock options, which is expected to be recognized over a weighted average remaining vesting period of approximately 2.3 years. As of December 31, 2018, there were approximately 3.9 million stock options exercisable with a weighted average exercise price of $31.07 and a weighted-average remaining contractual term of 5.9 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, 2018, 2017, and 2016 was $117.0 million, $61.4 million, and $13.2 million, respectively. As of December 31, 2018, the total intrinsic value of stock options outstanding and exercisable was $186.3 million and $158.2 million, respectively. Cash received from stock option exercises for the years ended December 31, 2018, 2017, and 2016 was $29.5 million, $13.9 million, and $2.4 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. For the year ended December 31, 2018, 2017, and 2016, share-based compensation expense related to RSUs was $21.9 million, $13.9 million, and $8.3 million, respectively. As of December 31, 2018, there was approximately $51.6 million of unamortized compensation cost related to RSUs, which is expected to be recognized over a weighted average remaining vesting period of approximately 2.3 years.

The total intrinsic value of RSUs converted into common shares during the years ended December 31, 2018, 2017, and 2016 was $35.5 million, $14.9 million, and $12.2 million, 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, 2018 was $80.9 million based on the Company's closing stock price on that date.

A summary of the status of the Company's RSUs as of December 31, 2018, 2017, and 2016 and of changes in RSUs outstanding under the plans for the three years ended December 31, 2018 is as follows:

	2018		2017		2016	
(in thousands, except weighted average data)	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	1,080	$ 40.30	883	$ 29.33	910	$ 24.23
Granted	540	85.29	588	47.21	326	36.73
Cancelled	(58)	36.21	(41)	40.62	(69)	32.50
Converted into common shares	(429)	59.23	(350)	24.19	(284)	20.71
Outstanding at December 31	1,133	$ 62.31	1,080	$ 40.30	883	$ 29.33

Performance-Based Restricted Stock Units. During each of the years ended December 31, 2018 and 2016, the Company granted approximately 0.2 million PRSUs that vest based on the achievement of certain pre-defined Company-specific performance criteria and expire approximately 4 to 5 years from the grant date. No PRSUs were granted during the year ended December 31, 2017. Additionally, 0.2 million PRSUs were earned during the year ended December 31, 2017. The fair value of PRSUs is estimated based on the closing sale price of the Company’s common stock on the date of grant. Expense recognition for PRSUs commences when attainment of the performance-based criteria is determined to be probable. During 2018, the Company recognized no expense related to PRSUs. During 2017 and 2016, the Company recognized approximately $0.4 million and $1.8 million, respectively, in expense related to PRSUs. At December 31, 2018, the total unrecognized estimated compensation expense related to PRSUs was $19.7 million

and the total intrinsic value of PRSUs outstanding was $23.6 million based on the Company's closing stock price on that date. The total intrinsic value of PRSUs converted into common shares was $8.8 million during the year ended December 31, 2017. No PRSUs were earned during the years ended December 31, 2018 or 2016.

Employee Stock Purchase Plan. Under the ESPP, eligible employees may purchase shares of the Company's common stock at a discount semi-annually based on a percentage of their annual compensation. The ESPP provides for the granting of up to 300,000 shares of the Company's common stock to eligible employees. The discounted purchase price is equal to the lower of 85% of (i) the market value per share of the common stock on the first day of the offering period or (ii) the market value per share of common stock on the purchase date. Share-based compensation expense recognized under the ESPP was $0.8 million for the year ended December 31, 2018.

NOTE 9. INCOME TAXES

The components of the income tax expense for continuing operations are as follows:

(in thousands)	2018	2017	2016
Current:			
Federal	$(100)	$ —	$ —
State	830	—	—
Total income tax expense	$730	$ —	$ —

The provision for income taxes on earnings subject to income taxes differs from the statutory federal rate at December 31, 2018, 2017 and 2016, due to the following:

(in thousands)	2018	2017	2016
Federal income taxes at 21% for 2018 and 35% for 2017 and 2016	$4,587	$(49,889)	$(49,383)
State income tax, net of federal benefit	361	(4,013)	2
Tax effect on non-deductible expenses	446	433	(321)
Share-based compensation expense	(9,778)	(19,589)	(5,077)
Officer compensation	915	2,163	—
Change in tax rate	(198)	154,415	—
Expired tax attributes	13,874	2,998	6,708
Research credits	(13,526)	(5,596)	(5,554)
Change in valuation allowance	4,306	(79,966)	53,414
Other	(257)	(956)	211
	$730	$—	$—

