

NEUROCRINE BIOSCIENCES INC

Form 10-K

February 13, 2018

[Table of Contents](#)

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, 2017

OR

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

Commission file number: 0-22705

NEUROCRINE BIOSCIENCES, INC.

(Exact name of registrant as specified in its charter)

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Delaware
(State or other jurisdiction of
incorporation or organization)
12780 El Camino Real, San Diego, CA
(Address of principal executive offices)

33-0525145
(I.R.S. Employer
Identification Number)
92130
(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 and posted on its corporate Web site, if any, every Interactive Data File required to be submitted and posted pursuant to Rule 405 of Regulation S-T (§ 232.405 of this chapter) during the preceding 12 months (or for such shorter period that the registrant was required to submit and post such files). Yes No

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

Indicate by check mark whether the registrant is a large accelerated filer, an accelerated filer, a non-accelerated filer, 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

(Do not check if a 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

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The aggregate market value of the common equity held by non-affiliates of the registrant as of June 30, 2017 totaled approximately \$3,407,988,476 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, 2017. The identification of 10% or greater stockholders as of June 30, 2017 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 2, 2018, there were 89,273,537 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, 2017 are incorporated by reference into Part III of this report	III

Table of Contents

TABLE OF CONTENTS

	Page
<u>PART I</u>	
Item 1. <u>Business</u>	3
Item 1A. <u>Risk Factors</u>	26
Item 1B. <u>Unresolved Staff Comments</u>	46
Item 2. <u>Properties</u>	46
Item 3. <u>Legal Proceedings</u>	46
Item 4. <u>Mine Safety Disclosures</u>	46
<u>PART II</u>	
Item 5. <u>Market for Registrant's Common Equity, Related Stockholder Matters and Issuer Purchases of Equity Securities</u>	47
Item 6. <u>Selected Financial Data</u>	49
Item 7. <u>Management's Discussion and Analysis of Financial Condition and Results of Operations</u>	50
Item 7A. <u>Quantitative and Qualitative Disclosures about Market Risk</u>	65
Item 8. <u>Financial Statements and Supplementary Data</u>	66
Item 9. <u>Changes in and Disagreements with Accountants on Accounting and Financial Disclosure</u>	95
Item 9A. <u>Controls and Procedures</u>	95
Item 9B. <u>Other Information</u>	98
<u>PART III</u>	
Item 10. <u>Directors, Executive Officers and Corporate Governance</u>	99
Item 11. <u>Executive Compensation</u>	99
Item 12. <u>Security Ownership of Certain Beneficial Owners and Management and Related Stockholder Matters</u>	99
Item 13. <u>Certain Relationships and Related Transactions, and Director Independence</u>	99
Item 14. <u>Principal Accounting Fees and Services</u>	99
<u>PART IV</u>	
Item 15. <u>Exhibits, Financial Statement Schedules</u>	100

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.

Table of Contents

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

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

ITEM 1. BUSINESS

Overview

We were originally incorporated in California in January 1992 and were 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 R&D platform, focused on neurological and endocrine based diseases and disorders. Our portfolio of products and product candidates is led by INGREZZA® (valbenazine), a vesicular monoamine transporter 2 (VMAT2) inhibitor for the treatment of movement disorders which was approved by the U.S. Food and Drug Administration (FDA) on April 11, 2017 for the treatment of tardive dyskinesia (TD). Our three lead late-stage clinical programs are INGREZZA (valbenazine) for Tourette syndrome, elagolix, a gonadotropin-releasing hormone (GnRH) antagonist for women's health that is partnered with AbbVie Inc. (AbbVie), and opicapone, a highly-selective catechol-O-methyltransferase inhibitor (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 - Portela & CA, S.A. (BIAL).

We believe that INGREZZA has the potential to address important unmet medical needs in neurological and psychiatric disorders beyond TD and we plan to continue to study the use of INGREZZA in other disease states. We are currently investigating the utilization of INGREZZA in Tourette syndrome. We have completed three clinical trials in Tourette's patients and a Phase IIb study in children with Tourette syndrome is currently ongoing. We intend to utilize the results of these studies to discuss with the FDA a plan for New Drug Application (NDA) submission for INGREZZA in Tourette syndrome patients.

Table of Contents

Our partner AbbVie has successfully completed the placebo-controlled portion of two Phase III studies of elagolix in women with endometriosis. Based on the positive results of these studies, AbbVie submitted an NDA to the FDA for elagolix to treat women with endometriosis during the third quarter of 2017. The NDA was accepted for priority review by the FDA and given a Prescription Drug User Fee Act (PDUFA) date in the second quarter of 2018. In addition, AbbVie is also assessing elagolix in women with uterine fibroids. The Phase III program began in early 2016 with two replicate studies of women with heavy uterine bleeding associated with uterine fibroids. AbbVie expects initial top-line efficacy data from the Phase III uterine fibroids program to be available in the first quarter of 2018, and based on the results of the study anticipates a subsequent NDA submission in 2019.

On February 9, 2017, we entered into an exclusive licensing agreement with BIAL for the development and commercialization of opicapone in the United States and Canada. Opicapone is a once-daily, peripherally-acting, highly-selective COMT inhibitor that was approved in June 2016 by the European Medicines Agency (EMA) as an adjunct therapy to preparations of levodopa/DOPA decarboxylase inhibitors for adult patients with Parkinson's disease and end-of-dose motor fluctuations who cannot be stabilized on those combinations. We held a meeting with the FDA in January 2018 to discuss a potential NDA submission for opicapone and we are currently awaiting the final summary meeting minutes which we expect to receive in February 2018. We intend to commercialize opicapone in the United States and Canada upon the receipt of applicable regulatory approvals.