Significant components of the Company’s deferred tax assets and liabilities as of December 31, 2018 and 2017 are listed below. A valuation allowance of $335.2 million and $330.9 million at December 31, 2018 and 2017, respectively, has been recognized to offset net deferred tax assets as realization of such assets is uncertain. Amounts are shown as of December 31 as of each respective year:

(in thousands)	2018	2017
Deferred tax assets:		
Net operating losses	$223,800	$238,500
R&D credits	62,200	47,500
Capitalized R&D	34,800	47,500
Share-based compensation	17,300	14,600
Other	28,600	14,600
Total deferred tax assets	366,700	362,700
Deferred tax liabilities:		
Convertible senior notes	(26,400)	(31,300)
Fixed assets	(5,100)	(500)
Total deferred tax liabilities	(31,500)	(31,800)
Net of deferred tax assets and liabilities	335,200	330,900
Valuation allowance	(335,200)	(330,900)
Net deferred tax assets	$—	$—

At December 31, 2018, the Company had federal and state income tax net operating loss carry forwards of approximately $1.0 billion and $398.0 million, respectively. The federal net operating losses will begin to expire in 2021, unless previously utilized.

A portion of the California net operating loss carry forwards expired in 2018. The remaining California net operating losses will begin to expire in 2028 and the net operating losses related to other states will begin to expire in 2026.

In addition, the Company has federal and California R&D tax credit carry forwards of $63.6 million and $41.6 million, respectively. A portion of the federal R&D tax credit carry forwards expired in 2018. The remaining federal R&D tax credits will continue to expire beginning in 2019, unless previously utilized. The California R&D tax credits carry forward indefinitely.

Additionally, the future utilization of the Company’s net operating loss and R&D tax credit carry forwards to offset future taxable income may be subject to annual limitations, pursuant to Internal Revenue Code Sections 382 and 383, as a result of ownership changes that could result in the future. The Company has determined that no ownership changes have occurred through December 31, 2018.

On December 22, 2017, the Tax Cuts and Jobs Act (TCJA) was enacted, reducing the corporate income tax rate from 35% to 21% effective on January 1, 2018. The carrying value of the Company's deferred tax assets is also determined by the enacted U.S. corporate income tax rate. Consequently, any changes in the U.S. corporate income tax rate have impacted the carrying value of the Company’s deferred tax assets. Under the new corporate income tax rate of 21%, deferred income taxes decreased, with a corresponding decrease to the valuation allowance. Therefore, the TCJA had no impact on the Company's 2017 earnings. As of December 31, 2018, the Company has completed its accounting of the tax effects from the enactment of the TCJA.

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 FASB provides accounting guidance on derecognition, classification, interest and penalties, accounting in interim periods, disclosure, and transition.

The Company’s policy is to recognize interest or penalties related to income tax matters in income tax expense. Interest and penalties related to income tax matters were not material for the years ended December 31, 2018 or 2017.

The Company is subject to taxation in the U.S. and various state jurisdictions. The Company’s tax years for 2001 (federal) and 2008 (California) and forward are subject to examination by the U.S. and state tax authorities due to the carry forward of unutilized net operating losses and R&D tax credits.

The following table summarizes the activity related to unrecognized tax benefits:

(in thousands)	2018	2017	2016
Balance as of the beginning of the year	$37,403	$34,112	$33,074
Increases related to prior year tax positions	6,103	—	260
Increases related to current year tax positions	11,726	3,291	2,211
Expiration of the statute of limitations for the assessment of taxes	(457)	—	(1,433)
Balance as of the end of the year	$54,775	$37,403	$34,112

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 $11.7 million for current year tax positions, as reflected in the table above.

As of December 31, 2018, the Company had $50.1 million of unrecognized tax benefits that, if recognized and realized, would affect the effective tax rate.

In the next 12 months, the Company does not expect a significant change in its unrecognized tax benefits.

NOTE 10. LEASES

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. The ultimate result of this real estate sale was a net deferred gain of $39.1 million, of which the Company recognized $0.7 million in 2018, $2.1 million in 2017, and $3.4 million in 2016. As of December 31, 2018, the remaining balance of the net deferred gain was approximately $7.3 million, which the Company expects to recognize as a cumulative-effect adjustment to equity upon adoption of Topic 842 on January 1, 2019. Refer to Note 1 to the consolidated financial statements for more information on the impact of adoption.