Our Product Pipeline

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

Program	Target Indication(s)	Status	Rights
Approved products:			
INGREZZA® (valbenazine)	Tardive Dyskinesia	Marketed	Neurocrine/Mitsubishi Tanabe (Asia-Pacific)
Product candidates in clinical development:			
elagolix	Endometriosis	Phase III	AbbVie
elagolix	Uterine Fibroids	Phase III	AbbVie
opicapone	Parkinson's Disease	Phase III	Neurocrine (U.S. and Canada)/BIAL
INGREZZA® (valbenazine)	Tourette Syndrome	Phase IIb	Neurocrine/Mitsubishi Tanabe (Asia-Pacific)
NBI-74788	Classic Congenital	Phase II	Neurocrine
	Adrenal Hyperplasia		
Research programs:			
Neurological/Neuropsychiatric (e.g. VMAT2 Inhibitors)	Movement Disorders,	Research	Neurocrine
	Bipolar Disorder and		
	Schizophrenia		
CNS Disorders (Targeted by G Protein-Coupled Receptors and Ion Channels)	Epilepsy, Essential Tremor, Dystonia, Other Indications	Research	Neurocrine

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

Table of Contents

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.

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

INGREZZA® (valbenazine) Vesicular Monoamine Transporter 2 Inhibitor (VMAT2)

VMAT2 is a protein concentrated in the human brain that is essential for the transmission of nerve impulses between neurons. VMAT2 is primarily responsible for packaging and transporting monoamines (dopamine, norepinephrine, serotonin, and histamine) in neurons. Specifically, dopamine enables neurotransmission among nerve cells that are involved in voluntary and involuntary motor control. Disease states such as 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 Tardive Dyskinesia. TD is defined by hyperkinetic involuntary movements which arise after months or years of treatment with dopamine receptor blocking agents, e.g. antipsychotics 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 United States 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 have committed to conduct certain post-marketing studies including Phase 1 (e.g., pharmacokinetics (PK) in volunteers with renal impairment) and Phase 4 (e.g., randomized placebo-controlled withdrawal in TD patients). We expect to conduct these studies over the next four years in accordance with FDA guidance.

Tourette syndrome. Tourette syndrome is a neurological disorder that consists of rapid, non-rhythmic stereotyped motor and vocal tics. Motor tics are typically characterized by facial grimacing, head jerks, extremity movements and other dystonic movements. Vocal tics typically include grunting, throat clearing, and repeating words and phrases. The average age of onset for Tourette syndrome is approximately six years, with symptoms reaching their peak severity at approximately age ten. Tourette syndrome is more commonly diagnosed in males than females and may also be associated with attention deficit hyperactivity disorder and obsessive compulsive disorder. We were granted FDA Orphan Drug Designation for valbenazine for the treatment of pediatric patients with Tourette's syndrome in 2017. Orphan drug designation is granted by the FDA to drugs that are intended to treat rare diseases or conditions affecting fewer than 200,000 people in the United States. The orphan drug

Table of Contents

designation allows the orphan drug indication for the drug to be eligible for a seven-year period of U.S. marketing exclusivity upon approval of the drug, as well as other development assistance and financial incentives.

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

The T-Forward study was a randomized, double-blind, placebo-controlled, multi-dose, parallel group, study that enrolled 124 adults with moderate to severe Tourette syndrome. Two once-daily fixed doses of INGREZZA were evaluated versus placebo in a 1:1:1 randomization. The three-arm study included eight weeks of dosing followed by two weeks off-drug at 32 study centers in the United States to assess the safety, tolerability and efficacy of INGREZZA in Tourette patients. The primary endpoint of this study was a change from baseline of placebo versus active scores utilizing the Yale Global Tic Severity Scale at the end of week 8. Tourette symptoms were also be evaluated via the Premonitory Urge for Tics Scale as well as Clinical Global Impression of Change scales, among others. While the T-Forward study showed a significant improvement in overall symptoms of Tourette syndrome as evidenced by the Clinical Global Impression of Change ($p=0.015$), the pre-specified primary endpoint, the change-from-baseline in the Yale Global Tic Severity Scale at week 8 was not met ($p=0.18$). Adverse events were dose dependent and consistent with earlier clinical studies.

The T-Force GREEN study was a multicenter, randomized, double-blind, placebo-controlled, multi-dose, parallel group, Phase II study to evaluate the safety, tolerability and efficacy of INGREZZA in up to 90 pediatric patients with moderate to severe Tourette syndrome. Once-daily fixed doses of INGREZZA were evaluated versus placebo in a 1:1:1 randomization. The three-arm study evaluated 98 children and adolescents over six weeks of dosing followed by two weeks off-drug at approximately 40 study centers in the United States. The primary endpoint of this study is the change from baseline of the Yale Global Tic Severity Scale between placebo and active treatment groups at the end of week six. Exposure-response analysis showed that selected doses for the T-Force GREEN study were below the therapeutic range for adequate tic reduction in the majority of subjects. For the subset of subjects with pharmaceutical exposure in the appropriate range, there was a substantial reduction in tics. For subjects with sub-therapeutic exposure, tic reduction was comparable to placebo. Adverse events were consistent with those observed in previous INGREZZA studies.

Based on the results of the T-Force GREEN study and earlier studies of INGREZZA in Tourette patients, we initiated the T-Force GOLD study in October 2017. This study is a multicenter, randomized, double-blind, placebo-controlled, parallel group, Phase IIb study to evaluate the safety, tolerability, efficacy and optimal dose of once-daily INGREZZA in up to 120 pediatric patients with moderate to severe Tourette syndrome. Patients will receive either once-daily dosing of INGREZZA or placebo using a 1:1 randomization over 12 weeks of dosing followed by two weeks off-drug. The primary endpoint of this study is the change from baseline of the Yale Global Tic Severity Scale between placebo and active treatment groups at the end of week 12. Tourette symptoms will also be evaluated via the Premonitory Urge for Tics Scale as well as Clinical Global Impression Scales. Top-line data from this study is expected in late 2018.

Table of Contents

elagolix Gonadotropin-Releasing Hormone (GnRH) Antagonist

GnRH is a peptide that stimulates the secretion of the pituitary hormones that are responsible for sex steroid production and normal reproductive function. Researchers have found that chronic administration of GnRH agonists, after initial stimulation, reversibly shuts down this transmitter pathway and is clinically useful in treating hormone-dependent diseases such as endometriosis and uterine fibroids. Several companies have developed peptide GnRH agonists on this principle, such as Lupron® and Zoladex®. However, since these molecules are peptides, they must be injected via a depot formulation rather than the preferred oral route of administration. In addition, GnRH agonists can take up to several weeks to exert their desired effect once the initial stimulation has occurred, a factor not seen with the use of GnRH antagonists. Upon administration, GnRH agonists have shown a tendency to exacerbate the condition via a hormonal flare. More importantly the profound suppression effect observed with GnRH agonists is similar to that seen after menopause and can be associated with hot 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 elagolix and all next-generation non-peptide GnRH antagonists (collectively, GnRH Compounds) for women's and men's health indications. Under the terms of the agreement, AbbVie is responsible for all development, marketing and commercialization costs and has primary responsibility for all regulatory interactions with the FDA related to elagolix and other GnRH Compounds covered by the collaboration. AbbVie is currently in Phase III evaluation of elagolix in two indications, endometriosis and uterine fibroids.

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

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

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

The observed safety profile of elagolix in the Violet PETAL study was consistent with observations from earlier clinical studies. Among the most common adverse events were hot flush, headache, nausea and fatigue.

Table of Contents

While most adverse events were similar across treatment groups, some, such as hot flush and bone mineral density loss, were dose-dependent. Overall discontinuation rates were similar across treatment groups and discontinuations specifically due to adverse events were 5.9%, 6.4%, and 9.7% for placebo, 150 mg once daily and 200 mg twice daily, respectively.

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

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

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 and given a PDUFA date in the second quarter of 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 United States, with approximately 250,000 hysterectomies performed each year related to uterine fibroids (Whiteman *et al AJOG* 2008, 198, e1). We believe that a safe and effective oral therapy would be a preferred treatment regimen rather than surgical intervention.

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

Results from this Phase IIb study show elagolix reduced heavy menstrual bleeding in all treatment arms. The study's primary endpoint, a composite design where subjects had to achieve a menstrual blood loss (MBL)

Table of Contents

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

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

AbbVie initiated Phase III studies of elagolix in patients with uterine fibroids in early 2016. The Phase III program includes two replicate, pivotal, six-month efficacy and safety studies followed by a six-month safety and efficacy extension study. AbbVie is evaluating 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 will be the same as that employed in the Phase IIb study: percent of subjects with reduction in uterine blood flow as measured by the alkaline hematin method. AbbVie expects initial top-line data from this Phase III program in the first quarter of 2018, and based on the results of the study anticipates a subsequent NDA submission in 2019.

opicapone, Catechol-O-methyltransferase (COMT) Inhibitor

COMT inhibitors are utilized to prolong the duration of effect of levodopa which is utilized as a 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 are considered off-time. Opicapone is a novel, once-daily, peripherally-acting, highly-selective COMT inhibitor utilized as adjunct therapy to levodopa in Parkinson's patients. 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 United States and Canada. Under the terms of the agreement, we will be responsible for the development and commercialization of opicapone in the United States and Canada.

Parkinson's Disease. Parkinson's disease is a chronic and progressive movement disorder that affects approximately one 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 end-of-dose motor fluctuations. These end of dose motor fluctuations are improved with the addition of a COMT inhibitor to levodopa.

In June 2016, the EMA authorized ONGENTYS® (opicapone) as an adjunct therapy to preparations of levodopa/DOPA decarboxylase inhibitors (DDCIs) 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 European approval, BIPARK-I and BIPARK-II, demonstrated that opicapone once-daily achieved a statistically significant decrease in off-time periods for Parkinson's patients

Table of Contents

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 and we are currently awaiting the final summary meeting minutes which we expect to receive in February 2018. We intend to commercialize opicapone in the United States and Canada, subject to regulatory approvals.

NBI-74788- Corticotropin-Releasing Factor (CRF) Receptor₁ Antagonist

CRF is a hypothalamic hormone released directly into the hypophyseal portal vasculature which acts on specific CRF₁ receptors on corticotropes in the anterior pituitary to stimulate the release of adrenocorticotropin hormone (ACTH). The primary role of ACTH is the stimulation of the synthesis and release of adrenal steroids including cortisol. Cortisol from the adrenals have a negative feedback role at the level of the hypothalamus that decreases CRF release as well as at the level of the pituitary to inhibit the release of ACTH. This tight control loop is known as the hypothalamic-pituitary-adrenal (HPA) axis. Blockade of CRF receptors at the pituitary has been shown to decrease the release of ACTH and subsequently attenuate the production and release of adrenal steroids.

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

Corticosteroids are the current standard of care for classic CAH and are used chronically to both correct the endogenous cortisol deficiency and 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 receptor antagonist as demonstrated in a range of in vitro and in vivo assays. Blockade of CRF receptors at the pituitary has been shown to decrease the release of ACTH, which in turn decreases the production of adrenal steroids including androgens, and potentially the symptoms associated with classic CAH. Lower ACTH levels would also reduce the amount of exogenous corticosteroid necessary for classic CAH patients to thrive avoiding the side-effects currently associated with excessive steroid therapy.