Upon the closing of the sale of the facility and associated real property, the Company entered into an agreement (original lease) whereby it leased back the Company’s corporate headquarters, comprised of two buildings located in San Diego, California, for an initial term of 12 years. In 2008 through 2011, the Company entered into a series of subsequent amendments to the original lease, whereby the Company vacated a building and continued to occupy one building.

In June 2017, the Company entered into an amendment to extend the current term of the original lease through December 31, 2029. Under the terms of the amendment, the Company reduced the base rental rate by approximately 8% and will continue to pay base annual rent (subject to an annual fixed percentage increase), plus a 3.5% annual management fee, property taxes, and other normal and necessary expenses, such as utilities, repairs, and maintenance. Certain incentives were included in the lease, including approximately $13.1 million in tenant improvement allowances, three months of rent abatement, and a reduction in the required security deposit amount from $4.7 million to $3.0 million. In lieu of a cash security deposit, Wells Fargo Bank, N.A. issued on the Company’s behalf a $3.0 million letter of credit, which is secured by a deposit of equal amount with the same bank. The Company has the right to extend the lease for 2 consecutive 10-year terms and right of first offer for future rental of adjacent office space owned by the landlord.

In May 2018, the Company entered into an agreement to lease 44,718 square feet of office space, which commenced on July 1, 2018, for a term of 10 years and 10 months. Under the terms of the lease, the Company will pay base annual

rent (subject to an annual fixed percentage increase), plus property taxes, and other normal and necessary expenses, such as utilities, repairs, and maintenance. Certain incentives were included in the lease, including approximately $4.2 million in tenant improvement allowances and twelve months of rent abatement. In lieu of a cash security deposit, Wells Fargo Bank, N.A. issued on the Company's behalf a $1.0 million letter of credit, which is secured by a deposit of equal amount with the same bank. The Company does not have the right to extend the lease or right of first offer for future rental of adjacent office space owned by the landlord.

The Company recognizes rent expense on a straight-line basis over the term of the associated lease. Accordingly, rent expense recognized in excess of rent paid is reflected as a liability in the Company's consolidated balance sheets. Gross rent expense was approximately $6.9 million for 2018, $5.9 million for 2017, and $6.0 million for 2016.

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 $1.8 million, $1.1 million, and $0.6 million for the years ended December 31, 2018, 2017 and 2016, respectively.

NOTE 12. COMMITMENTS AND CONTINGENCIES

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 entered into in-licensing 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 received licenses to research tools, know-how, and technology claimed in certain patents or patent applications. The Company is 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 in-licensed technology. The Company continually reassesses the value of the license agreements and cancels them when research efforts are discontinued on these programs. As of December 31, 2018, the Company may be required to pay milestone payments of up to $1.0 billion over the lives of these agreements, in addition to royalties on sales of the affected products at rates ranging up to 6%. Due to the uncertainties of the development process, the timing and probability of the milestone and royalty payments cannot be accurately estimated.

The Company is not aware of any 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 13. SUBSEQUENT EVENTS

On January 28, 2019, the Company entered into a collaboration and license agreement with a clinical-stage gene therapy company, Voyager Therapeutics, Inc., or Voyager. The collaboration is focused on the development and commercialization of four programs using Voyager's proprietary gene therapy platforms. The four programs consist of Voyager's VY-AADC program for Parkinson's disease, Voyager's VY-FXN01 program for Friedreich's ataxia, as well as rights to two programs to be determined by the parties in the future. In connection with the agreement, the Company agreed to pay Voyager a $115 million upfront cash payment and entered into an agreement to purchase $50 million of Voyager's common stock. Pursuant to development plans agreed to by the Company and Voyager, unless Voyager exercises the co-development and co-commercialization rights that are described below, the Company has agreed to be responsible for all development costs. Upon the occurrence of a specified event for each program, the Company has agreed to assume responsibility for development, manufacturing, and commercialization activities for

such program. Additionally, Voyager may be entitled to earn up to $1.7 billion in development, regulatory, and commercial milestones across the four programs and royalties for net sales in and outside the U.S.

Under the terms of the agreement, on a program-by-program basis, upon the achievement of milestones or metrics specified in the agreement for VY-AADC and VY-FXN01, Voyager will have the option to co-develop and co-commercialize such program with the Company in the U.S. under cost- and profit-sharing arrangements, and Voyager agrees to forfeit certain milestones and royalties related to such program for which Voyager has exercised its co-develop and co-commercialize option.

The effectiveness of the agreement and the closing of the sale and issuance of the Voyager common stock described above are subject to certain conditions, including the expiration or termination of the applicable waiting period under the Hart-Scott-Rodino Antitrust Improvements Act of 1976, as amended, and other customary closing conditions.

NOTE 14. SELECTED QUARTERLY FINANCIAL DATA (UNAUDITED)

The following is a summary of the quarterly results of the Company for the years ended December 31, 2018 and 2017:

(in thousands, except per share data)	First Quarter	Second Quarter	Third Quarter	Fourth Quarter
2018:				
Revenues	$71,086	$96,905	$151,757	$131,492
Operating expenses	$108,533	$98,757	$97,434	$109,621
Net (loss) income	$(41,818)	$(5,913)	$50,764	$18,078
Net (loss) income per share:				
Basic	$(0.47)	$(0.07)	$0.56	$0.20
Diluted	$(0.47)	$(0.07)	$0.52	$0.19
Shares used in the calculation of net (loss) income per share:				
Basic	89,526	90,100	90,555	90,742
Diluted	89,526	90,100	96,798	95,724
2017:				
Revenues	$—	$6,335	$60,774	$94,517
Operating expenses	$79,932	$63,603	$66,769	$82,683
Net (loss) income	$(78,326)	$(59,985)	$(11,125)	$6,894
Net (loss) income per share:				
Basic	$(0.90)	$(0.68)	$(0.13)	$0.08
Diluted	$(0.90)	$(0.68)	$(0.13)	$0.07
Shares used in the calculation of net (loss) income per share:				
Basic	87,283	88,063	88,325	88,665
Diluted	87,283	88,063	88,325	92,659

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.

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, 2018. 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, 2018, 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.

Report of Independent Registered Public Accounting Firm

To the Shareholders and the Board of Directors of

Neurocrine Biosciences, Inc.

Opinion on Internal Control over Financial Reporting

We have audited Neurocrine Biosciences, Inc.'s internal control over financial reporting as of December 31, 2018, 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). In our opinion, Neurocrine Biosciences, Inc. (the Company) maintained, in all material respects, effective internal control over financial reporting as of December 31, 2018, based on the COSO criteria.

We also have audited, in accordance with the standards of the Public Company Accounting Oversight Board (United States) (PCAOB), the consolidated balance sheets of the Company as of December 31, 2018 and 2017, the related consolidated statements of operations and comprehensive income (loss), stockholders' equity, and cash flows, for each of the three years in the period ended December 31, 2018, and the related notes and our report dated February 7, 2019 expressed an unqualified opinion thereon.

Basis for Opinion

The Company'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 are a public accounting firm registered with the PCAOB and are required to be independent with respect to the Company in accordance with the U.S. federal securities laws and the applicable rules and regulations of the Securities and Exchange Commission and the PCAOB.

We conducted our audit in accordance with the standards of the PCAOB. 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.

Definition and Limitations of Internal Control Over Financial Reporting

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.

/s/ Ernst & Young LLP

San Diego, California

February 7, 2019

ITEM 9B. OTHER INFORMATION

None.

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 2019 Annual Meeting of Stockholders, to be filed pursuant to Regulation 14A with the Securities and Exchange Commission within 120 days of December 31, 2018. 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 2019 Annual Meeting of Stockholders, to be filed pursuant to Regulation 14A with the Securities and Exchange Commission within 120 days of December 31, 2018. 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 2019 Annual Meeting of Stockholders, to be filed pursuant to Regulation 14A with the Securities and Exchange Commission within 120 days of December 31, 2018. 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 2019 Annual Meeting of Stockholders, to be filed pursuant to Regulation 14A with the Securities and Exchange Commission within 120 days of December 31, 2018. Such information is incorporated herein by reference.

ITEM 14. PRINCIPAL ACCOUNTING FEES AND SERVICES

Information required by this item will be contained in our Definitive Proxy Statement for our 2019 Annual Meeting of Stockholders, to be filed pursuant to Regulation 14A with the Securities and Exchange Commission within 120 days of December 31, 2018. Such information is incorporated herein by reference.