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

Table of Contents

refractory classic CAH. This pilot study is designed to be an open-label, pharmacokinetic/pharmacodynamic study assessing two single, ascending doses of NBI-74788 in up to twenty study participants. Key pharmacodynamic biomarker measurements include ACTH, 17-hydroxyprogesterone (17-OHP), androgen, and cortisol levels collected the morning following bedtime dosing.

We intend to apply for orphan drug designation for NBI-74788 in the treatment of congenital adrenal hyperplasia. 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 United States and provides sponsors with development and commercial incentives for such designated compounds and medicines.

Research Programs

Our research and development focus is on addressing diseases and disorders of the central nervous and endocrine systems, which include therapeutic categories ranging from HPA disorders to stress-related disorders and neurological/neuropsychiatric diseases. Central nervous system and endocrinology drug therapies are among the largest therapeutic categories, accounting for over \$150 billion in worldwide drug sales according to GlobalData (2014).

Neurological/Neuropsychiatric: VMAT2 Inhibitors

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

Essential Tremor

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

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

G Protein-Coupled Receptors (GPCRs) are the largest known gene superfamily of the human genome. Greater than thirty percent of all marketed prescription drugs act on GPCRs; which makes this class of proteins historically the most successful therapeutic target family. However, only a small fraction of the GPCR gene superfamily has been exploited. Ion channels appear to be represented by approximately 400 genes in the human genome and are currently the targets for approximately seven percent of the current marketed drugs. Next-generation therapies derived from targeting GPCRs and ion channels will be discovered through the understanding of the complex relationships of drug/receptor interactions and their subsequent impact on efficacy, downstream signaling networks and regulation.

Our GPCR research platform has met this requirement by integrating drug discovery research efforts with a suite of assays and assay systems and automated analytical techniques. This process, now also applied to ion channels, provides an unbiased profile of pharmacological protein/ligand interactions coupled with *in vivo* efficacy using discrete animal models allowing for rapid discovery of initial leads and advancement into

Table of Contents

preclinical and clinical development. Importantly, this design cycle is not limited to GPCRs or ion channel targets, but can be utilized for other recently identified proteins that play a role in human disease where current treatments or therapies are either inadequate or nonexistent.

Our Business Strategy

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

Continuing to Advance and Build Our Product Portfolio Focused on Neurological and Endocrine-Related Diseases and Disorders. We believe that by continuing to advance and extend our product pipeline, we can mitigate some of the clinical development risks associated with drug development. We currently have multiple programs in various stages of research and development. Our three lead late-stage clinical programs are elagolix, a GnRH antagonist in Phase III development for endometriosis and uterine fibroids that is partnered with AbbVie, INGREZZA (valbenazine), our VMAT2 inhibitor for the treatment of movement disorders which is in Phase IIb development for Tourette syndrome, 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. 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.

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 United States through our specialty sales force focused primarily on physicians who treat TD patients, including psychiatrists and neurologists. The commercial launch of INGREZZA, with our field-based sales team of approximately 160 personnel, occurred on May 1, 2017. This entire 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.

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, as in the case of our collaboration with Mitsubishi Tanabe. We intend to further leverage our resources by selectively entering into additional strategic alliances to enhance our internal development and commercialization capabilities by licensing our technology.

Identifying Novel Drugs to Address Unmet Market Opportunities. We seek to identify and validate novel drugs on characterized targets for internal development or collaboration. For example, GnRH antagonists, compounds designed to reduce the secretions of sex steroids, may represent the first novel non-peptide, non-injectable means of treatment of endometriosis. We believe the creativity and productivity of our discovery research group will continue to be a critical component for our continued success. Research and development costs were \$121.8 million, \$94.3 million and \$81.5 million for the years ended December 31, 2017, 2016 and 2015, respectively.

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

Table of Contents

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

Mitsubishi Tanabe Pharma Corporation (Mitsubishi Tanabe). In March 2015, we entered into a collaboration and license agreement with Mitsubishi Tanabe for the development and commercialization of 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 clinical trial to be performed by us, at an estimated cost of approximately \$12 million, should Mitsubishi Tanabe request the clinical trial. We will be entitled to a percentage of sales of 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 \$15.0 million in milestone revenue.

BIAL - Portela & Ca, S.A. (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 United States 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 United States and Canada. Under the terms of the agreement, we paid BIAL an upfront license fee of \$30 million, and we may also be required to pay up to an additional \$115 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.

Table of Contents

Upon commercialization, BIAL and Neurocrine will agree on annual sales forecasts. If we fail to meet the minimum sales requirements for a particular year, we will be required to pay BIAL an amount corresponding to the difference between the actual net sales and the minimum sales requirements for such year, and if we fail to meet the minimum sales requirements for any two consecutive years, BIAL may terminate the agreement. The agreement also contemplates that we will purchase, and BIAL will supply, all drug product and investigation medicinal product for our development and commercialization activities. BIAL has the right to co-promote opicapone within the United States and Canada during certain periods of time. If BIAL exercises its option to co-promote the licensed products, we will enter into a co-promotion agreement with BIAL at a future time.

The agreement, unless terminated earlier, will continue on a licensed product-by-licensed 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. 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. In certain circumstances where BIAL elects to terminate the agreement in connection with our change of control, BIAL shall pay us a termination fee. We can 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 United States, and upon nine months written notice to BIAL if such notice is given after the first NDA approval in the United States. If our termination request occurs prior to the first NDA approval in the United States, we will have to pay BIAL a termination fee except under certain conditions specified in the agreement.

Intellectual Property

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

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

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

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

INGREZZA (valbenazine), our highly selective VMAT2 inhibitor, currently in clinical trials for the treatment Tourette syndrome, is covered by U.S. Patent No. 8,039,627, which expires in 2029 (not including a

Table of Contents

potential patent term extension of up to two years) and U.S. Patent No. 8,357,697, which expires in 2027. INGREZZA is also covered by European Patent No. 2,081,929, which expires in 2027.

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.

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 select pharmacies (SP) and select distributors (SD), and all of our product sales are to these customers. SPs subsequently dispense INGREZZA to patients based on the fulfillment of a prescription and SDs sell INGREZZA primarily to government facilities and in-patient hospital pharmacies. Our agreements with SPs and SDs provide for transfer of title to the product at the time the product is delivered to the SP or SD. Our three largest customers represented 99% of our product revenue for the year ended December 31, 2017.

Master Manufacturing Services Agreement and Product Agreement

We entered into a Master Manufacturing Services Agreement with Patheon UK Limited (Patheon) in November 2016, and a related Amended and Restated Product Agreement in July 2017, for Patheon's manufacture of commercial supplies of INGREZZA at Patheon's manufacturing site. Under the terms of the agreements, we are responsible for supplying the active pharmaceutical ingredients 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.

Table of Contents

Commercial Packaging Agreement

We entered into a Commercial Packaging Agreement with AndersonBrecon Inc., doing business as PCI of Illinois (PCI), in December 2016, for PCI's commercial packaging services. Under the terms of the agreement, PCI will be responsible for, among other things, the packaging of certain of our products, tooling purchases and repair, analytical work, stability testing, auditing of suppliers and storage. We are responsible for supplying the product materials to PCI. Pursuant to the agreement, we have agreed to submit rolling forecasts, some of which will be binding on us. We will compensate PCI for services rendered, based on an agreed upon fee schedule and subject to certain price adjustments.

The agreement has an initial term ending in September 2019, unless earlier terminated in accordance with its terms. The agreement will automatically renew after the initial term for successive terms of two years, unless either party gives notice of its intention to terminate the agreement at least one year prior to the end of the then current term.

Marketing and Sales

During 2017, we established the balance of our commercial team to launch INGREZZA in TD. This commercial team is comprised of experienced professionals in marketing, access and reimbursement, managed markets, market research, commercial operations, and sales force planning and management.

We have built a specialty sales force in the United States of approximately 160 experienced sales professionals. This specialty sales force focuses on promotion to physicians who treat TD patients, primarily neurologists and psychiatrists.

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 United States and other countries. Regulation by government authorities in the United States and foreign countries is a significant factor in the development, manufacture, distribution, marketing and sale of our proposed products and in our ongoing research and product development activities. All of our products 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 United States, various federal and state statutes and regulation also govern or influence testing, manufacturing, safety, labeling, storage, and record-keeping of human therapeutic products and their marketing. Recent federal legislation imposes additional obligations on pharmaceutical manufacturers regarding product tracking and tracing.

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

The federal Anti-Kickback Statute makes it illegal for any person or entity, including a prescription drug manufacturer (or a party acting on its behalf) to knowingly and willfully, directly or indirectly, solicit, receive, offer, or pay any remuneration that is intended to induce the referral of business, including the purchase, order,

Table of Contents

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

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

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

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

Failure to comply with these laws, where applicable, can result in significant penalties, including the imposition of significant civil, criminal and administrative penalties, damages, monetary fines, disgorgement, individual imprisonment, possible exclusion from participation in Medicare, Medicaid and other federal healthcare programs, 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.

Table of Contents

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

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

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

Once Phase III trials are completed, drug developers submit the results of preclinical studies and clinical trials to the FDA in the form of an NDA or a biologics license application for approval to commence commercial sales. In most cases, the submission of an NDA is subject to a substantial application user fee. Under the PDUFA guidelines that are currently in effect, the FDA has a goal of ten months from the date of filing of a standard NDA for a new molecular entity to review and act on the submission. This review typically takes twelve months from the date the NDA is submitted to FDA because the FDA has approximately two months to make a filing decision.

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

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

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

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

Table of Contents

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 REMS, which can materially affect the potential market and profitability of the product. The FDA may prevent or limit further marketing of a product based on the results of post-marketing studies or surveillance programs. After approval, some types of changes to the approved product, such as adding new indications, manufacturing changes, and additional labeling claims, are subject to further testing requirements and FDA review and approval.

We will also have to complete an approval process similar to that in the United States in virtually every foreign target market for our products in order to commercialize our product candidates in those countries. The approval procedure and the time required for approval vary from country to country and may involve additional testing. Foreign approvals may not be granted on a timely basis, or at all. In addition, regulatory approval of prices is required in most countries other than the United States. The resulting prices may not be sufficient to generate an acceptable return to us or our corporate collaborators.

Special FDA Expedited Review and Approval Programs

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

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

The FDA may give a priority review designation to drugs that offer major advances in treatment, or provide a treatment where no adequate therapy exists. A priority review means that the goal for the FDA to review an

Table of Contents

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 user fee requirements for any marketed products and the establishments at which such products are manufactured, as well as new application fees for supplemental applications with clinical data.

The FDA may impose a number of post-approval requirements as a condition of approval of an NDA. For example, the FDA may require post-marketing testing, including Phase 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.

Table of Contents

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

restrictions on the marketing or manufacturing of the product, complete withdrawal of the product from the market or product recalls;

fines, warning letters or holds on post-approval clinical trials;

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

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

injunctions or the imposition of civil or criminal penalties.

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

Reimbursement

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

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

Table of Contents

expect will continue to increase the pressure on pharmaceutical pricing. Coverage policies and third-party reimbursement rates may change at any time. Even if favorable coverage and reimbursement status is attained for one or more products for which we receive regulatory approval, less favorable coverage policies and reimbursement rates may be implemented in the future.

Healthcare Reform

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

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

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

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

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

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

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

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

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

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

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

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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, President Trump has signed two executive orders

Table of Contents

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 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 . Congress may consider other legislation to repeal or replace elements of 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 2025 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(MACRA), 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, Congress and the Trump 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 become increasingly aggressive in passing legislation and implementing 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.