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, 2018 and 2017

Consolidated Statements of Comprehensive Income (Loss) for the years ended December 31, 2018, 2017 and 2016

Consolidated Statements of Stockholders' Equity for the years ended December 31, 2018, 2017 and 2016

Consolidated Statements of Cash Flows for the years ended December 31, 2018, 2017 and 2016

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, as amended(1)
3.2	Bylaws, as amended(2)
4.1	Form of Common Stock Certificate(3)
4.2	Indenture, dated as of May 2, 2017, by and between the Company and U.S. Bank National Association, as Trustee(4)
4.3	Form of Note representing the Company's 2.25% Convertible Notes due 2024(5)
Collaboration and License Agreements	
10.1*	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(6)
10.2*	First Amendment to Collaboration and License Agreement Dated August 31, 2011 between the Company and Abbott International Luxemburg S.a.r.l.(7)

10.3*	Collaboration and License Agreement dated March 31, 2015 between Mitsubishi Tanabe Pharma Corporation and the Company(8)
10.4*	License Agreement dated February 9, 2017 between BIAL– Portela & CA, S.A. and the Company(9)
10.5*	Collaboration and License Agreement dated January 28, 2019 between Voyager Therapeutics, Inc. and the Company
10.6	Stock Purchase Agreement dated January 28, 2019 between Voyager Therapeutics, Inc. and the Company
10.7	Investor Agreement dated January 28, 2019 between Voyager Therapeutics, Inc. and the Company

Manufacturing Agreements

10.8*	Master Manufacturing Services Agreement dated November 28, 2016, by and between Patheon UK Limited and the Company(10)
10.9*	Product Agreement dated November 28, 2016, by and between Patheon UK Limited and the Company(11)
10.10*	Commercial Supply Agreement dated March 9, 2017 between F.I.S. – FABBRICA ITALIANA SINTETICI S.p.A. and the Company
10.11*	Amended and Restated Product Agreement dated June 27, 2017 by and between Patheon UK Limited and the Company(12)

Equity Plans and Related Agreements

10.12** Neurocrine Biosciences, Inc. 2003 Incentive Stock Plan, as amended and form of stock option agreement and restricted

stock unit agreement(13)

10.13** Neurocrine Biosciences, Inc. 2011 Equity Incentive Plan, as amended(14)

10.14** Form of Stock Option Grant Notice and Option Agreement for use under the Neurocrine Biosciences, Inc. 2011 Equity Incentive Plan, and Form of Restricted Stock Unit Grant Notice and Restricted Stock Unit Agreement for use under the Neurocrine Biosciences, Inc. 2011 Equity Incentive Plan(15)

10.15** Neurocrine Biosciences, Inc. Inducement Plan, as amended(16)

10.16** Form of Stock Option Grant Notice and Option Agreement for use under the Neurocrine Biosciences, Inc. Inducement Plan, and Form of Restricted Stock Unit Grant Notice and Restricted Stock Unit Agreement for use under the Neurocrine Biosciences, Inc. Inducement Plan(17)

10.17** Neurocrine Biosciences, Inc. 2018 Employee Stock Purchase Plan dated May 30, 2018(18)

Agreements with Officers and Directors

10.18** Amended and Restated Employment Agreement effective August 1, 2007 between the Company and Kevin C. Gorman, Ph.D.(19)

10.19** Amended and Restated Employment Agreement effective August 6, 2007 between the Company and Christopher F. O'Brien M.D.(20)

10.20** Amended and Restated Employment Agreement effective August 14, 2007 between the Company and Haig P. Bozigian, Ph.D.(21)

10.21** Form of Amendment to Employment Agreement for executive officers, effective as of December 15, 2010(22)

10.22** Employment Agreement dated May 26, 2015 between the Company and Eric Benevich(23)

10.23** Employment Agreement effective November 29, 2017 between the Company and Matthew C. Abernethy(24)

10.24** Form of Indemnity Agreement entered into between the Company and its officers and directors(25)

Agreements Related to Real Property

10.25 Amended and Restated Lease dated November 1, 2011 between the Company and Kilroy Realty, L.P.(26)

10.26 First Amendment to Amended and Restated Lease between the Company and Kilroy Realty, L.P., dated June 5, 2017(27)

10.27 Second Amendment to Amended and Restated Lease between the Company and Kilroy Realty, L.P., dated October 12, 2017(28)

10.28

	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 and June 19, 2017(29)
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 Exhibit 3.1 of the Company’s Quarterly Report on Form 10-Q filed on November 5, 2018

(2) Incorporated by reference to Exhibit 3.2 of the Company’s Quarterly Report on Form 10-Q filed on November 5, 2018