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. We are performing research on or developing products for the treatment of several disorders including endometriosis, TD, uterine fibroids, Tourette syndrome, classic congenital adrenal hyperplasia, essential tremor, pain, and other neurological and endocrine-related diseases and disorders.

In April 2017, INGREZZA (valbenazine), was approved by the FDA for TD, and is also currently in Phase IIb development for Tourette syndrome. There are currently two FDA approved drug therapies for TD; INGREZZA® and AUSTEDO® (deutetrabenazine), a deuterium labeled VMAT2 inhibitor which 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.

Table of Contents

Generic neuroleptic medications (pimozide and haloperidol) as well as ABILIFY® (apripizole) are approved by the FDA to control the tics associated with Tourette syndrome. Teva is also investigating AUSTEDO for utility in Tourette syndrome. Other potential indications for our VMAT2 inhibitor include the chorea associated with Huntington's disease, schizophrenia and tardive dystonia. Currently, Austedo (deutetrabenazine) and XENAZINE® (tetrabenazine), marketed by Lundbeck, as well as its generic alternatives to Xenazine, are approved for the chorea associated with Huntington's disease.

We, in conjunction with our partner AbbVie, are developing elagolix for the treatment of heavy menstrual bleeding associated with uterine fibroids. There are no current pharmaceutical therapies approved in the United States for the chronic treatment of uterine fibroids. During 2017, Allergan Pharmaceuticals, Inc. filed an NDA with the FDA for potential use of ESMYA® (ulipristal), a selective progesterone receptor modulator in the treatment of heavy menstrual bleeding associated with 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®, 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 United States as a direct result of uterine fibroids, as well as myomectomies (surgery) to remove the fibroids. Our oral small molecule pharmaceutical agent, elagolix, would compete directly with these current invasive standards of care.

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

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 ACAT1 inhibitor ATR-101, and Spruce Biosciences, with its CRF antagonist SPR001 are in clinical development for 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;

Table of Contents

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, 2017, we had approximately 400 full-time employees. None of our employees are represented by a collective bargaining arrangement, and we believe our relationship with our employees is good. In addition, we rely on a number of consultants to assist us.

Insurance

We maintain limited product liability insurance coverage for our clinical trials in the amount of \$10 million per occurrence and \$10 million in the aggregate. 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 \$20 million per occurrence and \$20 million in the aggregate. 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 website at www.sec.gov.

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

Table of Contents

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 begun establishing our sales force, distribution and reimbursement capabilities, and we may not be able to successfully commercialize INGREZZA, or any of our product candidates if they are approved in the future.

Our ability to produce revenues ultimately depends on our ability to sell our products and secure adequate third-party reimbursement if and when they are approved by the FDA. We currently have limited experience in marketing and selling pharmaceutical products. With respect to INGREZZA in particular, we have only recently hired our sales force to sell INGREZZA, and have only recently begun establishing our distribution and reimbursement capabilities, all of which will be necessary to successfully commercialize INGREZZA. While we have recently hired personnel, and engaged consultants with experience marketing and selling pharmaceutical products, there can be no guarantee that we will be able to establish or 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 establish or maintain successful marketing, sales and reimbursement capabilities or fail to enter into successful marketing arrangements with third parties, our product revenues may suffer.

We currently depend on a single source supplier for each of the production of INGREZZA and its active pharmaceutical ingredients. The loss of either 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 United States, state and non-United States regulations. 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.

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.

Table of Contents

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

drug manufacturers are subject to ongoing periodic unannounced inspection by the FDA, the United States Drug Enforcement Administration, and other agencies to ensure strict compliance with current Good Manufacturing Practices and other government regulations and corresponding foreign standards. We do not have control over third-party manufacturers' compliance with these regulations and standards.

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.

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 Investigational New Drug (IND) application or foreign equivalent filings required to initiate human clinical studies for our drug candidates or the FDA may require additional preclinical 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;

Table of Contents

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

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

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

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

the results may not be statistically significant;

patient recruitment may be slower than expected;

patients may drop out of the trials; and

regulatory requirements may change.

These risks and uncertainties impact all of our clinical programs. Specifically, our VMAT2 inhibitor program will be impacted if any of the events above lead to delayed timelines for the enrollment in, or completion of, clinical trials of INGREZZA for Tourette syndrome. With respect to our gonadotropin-releasing hormone (GnRH) program with AbbVie, any of the clinical, regulatory or operational events described above could delay timelines for the elagolix endometriosis program, for which an NDA has been submitted to the FDA; or the completion of the Phase III uterine fibroids program. Likewise, any of these events could change our planned clinical and regulatory activities for the opicapone program in Parkinson's disease. 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.

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

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

failed to gain the requisite regulatory approval of elagolix;

Table of Contents

did not successfully launch and commercialize elagolix;

did not conduct its collaborative activities in a timely manner;

did not devote sufficient time and resources to our partnered program;

terminated its agreement with us;

developed, either alone or with others, products that may compete with elagolix;

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

merged with a third party that wants to terminate our agreement.

In March 2015, we entered into a collaboration and license agreement with Mitsubishi Tanabe to develop and commercialize 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 United States 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 product candidates we licensed to AbbVie.

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

Table of Contents

would not have made had we been fully informed, which may materially and adversely affect our business and operations.

In April 2017, we received FDA approval for INGREZZA for TD and that approval subjects us to ongoing obligations and continued regulatory review, 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, 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.

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.

Table of Contents

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

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

If physicians and patients do not accept INGREZZA or any of our other products, 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

Table of Contents

limited sales and marketing experience. If 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.

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 exception of INGREZZA, which has been approved by the FDA for TD. 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.