(3) Incorporated by reference to the Company's Registration Statement on Form S-1 (Registration No. 333-03172)
(4) Incorporated by reference to Exhibit 4.1 of the Company's Current Report on Form 8-K filed on May 2, 2017
(5) Incorporated by reference to Exhibit 99.1 of the Company's Current Report on Form 8-K filed on May 2, 2017
(6) Incorporated by reference to Exhibit 10.2 of the Company's Quarterly Report on Form 10-Q filed on July 29, 2010
(7) Incorporated by reference to Exhibit 10.2 of the Company's Quarterly Report on Form 10-Q filed on October 31, 2011
(8) Incorporated by reference to Exhibit 10.1 of the Company's Quarterly Report on Form 10-Q filed on April 30, 2015
(9) Incorporated by reference to Exhibit 99.4 of the Company's Current Report on Form 8-K filed on April 25, 2017
(10) Incorporated by reference to Exhibit 99.1 of the Company's Current Report on Form 8-K filed on April 25, 2017
(11) Incorporated by reference to Exhibit 99.2 of the Company's Current Report on Form 8-K filed on April 25, 2017
(12) Incorporated by reference to Exhibit 10.2 of the Company's Quarterly Report on Form 10-Q filed on November 1, 2017
(13) Incorporated by reference to Exhibit 10.1 of the Company's Quarterly Report on Form 10-Q filed on July 30, 2009
(14) Incorporated by reference to Exhibit 99.1 of the Company's Current Report on Form 8-K filed on May 30, 2018
(15) Incorporated by reference to Exhibit 99.1 of the Company's Current Report on Form 8-K filed on June 1, 2015
(16) Incorporated by reference to Exhibit 10.17 of the Company's Annual Report on Form 10-K filed on February 13, 2018
(17) Incorporated by reference to Exhibit 10.1 of the Company's Quarterly Report on Form 10-Q filed on July 29, 2015
(18) Incorporated by reference to Exhibit 99.2 of the Company's Current Report on Form 8-K filed on May 30, 2018
(19) Incorporated by reference to Exhibit 10.3 of the Company's Quarterly Report on Form 10-Q filed on August 3, 2007
(20) Incorporated by reference to Exhibit 10.35 of the Company's Annual Report on Form 10-K filed on February 10, 2011
(21) Incorporated by reference to Exhibit 10.37 of the Company's Annual Report on Form 10-K filed on February 11, 2008
(22) Incorporated by reference to Exhibit 10.35 of the Company's Annual Report on Form 10-K filed on February 11, 2008
(23) Incorporated by reference to Exhibit 10.32 of the Company's Annual Report on Form 10-K filed on February 14, 2017
(24) Incorporated by reference to Exhibit 10.26 of the Company's Annual Report on Form 10-K filed on February 13, 2018
(25) Incorporated by reference to Exhibit 10.1 of the Company's Quarterly Report on Form 10-Q filed on November 1, 2017
(26) Incorporated by reference to Exhibit 99.2 of the Company's Current Report on Form 8-K filed on January 18, 2012
(27) Incorporated by reference to Exhibit 10.1 of the Company's Quarterly Report on Form 10-Q filed on August 3, 2017
(28) Incorporated by reference to Exhibit 10.3 of the Company's Quarterly Report on Form 10-Q filed on November 1, 2017
(29) Incorporated by reference to Exhibit 10.3 of the Company's Current Report on Form 8-K filed on December 10, 2007; Exhibit 10.5 of the Company's Annual Report on Form 10-K filed on February 9, 2015; and Exhibit 10.2 of the Company's Quarterly Report on Form 10-Q filed on August 3, 2017

* 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.

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
Chief Executive Officer

Date: February 7, 2019

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	Chief Executive Officer	February 7, 2019
Kevin C. Gorman	and Director	
	(Principal Executive Officer)	
/s/ Matthew C. Abernethy	Chief Financial Officer	February 7, 2019
Matthew C. Abernethy	(Principal Financial and Accounting Officer)	
/s/ William H. Rastetter	Chairman of the Board of Directors	February 7, 2019
William H. Rastetter		
/s/ Gary A. Lyons	Director	February 7, 2019
Gary A. Lyons		
/s/ George J. Morrow	Director	February 7, 2019
George J. Morrow		
/s/ Richard F. Pops	Director	February 7, 2019
Richard F. Pops		

/s/ Alfred W. Sandrock, Jr.	Director	February 7, 2019
Alfred W. Sandrock, Jr.		
/s/ Stephen A. Sherwin	Director	February 7, 2019
Stephen A. Sherwin		