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 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.

Table of Contents

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

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. Furthermore, even if holders of the 2024 Notes did not elect to convert their notes, we could be required under applicable accounting rules to reclassify all or a portion of the outstanding principal of the 2024 Notes as a current rather than long-term liability, which would result in a material reduction of our net working capital.

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, 2017. We do not expect to be profitable for the year ending December 31, 2018.

In April 2017, we received FDA approval of INGREZZA for TD, 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. We will need to generate significant revenues to achieve and maintain profitability and positive cash flow on an annual basis. We may not be able to generate these revenues, and we may never achieve profitability on an annual basis in the future. Our failure to achieve or maintain profitability on an annual basis could negatively impact the market price of our common stock. Even if we become profitable on an annual basis, we cannot assure you that we would be able to sustain or increase profitability on an annual basis.

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, 2017, we had approximately 400 employees. Although we substantially increased the size of our organization during 2017, 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.

Table of Contents

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:

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 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 file 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. For example, on December 1, 2015, The Mount Sinai School of Medicine of the City University of New York (Mount Sinai) filed a complaint against us, seeking unspecified monetary damages, future sublicensing fees and attorney's fees, alleging that we violated the terms of our license with Mount Sinai by inappropriately sublicensing Mount Sinai technology to AbbVie. While we believe that we have meritorious defenses to the claims made in the complaint and intend to vigorously defend ourselves against such claims, we are not able to predict the ultimate outcome of this action. Likewise, if we were to lose our rights under a license to use proprietary research tools, it could adversely affect our existing collaborations or adversely affect our ability to form new collaborations. We also face the risk that our licensors could, for a number of reasons, lose patent protection or lose their rights to the technologies we have licensed, thereby impairing or extinguishing our rights under our licenses with them.

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.

Table of Contents

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. 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.

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 United States or for uses in other jurisdictions that differ from those approved by the applicable regulatory agencies. Physicians, on the other hand, may prescribe products for off-label uses. Although the FDA and other regulatory agencies do not regulate a physician's choice of drug treatment made in the physician's independent medical judgment, they do restrict promotional communications from companies or their sales force with respect to off-label uses of products for which marketing clearance has not been issued. A company that is found to have promoted off-label use of its product may be subject to significant liability, including civil and criminal sanctions. 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

Table of Contents

companies have been the target of inquiries and investigations by various United States 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 United States 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 United States federal and state laws and regulations, including claims asserting antitrust violations, violations of the federal False Claims Act, the Prescription Drug Marketing Act, anti-kickback laws, and other alleged violations in connection with the promotion of products for unapproved uses, pricing and Medicare and/or Medicaid reimbursement. If the FDA or any other governmental agency initiates an enforcement action against us or if we are the subject of a *qui tam* suit and it is determined that we violated prohibitions relating to the promotion of products for unapproved uses, we could be subject to substantial civil or criminal fines or damage awards and other sanctions such as consent decrees and corporate integrity agreements pursuant to which our activities would be subject to ongoing scrutiny and monitoring to ensure compliance with applicable laws and regulations. Any such fines, awards or other sanctions would have an adverse effect on our revenue, business, financial prospects, and reputation.

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, 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. Because of these factors, our financial results in one or more future quarters may fail to meet the expectations of securities analysts or investors, which could cause our stock price to decline.

The recently passed comprehensive tax reform bill could adversely affect our business and financial condition.

On December 22, 2017, President Trump signed into law new legislation that significantly revises the Internal Revenue Code of 1986, as amended. The newly enacted federal income tax law, 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%, 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 new federal tax law 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 newly enacted federal tax law. The impact of this tax reform 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 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

Table of Contents

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.

Our ability to use net operating losses to offset future taxable income may be subject to limitations.

As of December 31, 2017, we had federal and state income tax net operating loss carry forwards of approximately \$978.7 million and \$535.3 million, respectively. These net operating loss carry forwards could expire unused and be unavailable to offset future income tax liabilities. Under the newly enacted federal income tax law, federal net operating losses incurred in 2018 and in future years may be carried forward indefinitely, but the deductibility of such federal net operating losses is limited. It is uncertain if and to what extent various states will conform to the newly enacted federal tax law. In addition, under Section 382 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 net operating loss carry forwards and other pre-change tax attributes to offset its post-change income or taxes may be limited. We have determined that no ownership changes have occurred through December 31, 2016 and we are currently evaluating whether any ownership changes occurred through December 31, 2017. 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. If an ownership change occurs and our ability to use our net operating loss carry forwards is materially limited, it would harm our future operating results by effectively increasing our future tax obligations.

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, the price of our common stock may be dependent upon 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. During 2017, the price of our common stock has ranged from approximately \$38.00 per share to approximately \$78.00 per share. The market price of our common stock may fluctuate in response to many factors, including:

sales of INGREZZA;

the status and cost of our post-marketing commitments for INGREZZA;

the results of our clinical trials;

developments concerning new and existing collaboration agreements;

announcements of technological innovations or new therapeutic products by us or others;

general economic and market conditions, including economic and market conditions affecting the biotechnology industry;

developments in patent or other proprietary rights;

developments related to the FDA;

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

comments by securities analysts;

Table of Contents

additions or departures of key personnel;

fluctuations in our operating results;

developments related to on-going litigation;

government regulation;

health care reimbursement;

failure of any of our product candidates, if approved, to achieve commercial success; and

public concern as to the safety of our drugs.

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 commercialize INGREZZA for TD, to continue our research and product development programs, to conduct preclinical studies and clinical trials, for operating expenses and to pursue regulatory approvals for additional product candidates and indications, for the costs involved in filing and prosecuting patent applications and enforcing or defending patent claims, if any, product in-licensing and any possible acquisitions, establish manufacturing capabilities in the future and we may require additional funding to expand commercial and marketing efforts for other product candidates or indications. 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, 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;

debt service obligations on the 2024 Notes;

continued scientific progress in our research and development programs;

the magnitude and complexity of our research and development programs;

progress with preclinical testing and clinical trials;

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the time and costs involved in obtaining regulatory approvals;

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

competing technological and market developments;

the establishment of additional strategic alliances;

developments related to on-going litigation;

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

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

We intend to seek additional funding through strategic alliances, and may seek additional funding through public or private sales of our securities, including equity securities. For example, 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

Table of Contents

currently on file with the Securities and Exchange Commission (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 United States, comprehensive health care reform legislation was enacted by the Federal government and we expect that there will continue to be a number of federal and state proposals to implement government control over the pricing of prescription pharmaceuticals. In addition, increasing emphasis on reducing the cost of health care in the United States will continue to put pressure on the rate of adoption and pricing of prescription pharmaceuticals. Moreover, in some foreign jurisdictions, pricing of prescription pharmaceuticals is already subject to government control. Additionally, other recent federal 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 to individuals and entities to which product ownership is transferred, label drug product with a product identifier, and keep certain records regarding distribution of the drug product. Further, under this new legislation, manufacturers will have drug product investigation, quarantine, disposition, notification and purchaser license verification responsibilities related to counterfeit, diverted, stolen, and intentionally adulterated products, as well as products that are the subject of fraudulent transactions or which are otherwise unfit for distribution such that they would be reasonably likely to result in serious health consequences or death.

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

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

Table of Contents

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

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

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

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

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

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

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

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, President Trump 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 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. Congress may consider other legislation to repeal or replace elements of 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 2025 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 MACRA, 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, Congress and the Trump 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 become increasingly aggressive in passing legislation and implementing 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.

Table of Contents

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

We are currently unable to predict what additional legislation or regulation, if any, relating to the health care industry may be enacted in the future or what effect recently enacted federal legislation or any such additional legislation or regulation would have on our business. The pendency or approval of such proposals or reforms could result in a decrease in our stock price or limit our ability to raise capital or to enter into collaboration agreements for the further development and commercialization of our programs and products.

We face intense competition, and if we are unable to compete effectively, the demand for our products 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, Tourette syndrome, essential tremor, classic congenital adrenal hyperplasia, pain, and other neurological and endocrine-related diseases and disorders, and there are a number of competitors to 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;

Table of Contents

preserve our trade secrets;

prevent third parties from infringing upon our proprietary rights; and

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

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

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

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

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 United States 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. Valbenazine has received an orphan drug designation for the treatment of

Table of Contents

pediatric patients with Tourette syndrome from the FDA. If we seek orphan drug designations for other indications or in other jurisdictions, we may fail to receive such orphan drug designations 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 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.

Table of Contents

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, including the 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;

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

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

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

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

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 United States will also likely subject us to foreign equivalents of the healthcare laws mentioned above, among other foreign laws.

Table of Contents

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 \$10 million per occurrence and \$10 million in the aggregate. However, our insurance may not reimburse us or may not be sufficient to reimburse us for any expenses or losses we may suffer. Moreover, insurance coverage is becoming increasingly expensive, and we may not be able to maintain insurance coverage at a reasonable cost or in sufficient amounts to protect us against losses due to liability. 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 \$20 million per occurrence and \$20 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.

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.

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. Despite security measures, however, our information technology and network infrastructure may be vulnerable to attacks by hackers or breached due to employee error, malfeasance, or other disruptions. Any such cyber-attack or breach could compromise our networks and data centers and the information stored there could be accessed, publicly disclosed, lost, or stolen. Any such access, disclosure, or other loss of information could result in legal claims or proceedings, liability under laws that protect the privacy of personal information, delays and impediments to our discovery, development, and commercialization efforts, and damage to our reputation.

Table of Contents

ITEM 1B. *UNRESOLVED STAFF COMMENTS*

None.

ITEM 2. *PROPERTIES*

We lease our corporate headquarters which consists of approximately 140,000 square feet of laboratory and office space located at 12780 El Camino Real in San Diego, California. The lease expires in December 2029 with options to extend the term of the lease for up to two consecutive ten year periods.

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

ITEM 3. *LEGAL PROCEEDINGS*

The information set forth under Note 7 – 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.

Table of Contents**PART II****ITEM 5. MARKET FOR REGISTRANT'S COMMON EQUITY, RELATED STOCKHOLDER MATTERS AND ISSUER PURCHASES OF EQUITY SECURITIES**

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

	High	Low
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
Year Ended December 31, 2016		
1st Quarter	\$ 55.94	\$ 31.25
2nd Quarter	53.00	39.01
3rd Quarter	55.15	44.69
4th Quarter	54.91	37.35

As of February 6, 2018, 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 2017.

Table of Contents

Stock Performance Graph and Cumulative Total Return*

The graph below shows the cumulative total stockholder return assuming the investment of \$100 on December 31, 2012 (and the reinvestment of dividends thereafter) in each of (i) Neurocrine Biosciences, Inc.'s common stock, (ii) the NASDAQ Composite Index and (iii) the NASDAQ Biotechnology Index. The comparisons in the graph below are based upon historical data and are not indicative of, or intended to forecast, future performance of our common stock or Indexes.

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

Table of Contents**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.

	2017	2016	2015	2014	2013
	(In thousands, except for net (loss) income per share data)				
STATEMENT OF COMPREHENSIVE LOSS DATA					
Revenues:					
Product sales, net	\$ 116,626	\$	\$	\$	\$
Milestones and license fees	45,000	15,000	19,769		2,919
Total revenues	161,626	15,000	19,769		2,919
Operating expenses:					
Cost of product sales	1,254				
Research and development	121,827				